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The Medicalization of Stress: Hans Selye and the Transformation of the Postwar Medical Marketplace

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Abstract

THE MEDICALIZATION OF STRESS: HANS SELYE AND THE TRANSFORMATION OF THE POSTWAR MEDICAL MARKETPLACE

By

Vanessa Burrows

Advisor: Gerald Markowitz

This dissertation employs historical methodology and public health theory to examine how critical changes in the culture and political economy of biomedical research shaped Hungarian-Canadian endocrinologist Hans Selye’s concept of biological stress, guiding him to develop a highly individualistic and commercially-appealing disease model that complimented major interests of the postwar medical marketplace: the state, the corporation and the consumer. In the mid-1930s Selye proposed that the human body adapted to a diverse range of stressors—including, extreme temperatures, intoxification, surgical trauma, physical exercise and complete immobilization—by releasing adrenocortical hormones to regulate bodily functions. For the next fifty years he devoted his career to studying the mechanisms by which stress operated, using his training in histology and biological assay to identify how stress altered biochemistry at the cellular level. Selye found that while the human body maintains homeostasis and mitigates damage from stressors by altering the balance of pro- and anti-inflammatory adrenocorticoids, a prolonged imbalance of these hormones can produce “diseases of adaptation,” such as arthritis, heart disease, hypertension and gastrointestinal ulceration. While this General Adaptation Syndrome (GAS) is universal, it is also highly individualized, as an individual’s exposure to unique “conditioning factors” determines the type and magnitude of diseases produced by stress.
Even though he complied with the reductionist methods of biomedical research, Selye’s theory was a radical departure from the orthodox biomedical doctrine of specific disease etiology. However, by offering a multicausal theory of disease causation that embraced the concept of attributable risk, Selye helped to reconcile mid-century biomedicine with the contemporaneous rise in chronic disease in North America. Selye was a visionary, but was not insulated from financial and cultural pressures. In order to attract funding from philanthropies, private enterprise and the US and Canadian federal governments, he catered his research to appeal to mid-century public health priorities and the health concerns of North American patient-consumers: relief from chronic diseases and anxiety neuroses.

Selye began using the term “stress” to describe the GAS at the end of the Second World War, after military neuropsychiatric research on combat stress had already given the term a medical valence. And in the early-1950s, as his controversial theory was vindicated by the therapeutic discovery of cortisone and ACTH, Selye began a vigorous public relations campaign to promote popular awareness of stress. In doing so, he appealed to the concurrent medicalization of anxiety and growing market for anxiolytic drugs, blurring the distinction between biological and psychological stress. Yet, he won validation for stress in the medical marketplace.

Selye inadvertently advocated a psychosomatic perspective of stress by advancing an ethical code of “altruitistic egotism.” He insisted that individuals must learn their own unique stress triggers and develop personal therapeutic strategies, especially in disrupting patterned “stress grooves” with useful “deviations,” like reading a book, taking a walk, listening to music, or smoking a cigarette. While anxiolytic and adrenocoritcal medications might be useful in managing chronic conditions, to Selye will power and self-awareness were the most effective
therapeutic weapons in combating stress. Stress, as Selye described it, offered patient-consumers a means of managing their own health. Yet, by advancing an individualistic and commercially-appealing theory of stress, Selye obscured ecosocial pathways of disease that distribute stress risk far beyond the control of individual interventions.
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**Introduction**

I. **Historicizing Stress**

Stress is a ubiquitous force in modern culture. It afflicts us all, assaulting our bodies and minds as we strive to endure the cultural demands and environmental risks to which we are exposed in our daily activities. We complain of physical stress that abuses our muscles, mental stress that taxes our cognitive abilities, and emotional stress that upsets our interpersonal relationships. Exposure to pathogens and toxins stresses our immune systems. We are “stressed-out” by excessive (or deficient) sound, light and other sensory stimulations, eating too much or too little, having too much to do at work, financial hardship and unemployment. And in all of these experiences, we have a sense that too much stress may inevitably cause physical sickness. The medical concept of stress has become so thoroughly naturalized that we rarely question its medical basis. However, our implicit understanding of stress as a psychosomatic phenomenon instigated by an overwhelmingly powerful adverse force (or a complex of forces), is itself a historical construct that arose from a process of cultural and structural change.

While “stress” very clearly has numerous social uses, the American Institute of Stress—a self-proclaimed “clearinghouse for information on all stress related subjects”—offers the disclaimer that, “stress is not a useful term for scientists because it is such a highly subjective phenomenon that it defies definition.”¹ Yet, perhaps more to the point, the current model of stress has diminished scientific value because it is an abstraction, an ambiguity, and a metaphor.²

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² Mark Jackson has argued that the medical concept of stress became gradually accepted by medical professionals and the public at large, in part, as a result of its discursive power as a metaphor for tension and hardship, arising from its pre-existing non-medical meanings. See Mark Jackson, *The Age of Stress: Science and the Search for Stability* (Oxford: Oxford University Press, 2013). Similarly, Andrew Abbott argues that because the meaning of stress has
Stress is meant to describe a force that is at once both physical and emotional, and as the American Institute of Stress notes, also highly subjective. Though a universal threat, stress is highly individualized and therefore defies consistent measurement. Moreover, because stress is generally used to suggest a relationship between mental and physical phenomena, it lacks specificity of meaning and therefore is quite open to interpretation. Stress is also commonly used to invoke the physical law of elasticity, in the sense that a physical force of stress is visited upon an organism causing strain, much like a heavy load stresses a rope and causes strain.

The confusion surrounding the concept of stress is the result of a persistent professional debate of semantics, metrics, disciplinary demarcation and most of all, specificity, which has endured over decades of medical research. At the center of this debate is a man who is widely recognized as the “Father of Stress,” the Hungarian-Canadian endocrinologist, Hans Selye. Generally credited with being the first medical scientist to use the term “stress” to describe a unique biological process, Selye has aroused controversy since the mid-1930s when he first announced his discovery of a General Adaptation Syndrome (GAS) that mobilized hormonal mechanisms to facilitate resistance to disease-causing risk factors. Though he did not consistently claim this process to be associated with “stress” until the mid-1940s, Selye’s theory of the GAS was broadly interpreted as a heretical defiance of a central tenet of mid-century biomedical theory: the doctrine of specific etiology, which holds that a specific disease must arise from a specific pathogen.

Abbott further offers the Foucaultian interpretation that the enhanced discourse of stress reified its existence, and as a consequence, to this day, confusion as to the meaning of biological stress arises from the fact that when used to describe an individual experience stress is a synecdoche, a unique instance viewed as a symbol of a larger social phenomena. See Andrew Abbott, “The Duality of Stress,” in Chaos of Disciplines, 3-33 (Chicago: University of Chicago Press, 2001).
The GAS was radical because it claimed that all diseases were caused by a derailment of natural adaptive responses. It held that hormones released from the adrenal cortex (the outer layer of the adrenal glands) and the pituitary gland were paramount in regulating the body’s response to damage. These hormones manipulate inflammation, heart rate, and blood sugar and mineral concentration, among other things, and in doing so, orchestrate repair and defense in damaged tissues. By ascribing universal etiological power to adrenocorticoid and pituitary hormones, Selye offered a means of understanding all disease as a product of cumulative exposures to a myriad of extremes—extreme exposure to chemicals and toxins, extreme temperatures, extremes of physical activity or immobility, to name a few. This formula also posited an explanation for the relationship between degenerative diseases associated with old age and the hastened pace of modern civilization. According to the GAS, diseases such as cancer, heart disease and arthritis were produced not by a specific etiological agent, but by a complex combination of multiple causes, which contributed to a process of maladaptation that occurred over time. Selye hoped that in flouting the revered doctrine of specific etiology, his unified theory of disease might correct what he perceived to be a woeful deficiency of biomedical research—the inability to recognize a multiplicity of pathological processes that may contribute to degenerative, chronic diseases. In doing so, Selye presaged an impending movement in the health sciences to develop a multicausal disease model that recognized contributory risk factors—a disease model that would ultimately help to reconcile biomedicine with the mid-century rise of chronic disease.

However, while Selye was principally concerned with expanding biomedical theory to recognize collateral mechanisms of disease causation and to emphasize the adaptational relationship between an organism and its environment, he was principally focused on the physical and not the psychological determinants of adaptive disease. Selye studied the biochemical, histological and morphological changes that were produced in experimental animals by various damaging agents, including extreme temperatures, surgical trauma, toxic exposure, malnutrition, intense physical activity and immobilization. In fact, because he was so concerned with conforming to strictures of biomedical methodology in order to validate his provocative theory, and because his training was based in laboratory research that evaluated morphological and biochemical changes in experimental animals, his research did not actually investigate mind-body interactions that mediate human health. Selye’s principal contributions to stress research were not in substantiating the psychosomatic basis of disease, but 1) documenting the actions of adrenocortical and pituitary hormones in regulating health, 2) advancing a multicausal theory of chronic disease, 3) uncovering the role of conditioning risk factors in diminishing resistance to disease, and 4) explaining the relationship between processes of adaptation and premature aging. And perhaps ironically, Selye’s orthodox methods—emphasizing above all, the positivistic premium for empirical, reproducible evidence and a reductionist clinical perspective—shaped his disease model of stress to take on a decidedly individualist orientation.

Yet, as Selye labored to achieve legitimacy for his theory by documenting histological evidence of the adaptive regulation of physiological diseases through the secretion of pituitary and adrenocortical hormones, at the same time, a growing field of dynamic psychiatry adapted the psychoanalytic concept of anxiety to explain how both psychological and physiological
deterioration resulted from adverse environmental stimuli. Catalyzed by military investment in neuropsychiatric research during World War II, the concept of “combat stress” gave rise to a professional and popular faith that even normal, healthy individuals could succumb to disease when faced with situations of extreme adversity. By the end of the war—just as Hans Selye began to embrace the term “stress” to describe the GAS—widespread belief in the idea that “every man has his breaking point” helped to destigmatize and universalize mental illness, while drawing attention to the potential risk to physical health caused by psychological stress.

Under Selye’s stewardship, biological stress essentially appropriated the medical valence of the new psychological disease model of stress, as well as the physics concept of stress and pre-existing cultural referents of tension, emotional strain and overexertion. Because Selye chose a word that already had many meanings, rather than invent a new one to describe a unique syndrome, he exploited laymen’s preconceived ideas about the existence and nature of stress, as well as the medical valence of psychological stress. He also contributed to a great deal of confusion and ambiguity within the scientific community and society at large as to what exactly stress is.

Thus, though Selye himself did not investigate psychological stressors quite unintentionally, he did help to resolve a fundamental conflict of Cartesian dualism. By demonstrating the physiological manifestations of physiological and environmental stressors, Selye was instrumental in the development of a new interdisciplinary field of stress research that did not ultimately unify all disease within one category, but used the developing field of endocrinology to unite the discrete disciplines of biochemistry, physiology and psychiatry. The question of whether the mind governs the body, or the body the mind, became moot under the new realization that the two were fundamentally interconnected through a complex matrix of
psychosensory, nervous, and endocrine communication. By the end of the 1940s, the psycho-neuro-endocrinological theory of health gained scientific endorsement with the discovery of the synthetic hormones cortisone and ACTH, which were reported to be effective in treating a myriad of diseases, including arthritis, Addison’s disease, cancer and even alcoholism. These new “wonder drugs” offered a powerful endorsement of Selye’s adaptive theory of disease, and at the same time transformed the medical marketplace by generating inordinate demand for pharmaceutical steroids.

The universalization of stress also created a vast pool of patient-consumers for anxiolytic drugs developed by pharmaceutical companies which had grown enormously wealthy during World War II, primarily through lucrative government contracts to mass produce penicillin. By 1955, when the first minor tranquilizer, meprobromate was commercially marketed as Miltown, any North American who felt slightly on edge, could coax themselves back to “normal” with a simple little pill. The entrance of mass psychopharmaceuticals into the medical marketplace generated a popular referendum on the legitimacy of “stress,” and blurred the distinction between psychological anxiety and physiological stress. Thus, the legitimization of Selye’s theory of stress developed in tandem with the transformation of the postwar medical marketplace, and the increasing power of corporations and medicinal consumerism.

Selye skillfully adapted his disease model of stress to conform to changes in the medical market. To appeal to newly prominent state and corporate funders, as well as disease foundations, Selye highlighted the applicable uses of his research in treating the increasingly predominant chronic diseases of heart disease and cancer, as well as arthritis and aging, while also highlighting the commercial value of developing hormonal pharmaceutical treatments for such conditions. Selye also appealed directly to the consuming public to promote health literacy.
regarding the medical concept of stress. He offered a self-help philosophy to reduce risk for
disease by managing stress, which primarily endorsed behavioral modifications such as dietary
changes, increased physical exercise and individual diversions, but also recommended
pharmaceutical interventions. In doing so, he promoted an individualistic model of disease that
complimented the individualistic orientation of postwar mass consumer society.

While Selye was far from the only scientist who had a hand in shaping the medical
concept of stress, his research was dedicated exclusively to the study of stress, while most of his
contemporaries branched out into auxiliary fields of research. He was also an impressively
savvy self-promoter, and extremely successful in attracting attention to his work, and creating a
popular association between his name and the medical concept of stress. He also survived many
of his colleagues, and continued to devote his career to the research and popularization of stress
for a full two decades after many of his contemporaries passed away. Selye was a formative
influence on how we think about stress because he produced pioneering research that challenged
professional reticence, because he skillfully adapted his research to changes in the political
economy of biomedical research, and because he actively sought to manipulate the public
discourse of stress.

Selye was so successful in promoting his reputation as the “father of stress” that to this
day many scholarly references to his work implicitly accept this heroic interpretation of his
legacy. Yet, this study uncovers a much more dynamic and complex story of how stress

4 Recently, a few notable exceptions have helped to complicate Selye’s legacy. Several
essays in Stress, Shock and Adaptation in the Twentieth Century, edited by David Cantor and
Edmund Ramsden, have interrogated Selye’s central place in the history of stress. Of
particularly note are those by Mark Jackson, Elizabeth Siegal Watkins, Theodore M. Brown and
Tully Long. In a separate monograph, Mark Jackson emphasizes Selye’s formative influence on
the development and popularization of stress—focusing on his endocrinological innovations
and his use of public relations, as well as the psychological crafting of the disease concept of
became recognized as a medical condition—a story in which we see Selye as one of many researchers that helped to shape the disease model of stress; a story that recognizes Selye’s true scientific contribution was not in documenting the psychosomatic nature of disease, but the endocrinological regulation of multicausal chronic disease; a story that examines how stress research was not exclusively concerned with uncovering natural law, but was in fact profoundly influenced by cultural and economic forces; and a story that critically analyzes the ramifications of the individualistic orientation of the biomedical model of stress.

A historical examination of Selye’s evolving theory of stress reveals how changes in biomedical culture and the medical market influenced the development of this particular disease model, which transformed how we perceive health. Similarly, because Selye tried so ardently to conform his theory of stress to comply with biomedical research standards and appeal to funders, an historical perspective also offers insight into the relationship between critical transformations in mid-twentieth century epidemiology and medical-consumerism. In this sense, we see stress as a quintessential medical construct of the second-half of the twentieth century, enabling research into newly prevalent chronic and mental diseases, while at the same time reconciling medical treatment with the increasingly individualistic and consumer-oriented nature of the postwar medical marketplace. And in a broad sense, the history of Selye’s development of the theory of stress emphasizes how cultural and economic forces influence the design and objectives of medical research, in general.

II. Contextualizing the Medicalization of Stress

The history of Selye’s “discovery” of stress is at its core a story about advancements in endocrinological knowledge, for the radicalism of Selye’s unified theory of disease was predicated upon an understanding of the hormonal mechanisms that regulate health. Yet, even though Selye conscientiously distinguished the GAS as a physiological phenomenon—emphasizing the difference between biological and psychological stress—he simultaneously participated in blurring this distinction. To promote the professional and social acceptance of the GAS, Selye chose to describe it using a word laden with cultural meanings of psychological tension. A word that had gained medical valence through neuropsychiatric research on “combat stress,” and could lend legitimacy to his radical theory. And in his popular discourse on stress, he habitually endorsed the psychosomatic basis of stress by implicating psychosocial stressors, such as the pace of modern life, feeling “keyed-up,” dissatisfied, or bored, or the lack of a moral code. Consequently, the conceptualization of stress grew from tangled roots of diverse psychosomatic theories of health that variably examined 1) the relationship between the mind and the body, 2) the relationship between a host and its environment, 3) the capacity for human adaptation, and 4) the biochemical mechanisms of self-preservation, and how these functions are altered during acute trauma or chronic exposure to harmful agents.

The Current Disease Model of Stress

We now know that when confronted with a stressful situation, such as a violent attack or a prolonged irritation, the body responds by initiating what is called a “stress cascade.” First, the threat is detected by the sensory components of the sympathetic nervous system—the branch of
the autonomic nervous system that enables the body to react to external sensations. When we see, hear, smell, feel or taste something that is perceived to be dangerous or destabilizing, these nervous signals are relayed through the central nervous system to the hypothalamus, an almond-size region of the brain that regulates body temperature, thirst, hunger, and circadian rhythms. The hypothalamus then signals the locus coeruleus of the brain stem to release the neurotransmitter norepinephrine, which signals a region of the brain known as the amygdala to initiate a heightened state of alertness and attention, while simultaneously increasing the heart rate to expedite the release of stored blood glucose, enhancing lung capacity to increase the availability of blood-oxygen, and increasing blood circulation to the extremities.

The hypothalamus also releases a hormone, known as corticotropin releasing factor (CRF) which communicates to the pituitary gland, the pea-sized “master” endocrine gland located just beneath the hypothalamus, which controls growth, blood pressure, hydration, and various reproductive functions. Within fifteen seconds, the anterior lobe of the pituitary gland then releases adrenocorticotropic hormone (commonly referred to as corticotropic hormone, or just ACTH), which signals the cortex of the adrenal glands to begin secreting glucocorticosteroids, especially the steroid cortisol, which initiates glucogenesis and along with glucagon released from the pancreas, acts to increase the availability of blood sugar that provides muscles with the fuel to hasten reaction time.

Cortisol also suppresses immune function, in order to redirect the body’s energy from rest and repair towards immediate action. Increased cardiovascular function, triggered by the anterior pituitary gland’s release of vasopressin, redistributes blood from central organs to the extremities, which enables faster blood clotting at the expense of parasympathetic functions, such as digestion and tissue maintenance. The pituitary halts the release of growth hormone,
which is responsible for tissue growth and repair, and the pancreas ceases secretion of insulin, a metabolic hormone that enables sugar storage. Reproductive functions are also suspended by the posterior pituitary’s release of prolactin, and the secretion of estrogen, progesterone and testosterone are inhibited.

This entire hypothalamic-pituitary-adrenal (HPA) chain—or, the “stress cascade”—occurs within just a few minutes, and facilitates what is known as the “fight-or-flight” or “stress” response. While it is vital to human survival in situations of extreme danger, such as being attacked by a wild animal, the stress response can become detrimental when it is prolonged or initiated too often. The tendency of emergency functions to disrupt normal rest and repair processes jeopardizes biological stability, or homeostasis. Not only do digestion, reproduction, growth and wound healing fail to occur when needed, but the increased blood pressure and levels of fatty acids in the blood can strain venous tone and contribute to cardiovascular disease. Chronic stress has also been linked with an increased susceptibility to cognitive and psychological disorders, as well as gastrointestinal ulcers, infertility, chronic fatigue, headaches, muscular pain, visceral obesity and the early onset of aging.\(^5\)

Now that the mechanisms of the HPA stress axis have been thoroughly documented, the medical concept of stress seems even more firmly grounded in scientific fact. However, the very association between stress and endocrine function is the result of a historical process that shaped cultural standards of scientific investigation and the interests of research funders. Mid-twentieth-century stress research was fundamentally influenced by a biomedical culture that privileged specific etiology and reductionist laboratory science. Epidemiologist Nancy Krieger has argued

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that reductionism became a principal lens of biomedicine in the mid-twentieth century United States due to its emphasis on “basic” research—that is, inductive investigation of fundamental biological processes aimed to enhance knowledge of physiology, rather than investigation the practical investigation of medical problems aimed to improve health outcomes. Krieger explains that the “key to defining a ‘reductionist’ approach is to postulate that ‘the parts’ explain ‘the whole.’” Krieger continues,

At an abstract level, a reductionist approach holds that the properties of phenomena at a ‘higher level’ can be ‘reduced’ to—and hence be solely determined and explained by—phenomena at a ‘lower level.’ Two corollaries are: (1) causal pathways run solely from the ‘lower’ to ‘higher’ levels, and (2) properties of ‘the whole’ cannot influence those of ‘the parts’ of which it is composed. Translated into concrete terms, in the case of biomedicine, this reductionist premise holds that the features of a biological organism and its diseases (i.e., the ‘higher level’) can be fully explained by genetics and molecular biology (i.e., the ‘lower level’)—and hence ultimately by chemistry and physics. The operational implication is that research at the ‘lower levels; is not only essential but also sufficient to explain the phenomena at ‘higher’ levels.⁶

As a consequence of the premium for reductionist methodology, Krieger asserts that biomedicine also adopted an “inherently mechanistic” view of the human body, perceiving disease as a product of specific physiological, biochemical, and genetic mechanisms. In addition to the perception of the human body as a machine, mid-twentieth-century biomedicine perceived of population health as the sum of individuals’ health, recognizing only biological determinants of health and rendering social determinants of health secondary or superfluous to understanding epidemiological concerns.⁷

⁶ Nancy Krieger, *Epidemiology and the People’s Health: Theory and Context* (New York: Oxford University Press, 2011), 136, emphasis in original. Krieger also notes that biomedicine in the United Kingdom departed from basic methods, and solely emphasized applied medical research. However, in the postwar United States, the National Institutes of Health fostered an “institutional linkage of biology and medicine,” that promoted the use of basic research methods to address medical problems, p. 127.

⁷ Krieger, *Epidemiology and the People’s Health*, 137.
Thus, while one might presume that stress researchers would have adopted a holistic framework in order to substantiate psychosomatic interpretations of health, on the contrary, the culture of biomedical research promoted adherence to an individualistic, reductionist and mechanical view of human health. While some stress researchers—particularly those with psychiatric training—did adopt a more holistic perspective of bio-psycho-social health, Selye’s doctrinaire assimilation of these hallmark biomedical principles was not anomalous in his time, but rather the prevailing perspective of his contemporaries. I concur with historian Mark Jackson that “Selye should be regarded as neither a pioneering genius nor an unmitigated pariah.”

Assigning praise or blame does little to advance understanding of his role in the medicalization of stress. Moreover, Selye’s work, like that of his contemporaries, was strongly influenced by the cultural terrain and funding economy of biomedical research.

Reductionism had such forceful staying power, in part, due to the disciplinary demarcation of the early-twentieth century. Rigid boundaries discouraged interdisciplinary collaboration that could have enabled the recognition of dynamic biological, psychological and social forces as etiological agents. Selye drew on a tradition of psychosomatic research that grew independently in the fields of psychology, neurology, sociology and endocrinology. While research conducted in these fields often overlapped, the lack of communication between distinct disciplines—and at times, outright competition over the legitimacy of research standards—impeded the development of a holistic theory of psychosomatic disease. In the decade following the Second World War, interdisciplinary biomedical research became more common, with several institutes forming teams of diverse scientific experts to investigate the dynamic interplay of physiological, psychological and social pathways of stress. Selye was at the forefront of the

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8 Jackson, *The Age of Stress*, 80.
postwar interdisciplinarity that helped to join these diverse strands of research in a single, unified framework of disease, yet in doing so, created a confusing and conflicted legacy of the very meaning of “stress.”

The Mind-Body Problem

The concept of stress is now associated with psychosomatic disease. However, the study of emotional and psychological effects on physical health is far from a modern trend. Scientists and medical practitioners have been fascinated with the mind-body relationship since the ancient Egyptians and Greeks. Until the seventeenth-century, most medical cultures accepted a holistic interpretation of the relationship between the mind and the body. However, in the 1640s, Rene Descartes challenged this tradition, outlining in his 1641 Meditationes de Prima Philosophia a new proposition that the mind and the body occupied distinct realms of existence, operating independently of one another. According to Descartes, both the body could affect the mind and the mind could affect the body, but the two were fundamentally different substances with different properties: the body, a material substance; the mind, an immaterial substance. In this schema, the body was seen as a machine that was susceptible to manipulation by the conscious mind, and the mind was “the ghost in the machine.”

By separating corporeal and spiritual health, Cartesian dualism advanced scientific investigation of the physical body without challenging the Catholic Church’s metaphysical authority. Descartes’ bifurcation of the body and mind drew credence from his innovative method of reasoning. By popularizing deductive logic for determining causality, Descartes modeled the legitimate methods of scientific investigation throughout the Enlightenment. And because deductive reasoning “proved” the logic of dualism, it gained legitimacy as the Scientific
Revolution placed a premium on objectivity and empiricism. As a consequence, the prevalence and persistence of this bargain reified the presumption that the mind and the body were indeed distinct, as well as the mechanistic metaphor of the body.  

By the nineteenth-century, Cartesian dualism was displaced by the monistic philosophy of materialism, in which matter superseded ideas as the fundamental basis of all existence. Materialism had a profound influence on the medical interpretation of physical and psychological health by denying that psychological phenomenon might have any influence on one’s physical health, and thus encouraging a somatic perspective in the medical sciences. The materialist perspective interpreted both physical and mental illness as purely physiological phenomena. Consequently, while the causes of bodily diseases were thought to originate from internal and external physical agents, investigations of psychological illness looked to cerebral physiology and functional nervous disorders. As such, behavioral theories of health lost scientific credence.

The materialist influence on the medical sciences created a standard for physiological evidence of disease that was in many ways complemented by the concurrent development of a scientific theory of evolutionary adaptation. The evolutionary concept of natural selection emphasized that human development resulted from a biological process driven by adaptive needs,

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9 Descartes’ epiphany revolutionized philosophy and medical science, though it was not without its critics. Most notably, Baruch Spinoza and Gottfried Wilhelm Leibniz offered their own alternative models for Cartesian dualism. Spinoza disputed the theory that the body and the mind are qualitatively different substances, arguing that there is only one universal substance, God. Under Spinoza’s double-aspect theory, the body and the mind were united through a divinely pre-ordained relationship. Leibniz argued that the expressions of the body and the mind were so patently dissimilar that they could neither affect one another, nor be produced by an independent third substance. He instead argued in favor of a parallelism between the body and mind, accepting a relationship of correlated mental and physical expressions, but denying any causal relationship between the two entities. See Spinoza, De Ethica in Opera Posthuma (1677), and Leibniz, Système Nouveau de la Nature (1695), Eclaircissement du Nouveau Sisteme (1696).
which led to a disproportionate focus on physiological traits that were chosen over generations of reproduction, and presumed to arise primarily through bio-structural and biochemical mechanisms. The zeitgeist of evolution, and its companion pseudo-sciences of social Darwinism and eugenics, infiltrated both psychiatric and physiological scientific research.\textsuperscript{10} An evolutionary perspective in the health sciences viewed sickness or weakness as a dynamic of natural selection—and failure to successfully adapt to environmental pathogens and psychosocial duress was viewed as a natural process for improving the genetic stock of the human race.

While evolutionary theory emphasized genetic determinants of health, contemporaneously, the rise of the “Germ Theory” of disease further endorsed a positivist ethos in the medical sciences by promoting empirical observation and reductionist research methods. Louis Pasteur and Robert Koch’s independent investigations of microbiological etiology (which led to Koch’s discoveries of the cholera vibrio, the tuberculosis bacillus and the anthrax vibrio), generated a methodological paradigm of scientific investigation oriented around the laboratory and the microscope. The great success of bacteriology and virology in combating devastating contagious diseases gave microbiology a privileged seat in the pantheon of the sciences, and recalibrated the standards for scientific legitimacy so that in order to be accepted as valid, studies were expected to comply with the microbiological methodological practices. The doctrine of specific etiology became the dominant model of medical theory, prompting researchers to focus

\textsuperscript{10} In 1864, five years after the publication of Darwin’s \textit{Descent of Man} examining evolution in humans, English polymath Herbert Spencer published \textit{Principles of Biology}, applying the adage “survival of the fittest” to describe natural selection. Spencer saw evolution as increasing in complexity from generation to generation, towards a determined end-point of supreme evolution. Applying his interpretations of the biological principles of evolution to society, Spencer theorized that complexity was the measure of social evolution, and that in order to attain the highest degree of civilization, men must exist in unfettered competition, so that the weakest and simplest could be weeded out. Darwin’s cousin, Sir Frances Galton interpolated the concept of natural selection, when applied to human beings exclusively, to recommend \textit{eugenic} selection, using human intervention to select desirable traits and to weed-out undesirable ones.
on laboratory methods to identify the microbiological causes of disease. Robert Koch’s four postulates to determine disease causation—1) the abundant presence of the germ in diseased, but not healthy organisms, 2) the isolation and growth of the germ in pure culture, 3) the reproduction of disease in a healthy organism when the cultured germ is introduced, and 4) the affirmation that the re-isolated germ from the experimental host is identical to the original source—became the principal standards of clinical laboratory research. This microscopic focus emphasized a reductionist perspective of disease, which sought to identify the most basic etiological mechanisms independently from their larger effects on an organism.

**Precedents of Psychosomatic Stress**

In the mid-nineteenth century, the professionalization of psychiatric medicine followed the dualistic paradigm that bifurcated mental and physical health, yet implicated the relationship between a host and its environment as a critical determinant of mental health. Nineteenth-century psychiatrists practiced a “moral cure” for mental illness oriented around the imposition of regiment spaces, routines and social relationships, ensured by the nearly-exclusive care for

psychiatric patients in institutional settings. Yet, the effectiveness of institutional moral therapy was restricted to the treatment of acute neurotic conditions, and even among such patients, it bore unreliable and in many cases fleeting results. Thus, by the end of the nineteenth-century, the limitations of this therapeutic program gave rise to an increasing number of incurable, chronic cases of psychoses and senility amongst institutionalized patients, and a high rate of recidivism amongst neurotic patients, which conveyed an impression that psychiatric methods were ineffective and unscientific. Specialists in the nascent field of neurology emerged as outspoken critics of psychiatrists’ methods, arguing that due to the scientific deficiency of their profession, psychiatrists’ behavioral theories of mental illnesses were unfounded and impeded effective treatment.

Neurologists’ rebuke of asylum psychiatry helped to demarcate the boundaries of their profession, and with the founding of the Neurological Society in 1875 and the circulation of its official organ, the Journal of Nervous and Mental Disease, neurology began to define itself as a legitimate, independent medical field. By seeking to discredit psychiatrists’ behavioral theories of mental illness, neurologists sought to establish a scientific foundation for the evaluation and treatment of mental illness that conformed to the biological-orientation of contemporary microbiological science. Yet, in doing so, they also helped to generate scientific investigation of the relationship between psychological and physical health.

12 Grob, Mental Illness and American Society; Rothman, Conscience and Convenience.

Neurologists advanced a somatic theory of mental illness, insisting that all psychological disorders must arise from a physical impairment to the central nervous system. This theory derived from several breakthrough discoveries in the 1860s and 1870s, including the revelation that locomotion could be induced by stimulating specific areas of the cerebral cortex and Paul Broca’s 1861 discovery of the area of the posterior inferior prefrontal gyrus of the brain that produces speech. Neurological science also arose from military research of soldiers’ psychosomatic complaints. During the Civil War, Dr. Jacob Mendes DaCosta leant his name to a syndrome, also colloquially known as “soldier’s heart” or “irritable heart,” in which soldiers suffered from symptoms of heart disease without any physiological cause. DaCosta studied 300 patients who suffered from chest pains and tightness, difficulty breathing, heart palpitations, dizziness and fatigue. He noted that their symptoms often set in after a fever or case of diarrhea, which he theorized weakened these men’s constitutions so that they were less capable of enduring the physical strain of soldiering. DaCosta published the results of his study in 1871, the same year that William Alexander Hammond, former Surgeon General of the Union Army, 


also published a highly influential treatise on the neurological foundations of physical health, heralding the emergence of a new field of neurological medicine.\textsuperscript{16}

Hammond’s \textit{Treatise on Diseases of the Nervous System}, also published in 1871, outlined the tenets and methods of neurology, based largely on the lectures of French neurologist, Jean-Martin Charcot. Remembered as the “father of modern neurology,” Charcot established the first neurological clinic in Europe at the Salpêtrière Hospital in Paris, where he taught numerous notable students, including Pierre Janet, Sigmund Freud and William James, that nervous diseases developed from a localized lesion in the brain, meninges or peripheral nervous system. Charcot helped to popularize the neurological explanation for \textit{hysteria}, which claimed that women who exhibited volatile emotional surges did so due to hereditary neurological deficiencies.\textsuperscript{17}

While hysteria interpreted emotional disturbances as a result of the physiological dysfunction of the uterus, neurologists also advanced an energetic theory of mental illness: \textit{neurasthenia}. Popularized by New York neurologist George M. Beard and his Philadelphia colleague Silas Weir Mitchell, neurasthenia was thought to arise from a depletion of one’s inherited finite nervous force through excessive mental, physical or sensory stimulation.\textsuperscript{18}


theorized that physical exercise, excessive exposure to noise, over-work, burdensome financial and social responsibilities and perhaps most significantly, the “pace of modern life” drained finite stores of nervous energy and induced mental and physical fatigue, and in some instances, acute episodes of manic behavior. Because this etiological formulation suggested that nervous weakness was strongly associated with modernization and urbanization it accordingly called for reclusive therapies, such as visits to rural spas or the rest cure, and in some cases, the invigorating and masculinizing antidote to an excess of civilization by embracing the “strenuous life” through physical activity in the great outdoors.¹⁹

While neurology proved to be a lasting formative influence on the development of medical fields of psychiatry and medical psychology,²⁰ by the turn of the century, the somatic


emphasis of neurology that had initially helped to legitimate the field, began to draw criticism as most causes of insanity could not be conclusively associated with specific lesions.\textsuperscript{21} By the early-twentieth century, both hysteria and neurasthenia, while still widely diagnosed, were becoming outmoded. Not only had their usefulness been stretched thin by over diagnosis, but the traditional therapies of rest, ascetism and hypnosis seemed decidedly un-scientific amidst the rise of microbiology, and passé by the standards of emerging behavioral and structural theories of mental illness. These vestiges of nineteenth-century psychiatric medicine increasingly fell into disuse in the Progressive Era, as unique fields of psychiatry and psychology sought to distinguish themselves from one another.

The first decades of the twentieth century witnessed a crisis of disciplinary demarcation that was critical to the development of the modern sciences.\textsuperscript{22} With regards to mental health, psychiatry became more closely allied with allopathic medicine and institutional treatment, assimilating Emil Kraeplin’s classification system for distinct mental diseases, symptoms and etiologies. Whereas, psychology was regarded as a heterodox off-shoot that existed independently from the mainstream medical establishment and was generally relegated to academic research and private practice. Psychology, was itself a composite of diverse subfields—most prominently, structuralism categorized mental structures of affections, images


and sensations, behavioralism emphasized the importance of observable human actions rather than abstract thoughts and feelings, and psychoanalysis placed primary importance on the influence of repressed emotional memories.

Following Sigmund Freud’s lectures at Clark University in 1909, psychoanalysis became a dominant influence on North American psychology. Under the teaching of Freud, talk therapy offered patients the opportunity to explore their own subconscious fears and desires, and through their own realization, resolve psychosomatic physical disorders, such as migraines, stutters, nervous twitches, and bedwetting. The psychoanalytical concept of anxiety proved to be particularly resonant among American practitioners and patients because it explained unique psychological problems as the product of suppressed emotions, while at the same time alleviating feelings of deviancy and irremediable by interpreting mental illness and wellness as two poles on a dynamic continuum. Any otherwise normal person could suffer from anxiety as a natural reaction to emotional repression, and through psychoanalytical therapy, they could regain full mental health.

The popularity of psychoanalysis attracted more and more practitioners, so that between the First and Second World Wars, the number of practicing psychologists in the United States...

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23 Behavioral psychology was largely inspired by the work Russian physiologist Ivan Petrovich Pavlov, who revolutionized the study of human behavior through his research on conditioned reflexes, for which he won the 1904 Nobel Prize in Physiology and Medicine. Pavlov demonstrated that animal physiology could be altered through environmental stimuli, emblematized by his famous study of behavioral conditioning in which he trained his dogs to salivate in expectation of food whenever he rang a bell.

grew from 300 to 3,000. But, aspects of psychoanalytical theory appealed to some psychiatrists, as well. Head of the Johns Hopkins Department of Psychiatry, Adolf Meyer incorporated aspects of Freudian psychoanalysis into the more traditional discipline of psychiatry, giving rise to a new field of psychobiology. The rise of psychobiology signifies the fading influence of neurology and organicism, and increasing attention to cumulative life events, including emotional, physical and social factors as precipitating factors in mental health. Meyer trained multiple generations of psychobiologists, who went on to lead their own psychiatric departments and institutes, evangelizing the tenets of psychobiology in the course of their professional research and service.

By the mid-1930s, the proselytization of psychoanalysis catalyzed the development of a formal field of psychosomatic medicine. Psychoanalysts, such as Helen Flanders Dunbar and Franz Alexander, documented the relationship between emotional disorders and physiological ailments, while physiologists and chemists, such as Walter Bradford Cannon and Otto Loewi compiled laboratory-based evidence of the alteration of internal neurological and endocrinological mechanisms by emotional and afferent stimuli. Yet, as dualism remained a


powerful force in biomedical research, psychosomatic medicine was largely regarded as an unorthodox and marginal field until the Second World War, when it became more professional organized.  

While psychiatric, psychological and neurological research did much to advance medical knowledge of the relationship between mental and physical health, psychosomatic medicine only gained scientific credence with the emergence of “hard” scientific evidence. Falsifiable and reproducible laboratory investigation documenting internal biochemical changes caused by emotional disturbances offered the positivist justification required by mainstream medical standards. Claude Bernard, the first chair of Physiology at the Sorbonne, revolutionized the study of psychosomatic medicine not by conducting experiments on the Mind-Body relationship himself, but by promoting standards of investigation through his insistence on the universal use of the scientific method and the importance of blind testing and falsifiable results. Bernard’s research focused on uncovering the effects of internal secretions, employing the controversial technique of animal vivisection to determine the effect of pancreatic secretions on digestion, as well as glycogenesis in the liver. Bernard also developed a unique insight that undergirded future stress research. He theorized that the human body was driven to maintain a constant “internal milieu,” a stable fluid matrix that regulated essential bodily functions, so that whenever this state was disrupted, by disease, temperature, shock, etc., the body would initiate repair processes to retain its prime steady state. Bernard’s theory of “internal milieu” intrigued


Harvard physiologist Walter Bradford Cannon. Cannon began his career investigating the effects of the emotions on bodily functions, such as peristalsis, leading him to identify the “flight or fight” response facilitated by the release of adrenaline. He later proposed the theory of homeostasis, a biological equilibrium maintained by nervous and endocrinological regulatory mechanisms, which built on Bernard’s theory of “internal milieu.”

Bernard and Cannon were at the forefront of a burgeoning field of endocrinological research that gained apace following the First World War, as it became associated with biochemistry. Following Charles Brown-Sequard’s research on the internal secretions of the reproductive organs in the 1880s, scientists were increasingly drawn to investigate these invisible mechanisms of internal regulation. In 1902, William Bayliss and Ernest Starling identified a chemical messenger, “secretin” that was produced in the intestines to signal the pancreas to secrete digestive enzymes. In 1904, Bayliss dubbed such chemical messengers that carry signals to regulate organ and tissue functions, “hormones.” In the first two decades of the twentieth-century, scientists found hormones produced by the ovaries, testes, pancreas, adrenal, thyroid and pituitary glands, each of which regulated various aspects of metabolism, reproduction, and growth. In 1921, the discovery by four Canadian researchers—Frederick Banting, Charles Best, John J.R. Macleod, and James Bertram Collip (the Chief of the McGill Biochemistry Department where Selye began his career in North America)—that blood sugar levels are regulated by the pancreas’ secretion of insulin, revolutionized the treatment of diabetes through pharmaceutical

30 Historian of endocrinology, Victor Medvei has argued that endocrinology developed not as a distinct discipline, but a diverse field that incorporated a range of scientific methods. By the 1920s, the dominant model of endocrinological research was based in biochemistry. See Victor Cornelius Medvei, The History of Clinical Endocrinology: A Comprehensive Account of Endocrinology from Earliest Times to the Present Day, rev. ed. (New York: Parthenon Publishing Group, 1993). On the development of biochemistry in North America see Robert E. Kohler, From Medical Chemistry to Biochemistry: The Making of Biomedical Discipline (New York: Cambridge University Press, 1982).
hormone preparations, and generated widespread excitement about the promise of hormonal research.

**Stress and the Political Economy of Biomedical Research**

Selye’s “discovery” of stress was profoundly influenced by both the medical culture and political economy of biomedical research that informed his education and early career. And biomedical culture was itself shaped by available sources of funding. Over time, these consisted of a matrix of state, philanthropic and corporate patrons. However, until the Second World War, Selye relied nearly exclusively on philanthropic grants, supplemented with limited financial and material support from pharmaceutical companies. In the early-twentieth-century, philanthropic organizations—especially the Rockefeller Foundation—offered the primary means of support for academic research, and in so doing exerted a powerful influence on the design of newly developing North American academic medical and public health institutions.31 Historian E. Richard Brown has written that, “the Rockefeller wealth became the *largest single source of capital* for the development of *medical science* in the United States, the conversion of *medical education* to a scientific research basis, and the development of *public health* programs in the United States and abroad,” donating more than $82 million to medical education in the United States.

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States and Canada from its founding in 1914 to 1930. Through large grants to universities strategically chosen to enhance North American regional centers of medicine, the GEB standardized scientific medicine, in accordance with clinical biomedical principles, and promoted the prestige and viability of academic researchers as a professional class. By 1920, the GEB had granted approximately $15 million for improvements in medical education, and by 1929 their total donations exceeded $78 million (more than half of the $150 million donated by all philanthropic foundations by 1938). The Biochemistry Department of McGill University (where Selye began has scientific career in North America), received substantial funding from the Rockefeller Foundation to “modernize” its scientific research facilities following the Johns Hopkins model.

The formative years of Selye’s professional career were framed by the international economic crisis of the Great Depression, which marked a turn towards state activism and government spending to promote economic recovery and development. Further enshrining the Keynesian liberalism of the Depression years in US federal policy, World War II radically transformed the funding of medical research and popular understandings of health, and directly contributed to the development of the disease concept of stress. As the state took on an active role in directing and funding research to support the war effort, academic and industrial scientists gained a new source of financial support that would permanently transform the political economy of medical research. Research sponsored by the US and Canadian National Research Councils (USNRC and CNRC, respectively) catalyzed the development of synthetic adrenocortical steroids, while neuropsychiatric research conducted under the US Army’s

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Medical Corps drew attention to the prevalence of and universal susceptibility to “combat stress” amongst servicemen. Together, these advances in endocrinology and psychiatry gave birth to a biomedical model of stress.

Following the war, a corporate liberal economy of biomedicine fueled both psychological and endocrinological research, which together advanced the medicalization of stress. The war also transformed the political economy of medical research by promoting the pharmaceutical industry to a newly powerful role in supporting academic research. Partnering with the federal government in wartime research programs, perhaps most notably the effort to develop a means of mass-producing penicillin, pharmaceutical companies emerged from the war with new laboratory facilities funded by state contracts, and revenue streams derived from the commercialization of antibiotics, which enabled further investment in product development. Wartime research on the synthesis of adrenocortical steroids considerably advanced medical understanding of the role of the adrenal cortex in adaptation, and forged a collaborative relationship between corporate and academic scientists, which by the end of the 1940s led to the mass production of the adrenocorticoids cortisone and ACTH. These new “wonder drugs” initially seemed a panacea for countless chronic diseases, from arthritis to hypertension, and consequently stood testament to Selye’s theory that the hormones of the pituitary-adrenal axis regulate diseases of adaptation.

While corporations took on a newly powerful role in the postwar biomedical economy, the state quickly emerged as the most powerful funder of scientific research. The great success of the military research programs during World War II stood testament to the immense benefits of state-funded scientific research, endorsing an ethos of corporate liberalism that guided postwar economic policy, while the new threat of the Cold War created an imperative to continue the model through an academic-military-industrial complex. State and corporate funders were
foundational in the development of a distinct field of stress research in the postwar period. Academic researchers were invited into influential policy making positions in new state agencies and institutions, such as the newly reorganized National Institutes of Health, the National Science Foundation and the USNRC’s Ad Hoc Committee on Stress. At the same time, an epidemiological transition resulting from the huge success of bacteriological interventions, led to fewer deaths from infectious disease and a collateral increase in the prevalence of chronic diseases. This drastic change in disease prevalence required extensive research to uncover new treatments and methods of disease prevention. US national medical research policy targeted diseases such as cancer, arthritis and heart disease, enlisting the advise of newly created disease associations, such as the Arthritis and Rheumatism Foundation, as well as academic and industrial “scientist statesmen” to serve on their various committees helped that determined research priorities and approved grant applicants.

The theory of stress was a crucial underpinning of the risk factor model that helped to reconcile biomedical science with the epidemiological transition of the mid-twentieth century, and consequently, served to medicalize a range of conditions previously considered to fall within the range of “normal” health or “natural” aging processes. Both state and corporate research funders found the emergent disease concept of psychoendocrine stress to be an exceptionally appealing field of research and investment, as it promised to address the unique therapeutic needs of the postwar patient population. As chronic diseases, such as heart disease, cancer and arthritis became increasingly prevalent, and as a dynamic theory of mental illness universalized susceptibility to anxiety, stress seemed to be a natural explanation for the most prevalent health complaints of North Americans.
While state and corporate funders continued to dominate the medical research economy, the increasing consumer-orientation of postwar economic liberalism elevated the interests of consumers as a deciding factor in the validation of research pursuits.\(^3^4\) In the decade after the close of World War II, the pharmaceutical industry prioritized research and development of adrenocortical steroids and anxiolytic drugs to meet the therapeutic needs of the postwar increase in chronic disease and the medicalization of anxiety. The return of veterans suffering from “combat stress” and other neuropsychiatric disorders encouraged the cultural assimilation of a dynamic model of mental illness which held that “every man has his breaking point.” The dynamic model of mental health universalized and normalized psychological distress, while the 1952 publication of the American Psychiatric Association’s first *Diagnostic and Statistical Manual* formally medicalized anxiety as diagnosable and treatable condition. As more and more Americans came to believe that even healthy individuals could suffer from slight mood disorders, they embraced the medicalization of anxiety, and sought pharmaceutical treatments to alleviate feelings of tension.\(^3^5\) Furthermore, as the paranoid culture of the Cold War spread


anticommunist fears and “atomic anxiety,” individuals who had already lived through the hardship of the Great Depression and the Second World War, developed new sources of psychological stress that might lead them to seek pharmaceutical relief. Thus, while World War II gave birth to the biomedical concept of stress, the Cold War created new psychological demands for this diagnosis.

While on the one hand, pharmaceutical firms sent their own in-house “detail men” into doctors’ offices around the nation to encourage professionals to prescribe these drugs, at the same time, the importance of consumerism to the postwar manufacturing economy offered power to patient-consumers in the medical marketplace, which encouraged direct-to-consumer marketing via advertisements in popular periodicals and on the radio. Drug firms influenced popular health literacy as they marketed both adrenocortical and anxiolytic medications as effective treatments for a diverse range of diseases, including heart disease, allergy and menopause. The medicalization and commercialization of anxiety helped to popularize belief in the psychosomatic nature of stress, and the consumer-orientation of the postwar medical market encouraged an individualistic perspective of disease that required individualized treatments.

**III. Cultural and Economic Forces Shaped Selye’s “Stress”**

A close examination of the evolution of Selye’s stress research reveals a process that was powerfully shaped by biomedical culture, the political economy of medical research, and the interpretive needs of changing patient demographics. Charting these forces from the mid-1930s to the mid-1970s, we see how Selye cleverly adapted to the changing terrain of his profession and adroitly responded to cultural changes.

Selye’s methods, career goals and research questions were shaped by the academic research structure of the 1930s, 40s, and 50s, which was itself, primarily shaped by funding sources that enabled research, investigative methods and principles that conformed with the dominant biomedical paradigm, and medical inquiries required by changing patient demographics. As Selye strove to conform to orthodox biomedical standards in order to legitimate his heterodox theory, he utilized clinical investigative methods which cast “stress” in an individualistic and reductionist framework. By the end of the Second World War, he recognized that the drastic rise in chronic diseases required a more dynamic etiological model that could account for multiple causes and risks for disease. Thus, biological stress helped to reconcile biomedical science with changing patient demographics, while yet retaining its individualistic and reductionist tenor.

Stress became the quintessential postwar disease, reflecting changing patient demographics, medical culture, and economic forces, and Selye gained professional prestige as the world’s preeminent expert on stress. He focused on investigating chronic and degenerative disease etiology as these disease categories were surpassing infectious diseases as the primary causes of death in North America. And over time, he adapted both his methods of research and of soliciting funding to the changing needs of the postwar medical market and North American public. Selye catered his research to attract lucrative philanthropic grants, federal research contracts, and support from pharmaceutical companies and the tobacco industry. He focused on dietary and behavioral risk factors for disease that enabled patient management of chronic diseases, while also complementing the consumer-orientation and corporate interests of the postwar medical market. However, in doing so, Selye developed a conflicted disease model that confused the causal relationship between psychological and physiological stress, and focused
exclusively on the individual causes of disease to the exclusion of social, political and economic
determinants of health. He also lent his authority as an expert on stress to endorse the
commercial interests of the pharmaceutical and tobacco industries. As Selye’s scientific
expertise was predicated on corporate support, so was corporate credibility bolstered by the
appropriation of scientific authority.

At the heart of Selye’s medical and philosophical theories of stress was a focus on
individual interventions, whether through pharmaceutical treatment, self-medication, or behavior
modification. Selye promoted a popular understanding of stress that focused exclusively on
individual causes and therapies, very much in accordance with mid-century biomedicine, which
seemed to offer patients the power to improve their own wellbeing. By avoiding salt and red
meat, indulging in stress-reducing diversions, and when necessary, taking stress relieving
medications, individuals could take control of their own health. However, this perspective
presumed that physical health is controlled by will power, reifying a belief in the psychosomatic
nature of disease: since your mind controls your behavior, and your behavior can influence your
physical health, then ultimately you can control your health with your mind. This logic has not
only contributed to the ambiguous psychosomatic interpretation of stress, but also failed to
account for social and environmental stress risk factors that are beyond individual control.

Selye helped to revolutionize our understanding of the causes of disease by substantiating
the concept of attributable risk and multicausal disease, and thereby reconciling biomedicine
with the mid-century rise of chronic disease mortality. His work on stress made a profound
foray into the medical investigation of holistic health and helped to legitimate the scientific
investigation of the relationship between the mind and the body. Yet, his individualistic and
reductionist focus hindered the recognition of ecosocial pathways of disease. Indeed, his advocacy of consumer-oriented and behavior-centered therapeutic and diversionary interventions insulated and obscured commercial pathways that influence the distribution of stress. And, perhaps ironically, these same potentially harmful commercial pathways helped “stress” to gain cultural currency. Selye’s theory upheld the primacy of the market as the principal point of therapeutic intervention, promoting the assimilation of a disease model that favored consumerist and behavior-oriented treatments, and therefore failed to acknowledge a full spectrum of risk. Consequently, while the scientific endorsement and functional value of biological stress encouraged its social assimilation, its meaning remains contested and shrouded in ambiguity.

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Chapter 1: Discovering Biological Stress

Introduction

Hans Selye’s research was profoundly shaped by the culture of early-twentieth-century biomedical research in which he was immersed. Both his methodology and research queries were informed by the forces that shaped this culture—namely, a professional standard that promoted positivistic research methods and a reductionistic perspective of biological processes, as well as a system of patronage oriented around philanthropic funding and a burgeoning market for the pharmaceutical commercialization of hormonal drugs. Guided by these influences, Selye created a disease model that focused on the development of disease within the individual, and failed to account for ecosocial pathways of disease.

By the early-1930s, this biomedical culture, developing since the late-nineteenth-century triumph of the “germ theory,” and encouraged by growing interest in the field of endocrinology, had created a professional standard relying on the methodological techniques of vivisection and histology. These professional standards were enforced by philanthropic patronage, particularly through the Rockefeller Foundation’s program of institution building in the medical sciences. Complimenting philanthropic support, an expanding market for hormonal drugs drove pharmaceutical corporations to offer grants-in-aid for endocrinological research, and in a few cases, to develop long-standing collaborative relationships with academic scientists.

Like all successful bench scientists of his day, Selye acclimated to the cultural hallmarks and political economy of biomedical research and competed for small, short-term philanthropic grants to fund specific projects. Selye’s early research investigated the actions of reproductive

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1 Vivisection is the surgical experimentation on a living organism for scientific purposes. Histology is the study of the microscopic anatomy of animal and plant tissues and cells. Bioassay is an experimental method that uses live animals or tissues to assess the activity of a substance, such as the potency of a drug or a hormone.
and adrenal hormones, as well as environmental influences on biological health. By 1936, these queries led him to discover a “General Adaptation Syndrome” (GAS) that the body mounted in response to a diverse array of harmful agents, including extreme temperatures, excessive physical exercise and intoxication.

Selye was not the first scientist to contribute to our understanding of what he would eventually name “stress.” Since the late-nineteenth century, neurologists, endocrinologists and psychologists had investigated the environmental and emotional propagation of physical diseases, and the physiological production of mental illness. Investigations into shock, hysteria, neurasthenia, and dyspepsia, to name a few, sought to draw a connection between the symbiotic health of the mind and the body. However, Selye did not seek to evaluate the mind-body connection. Rather, his theory was unique in its insistence on the nonspecific nature of disease.

The implication that the body responded in the same way to all antagonistic agents levied a direct challenge to a central tenet of biomedical theory: the doctrine of specific etiology, which held that each disease arises from a unique pathogen. Consequently, Selye’s theory was initially met with great skepticism.

Rather than discourage Selye, this criticism prompted him to hone his theory, using reductionist research methods to demonstrate its scientific legitimacy. As a result, Selye focused on identifying discrete hormonal processes initiated by adverse external, physical agents, and avoided any direct examination of the physiological afferents of emotional states. In doing so, his research was bound by biomedical standards of empirical investigation, reductionist methods, and the isolation of biochemical sciences in distinct departments. By the late-1930s, his research benefitted immensely from the development of synthetic adrenocorticoids, with which he was able to simulate the GAS in his laboratory animals. By establishing the biochemical mechanisms
of physiological adaptation to external stimuli, Selye’s theory of general adaptation would ultimately help to expand the investigative boundaries of biomedicine to enable a more holistic analysis of biological disease. However, in doing so, Selye’s primary concern was to reconcile what he considered a deficiency of biomedical theory—its strict adherence to the doctrine of specific etiology—and not to justify the scientific validity of a relationship between psychological and physical health.

I. Discovering the General Adaptation Syndrome

Hans Selye began working in the McGill University Biochemistry Department in the early-1930s at the height of the Great Depression. In the summer of 1932, after completing the second half of a one-year Rockefeller Foundation Fellowship at McGill, he intended to return home to the Czech Republic to assume a teaching post at his alma mater, the University of Prague. However, he arrived to discover his position had been eliminated due to insufficient funding generated by the worldwide financial crisis. Hearing of Selye’s misfortune, James Bertram “J.B.” Collip, the Chair of McGill’s Biochemistry Department offered Selye a position as a lecturer in biochemistry and a seat at the bench in Collip’s lab. Collip had first gained international professional acclaim for his participation in the isolation of the metabolic hormone insulin in 1921, but by the early-1930s his research interests gravitated towards reproductive endocrinology. In the late-1920s he developed an estrogenic placental extract, Emmenin that

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2 Selye served approximately half of his fellowship at McGill, after arranging a transfer from Johns Hopkins Medical School where he felt lonely and out of step with American culture.


4 J.B. Collip collaborated with Frederick Banting, Charles Best and John Macleod in the isolation of insulin, for which all four men shared the 1922 Nobel Prize in Medicine or Physiology.
was effective in promoting menstruation and treating postmenopausal estrogen deficiency—and ultimately became the best-selling prescription drug in twentieth-century North America.\(^5\) Collip was convinced that though only two female sex hormones had yet been identified by scientists (estrogen and progesterone), a third unidentified hormone was yet to be discovered, and he enlisted Selye and his lab mates in a departmental search for this mysterious unknown female sex hormone.

An aspiring endocrinologist, trained in allopathic medicine and histology, Selye was fortunate to work under Collip at McGill, and Collip was fortunate to have him on his team. The study of reproductive hormones required histological analysis—detailed microscopic examination of prepared tissues to detect sometimes very subtle changes in the shape and size of cells. Selye’s histological skills were an asset to the departmental work on female sex hormones, while at the same time his independent projects produced pioneering research on the neuroendocrine mechanisms that regulate pregnancy. Selye was especially interested in the relationship between the adrenal and pituitary glands in mediating the reproductive cycle. Through his work on reproductive hormones, Collip had also been drawn to study the anterior pituitary gland as the “conductor of the endocrine orchestra.”\(^6\) In order to assess the unique functions of each gland, Selye would remove rats’ pituitary glands and inject the hypophysectomized\(^7\) animals with hormonal extracts prepared from the missing gland. This


\(^6\) In his research on Emmenin, Collip had detected a second active principle, which he called anterior-pituitary-like substance (APL) that produced corpora lutea in female rats and increased the growth of the seminal vesicle and prostate in male rats. Li, *J.B. Collip and the Evolution of Medical Research in Canada*, 67, 76-77.

\(^7\) The suffix “ectomy” denotes the surgical removal of the root word. The hypophysis is a synonym for the pituitary gland.
enabled Selye to evaluate the extent to which the hormones produced by the pituitary acted upon the reproductive organs. In his first year in Collip’s lab, Selye improved upon University of California, Berkeley endocrinologist Philip Smith’s innovative method of removing pituitaries at the base of the rats neck (rather than through the scull), so that by the end of 1932 he was able to perform the operation in less than five minutes and could operate on as many as one hundred rats per day.⁸

Based on his strong training in histology and experimental surgery and morphology, Selye was delegated the responsibility for preparing ovarian extracts to be injected into ovariectomized and hypophysectomized female rats (to inhibit their capacity to naturally produce female sex hormones). Selye would then perform autopsies on the treated animals to evaluate the potency of the extracts and the extent to which they produced morphological changes.⁹ This involved collecting fresh cow ovaries from a local slaughterhouse, slicing the organs into microscopically thin particles, macerating them with a solute, and injecting the preparation into the post-surgical rats—a task which he found to be painfully monotonous.¹⁰ Perhaps the monotony sufficiently wore on Selye’s powers of concentration to distract him from the proper execution of this task, but for whatever reason, some of the extracts he prepared became contaminated with formalin, a highly caustic aqueous formaldehyde detergent used to clean laboratory instruments.

When Selye performed autopsies on the injected rats, he anticipated finding evidence that the hormone extracts had caused physical changes in their reproductive organs. Thus, he was

⁸ Alison Li, *J.B. Collip and the Evolution of Medical Research in Canada*, 98.


gratified to observe various lesions and other morphological alterations in the ovariectomized rats, but not in the hypophysectomized rats (which indicated that they failed to mount the same adrenocortical response). Notably, all of the ovariectomized rats exhibited three symptoms: 1) significant enlargement of the adrenal glands, 2) reduced size and weight of the thymus, and 3) the development of peptic ulcers in the upper intestine and duodenum. Selye excitedly interpreted these findings to arise from the unique hormonal content of the extractions.\textsuperscript{11} He was certain that he was on the right track of discovering Collip’s elusive female reproductive hormone when injections of progesterone and estrogen failed to produce this same battery of symptoms. He was however perplexed when anterior pituitary extracts, which could not possibly have contained ovarian hormones, produced the same effects.\textsuperscript{12} However, Selye assured himself that this peculiarity may in fact be evidence that an unknown hormone produced by the pituitary, placenta and ovaries might be responsible for instigating the syndrome.\textsuperscript{13}

However, when he repeated the experiment using extracts of kidney, spleen and other organs and found that these non-reproductive organs produced the same triad of symptoms, Selye began to question whether the unknown “active principle” that induced this response was in fact specific to the reproductive endocrine system. At the same time, he had noticed that contrary to his scientific intuition, the purest extract preparations were the least effective, and the least refined preparations produced the most pronounced reactions. Selye suddenly realized that the glandular lesions may have nothing at all to do with sex hormones, but may have been

\textsuperscript{11} Selye, \textit{The Stress of My Life}, 59-60.

\textsuperscript{12} Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH) were the only two gonadotropic (a substance that stimulates secretions from the gonads) sex hormones produced by the pituitary then known, and neither of them acted independently of the gonads.

\textsuperscript{13} Selye, \textit{The Story of the Adaptation Syndrome}, 26.
induced purely by the toxicity of his extracts. After months of experimentation, Selye finally recognized that the preparations he had been injecting into his rats were contaminated with formalin. To test this theory he injected his rats with a diluted formalin solution and to his great despair, found that they developed the exact same symptoms.

Months of research wasted, his hopes of achieving a monumental discovery dashed, Selye retreated into what he later described as a “period of introverted contemplation.” It was in the midst of his brooding and rumination that he had an epiphany: if the syndrome he observed was indeed a general biological response to any source of damage, it may be a great benefit to science if he could identify its specific biochemical mechanisms. This realization reminded him of something he had noticed during his clinical training at the German University of Prague. Selye was shown patient after patient that exhibited remarkably similar symptoms even though they each suffered from a different disease. They all looked and felt ill, often suffered non-specific pain in their muscles and joints, and experienced a loss of appetite and gastro-intestinal disturbances. At the time, Selye had been struck by the general response of the body to such diverse influences, but had been discouraged from pursuing the idea any further. Given that orthodox biomedicine of the time sought to identify specific causes and treatments for specific conditions, Selye’s fascination with generality was considered decidedly unscientific.

At the same time, Selye and his first graduate student, Thomas McKeown were working on another project examining the hormonal regulation of the female reproductive cycle. They injected female rats with extracts prepared from pituitary glands and placenta, and observed a subsequent disruption of the rats’ normal sexual cycle—they failed to initiate the phase of

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vaginal estrus in which ovarian follicles mature in preparation for fertilization. When Selye and McKeown performed experiments using different kinds of hormonal extracts to corroborate their results, they found that estrus could also be prevented by excessive doses of thyroid extract, induced vitamin deficiencies, starvation and the removal of the adrenal glands. Given the diverse range of catalysts, Selye and McKeown realized that this was a non-specific response and “promptly lost interest in it.”

Publishing their results in a 1935 edition of the Proceedings of the Royal Society of London, Selye and McKeown deduced that the sexual dysfunction caused by these diverse hormonal treatments must be a reaction to non-specific “stress” channeled through the pituitary and the glands it regulates. Throughout the article, Selye and McKeown repeatedly described estrus-preventing conditions as “stress,” emphasizing the nonspecific nature of this phenomenon wherein any number of traumatic factors could interrupt the reproductive cycle by preventing follicle growth. Yet, neither Selye nor McKeown appreciated the significance of this finding—that the disruption of normal biological processes in response to nonspecific stresses was in fact a biological tactic of self-preservation. Nor did Selye or McKeown intend for the term stress to be interpreted as a specific syndrome or medical condition—in this article, they used the term “stress” as a generic noun.

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15 Selye, The Story of the Adaptation Syndrome, 19.

16 Ibid., 20.


Though Selye initially failed to realize the significance of his observations of nonspecifically caused damage, over the next several months he became convinced that there was a profound link between his early observations of general sickness, and the response of the body to nonspecific damage. “If this were so,” he determined, “some degree of non-specific damage is undoubtedly superimposed upon the specific symptomatology of any disease and of any drug used to treat disease… [and] all the actually observed biologic effects of stimuli must represent the sum of their specific actions and of this non-specific response to damage that tends to mask the former!”

Contrary to mainstream medicine’s preoccupation with specific etiology, Selye was asserting the validity and importance of general sickness and general causation. What Selye was proposing was nothing short of biomedical heresy. Yet, he was certain that if his theory was correct, it would be of unparalleled value to medical science by offering the capacity to treat all diseases without requiring specific knowledge of their cause.

II. The “Pharmacology of Dirt”

Fearing that Selye was wasting his potential as a scientist, Collip attempted to draw Selye’s focus back to orthodox endocrinological concerns and “abandon this futile line of research.” But Selye was captivated by his current research and adamant that the study of nonspecific physiological mechanisms of self-preservation could revolutionize modern science. Selye later vividly recalled that in response to his stubborn insistence on the importance of his theory an exasperated Collip finally accused Selye of squandering his scientific skill only to pursue his study of “‘the pharmacology of dirt?’”

19 Selye, The Story of the Adaptation Syndrome, 27.

Selye not only deeply admired Collip, but considered him a “fatherly friend” and a great inspirational influence.\textsuperscript{21} Therefore he was extremely hurt by Collip’s blunt criticism. Yet, despite having lost the support of his Chief, Selye found support from another icon of Canadian endocrinology, Collip’s fellow discoverer of insulin Frederick Banting. As an advisor to the Canadian National Research Council (CNRC), Banting often conducted site inspections of CNRC-supported university labs throughout Canada. While conducting a site visit at McGill, he visited Selye’s lab and spoke with him about his theory of general biological response. Banting assured Selye that his theory did indeed have great potential, and even helped to secure him a $500 grant (approximately $6,000 in 2015 Canadian dollars) to support his research.\textsuperscript{22}

Encouraged by Banting’s faith in his theory, Selye dedicated himself whole-heartedly to investigating this syndrome. Though McKeown was no longer with him, by this time, Selye had acquired his own lab assistant, Kai Neilsen, to whom he delegated the mundane task of holding the experimental animals while Selye administered injections and measured their responses, as well as the tedious microscopic analysis of their samples. With Neilsen’s help, Selye first investigated the extent to which the syndrome was truly nonspecific by exposing rats to a diverse range of physical stimuli. He first experimented with extreme temperatures, leaving his rats in cages on the roof of his laboratory for an entire day in the middle of the Montreal winter. He then measured the effects of excessive exercise, forcing his rats to run constantly on electrically-powered exercise wheels in order to avoid being tossed upside-down. He also induced surgical shock through transcision of the spinal cord, exposed the rats to x-rays and assaulted their senses with intense light and sound. In every instance, the rats exhibited the same three symptoms that

\textsuperscript{21} Selye, \textit{The Stress of My Life}, 61.

\textsuperscript{22} Ibid., 62.
he had earlier inadvertently induced through intoxification. In fact, Selye concluded that he “could find no noxious stimulus that did not elicit” adrenal enlargement, thymico-lymphatic atrophy and gastrointestinal ulceration.\textsuperscript{23}

While studying the nonspecific nature of the syndrome, Selye noticed that the characteristic symptoms occurred in a specific temporal pattern. Within a few hours of the first exposure to injury, the body would initiate an emergency response of extreme vigilance, which Selye referred to as the “Alarm Reaction.” For up to 48 hours, the body would become engaged in the urgent distribution of glucose and oxygen to facilitate rapid physical response. Following the initial acute response of the “Alarm Reaction,” the characteristic three symptoms began to attenuate even despite the continued presence of the harmful agent. Selye reasoned that the decreased mechanisms of vigilant protection indicated not that the body had succumbed to the trauma, but that it had adjusted to its presence. This adjustment signified the body’s successful adaptation to an external threat by elevating its capacity for resistance, thus Selye called this second stage of his syndrome the “Stage of Resistance.” As the body became inured to the threat, it was able to revert to normal physiological functions of repair, growth and reproduction—blood pressure would decrease and the body would resume its normal weight. Yet, this acquired adaptation was not permanent. Eventually, the body would become so fatigued by the constant vigilance required by its adaptation that it would fall prey to a final “Stage of Exhaustion,” which ultimately culminated in death.

\textsuperscript{23} Selye, \textit{The Story of the Adaptation Syndrome}, 32.
III. Conceptualizing “Stress”

By the summer of 1936, Selye had identified a specific syndrome, which the body mounted in response to virtually any antagonistic force, and had identified three characteristic symptoms of this syndrome—enlargement of the adrenal glands, shrinking of the thymus and lymphatic tissues, and the development of ulcers in the intestines. Furthermore, he had discovered that the syndrome occurred in three specific stages: an initial Alarm Reaction, beginning within a few hours of injury and lasting for up to 48 hours, in which an animal develops a heightened capacity to resist diverse sources of damage; a subsequent Stage of Resistance, that lasts for an extended period of time and is signified by a prolonged adaptation to one specific damaging agent, but also an increased susceptibility to all other noxious stimuli; and a final Stage of Exhaustion, in which an animal lost its adaptive capacity to resist any damaging agent, and finally succumbed to death. These three stages represented a progressive adaptation to harmful agents, which Selye named the “General Adaptation Syndrome” (GAS).\(^\text{24}\)

Selye outlined the results of his experiments in a brief letter to the editor of *Nature* published on July 4, 1936 under the title “A Syndrome Produced By Diverse Nocuous Agents.”

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He explained the tri-phasic nature of the physiological response to bodily injury, as well as the characteristic symptoms of adrenal enlargement, thymico-lymphatic atrophy and gastro-intestinal ulceration. The concept of general adaptation offered a “unified theory of disease” that saw all illness as a product of the same central pathological mechanisms, as well as a new method of intervention in the processes of sickness, aging and degeneration. Yet, despite the revolutionary potential of Selye’s theory, this official announcement failed to elicit the radical paradigm shift that his theory foretold. In fact, the article drew very little interest at all, and what attention it did receive was largely critical. Critics charged that the GAS was irrelevant (much as Collip had suggested in likening Selye’s study of general sickness to a “pharmacology of dirt”), and that rather than emphasize the nonspecific causes of this syndrome, it would be more useful to examine the specific repercussions of the specific agents Selye employed in his experiments—extreme temperatures, intoxification, surgical shock, etc. Even those who accepted the validity of nonspecifically-caused sickness argued that the GAS was imprecise for it failed to identify the actual biochemical agents that induced the morphological changes of the Alarm Reaction and the crossed sensitization witnessed in the Stage of Resistance.

Before publishing these early findings, Selye made a deliberate decision to try to reduce resistance to his radical theory by conforming as much as possible to contemporary standards and mores of academic science. He anticipated that his attack on the sacred doctrine of discrete etiology would be met with skepticism, so in order to discourage opposition, he was especially careful in the phrasing he chose to describe his controversial theory. Though he had used the term “stress” in the article outlining the physiology of the rat placenta that he and McKeown had published just a year before he began to formulate the GAS, he later claimed to have intentionally shied away from introducing this neologism for fear that it would draw criticism
and detract from clinical significance of his theory. So, when the editors of Nature recommended that he use the term “nocuous agents” to describe the stressful stimuli used in his experiments, he gladly assented. It was not until 1946 that Selye began to consistently use the term “stress” to describe a specific biological phenomenon, often referring to the GAS as the “stress syndrome.”

The same year that Selye published this watershed article in Nature, the Chair of Harvard University’s Department of Physiology, Walter Bradford Cannon published an article in The American Journal of the Medical Sciences entitled “The Stresses and Strains of Homeostasis.”25 In this article, Cannon used the term “stress” to describe a dynamic physiological struggle to maintain equilibrium despite a constant flux in the bioavailability of fluids and nutrients. In Cannon’s usage, oxygen and glucose levels, as well as heart rate, blood volume and internal temperature were potential sources of stress when either excessive or deficient. However, Cannon did not seek to introduce a biological theory of stress, but rather used the physics concept as a metaphor for biological activity.

It is highly likely that Selye was familiar with this article, as he admittedly was a great admirer of Cannon’s work and was in fact in communication with Cannon in the mid-1930s. Correspondence between Selye and Cannon in April of 1936—three months before Selye’s article appeared in Nature—reveals that Cannon was aware of Selye’s research on adrenocortical hormones, and in fact strongly encouraged Selye to consider the possibility that the different layers of the adrenal cortex may perform different functions and produce different

hormones. Yet, this correspondence does not indicate that either man embraced the term stress as a biological concept at the time. It is quite possible that Selye’s eventual assimilation of the term stress to describe the GAS was influenced by Cannon’s 1935 article. However, this would suggest an interpretive leap on Selye’s part, as Cannon remained resistant to this terminology for the duration of his career, and contested the central tenets of Selye’s theory: the tri-phasic, prolonged nature of the GAS, and the nonspecific origins of diseases manifest through the GAS.27

Cannon’s criticism bore great weight because, perhaps more than any other scientist, his research presaged, and indeed enabled the discovery of biological stress. Cannon began his career investigating the effects of the emotions on bodily functions, such as peristalsis. As a graduate student at Harvard in the late-1890s, Cannon used cutting-edge x-ray technology to observe gastric motility in laboratory animals. By combining vivisection and radiology, he discovered that when his laboratory animals were nervous or frightened, their peristaltic activity abated.28 In 1915, his seminal monograph, Bodily Changes in Pain, Hunger, Fear and Rage identified the process initiated by the sympathetic nervous system in the “flight or fight” response to increase the bioavailability of oxygen and sugar triggered by adrenal secretions.29

26 Walter B. Cannon to Hans Selye, April 2, 1936, Box 132, folder 1864, RG H Ms c40, Walter B. Cannon Papers, Center for the History of Medicine, Francis A. Countway Library of Medicine, Harvard University, Boston, M.A. (hereafter WBC).


29 Bodily Changes in Pain, Hunger, Fear, and Rage drew upon Spencer and Darwin’s evolutionary theory, as well as psychologist William McDougall’s 1908 monograph, Introduction to Social Psychology, which attributed fear to a flight instinct, and anger to
He found that during times of extreme tension or excitement, the adrenal medulla (the inner core of the adrenal glands) secretes adrenaline (also known as epinephrine) to mobilize emergency energy reserves in order to escape or combat danger, liberating sugar and fatty acids from the liver into the blood stream to provide metabolic fuel for the muscles, while the blood supply is shifted from the abdomen to the lungs, heart, and limbs to support mobility and be readily available for immediate clotting in the case of injury.

Fear, anger, hunger and pain could all signal the adrenal medulla to secrete a burst of adrenaline to initiate the body’s emergency response mechanisms: increased heart rate, blood vessel constriction, lung passage dilation, pupil contraction, and glycogen production. All of these processes triggered by the release of adrenaline were intended to facilitate acute sensory perception and intensive muscular activity. In order to expedite the bioavailability of glucose and oxygen that nourish the muscles and the brain, the heart rate increased, enhancing blood circulation. And in order to preserve energy for the exclusive purpose of combating external threat, the body would divert blood and glucose from organs that were not essential to the fight or flight response, slowing digestion, interrupting growth and repair, and disrupting reproductive processes. At the same time, the sympathetic nervous system suspends all repair functions, in order to redirect the energy needed for functions such as digestion, growth and wound healing towards the immediate response to an external threat. While these mechanisms were highly effective in fighting or fleeing an external attack, if they were called upon too frequently, they

“pugnacity.” Cannon applied McDougall’s dichotomy of fight or flight to explain the physiological response to immediate external threats, which he deduced had developed as an adaptive response over many millennia. See, Cannon, Bodily Changes in Pain, Hunger, Fear and Rage (New York: D. Appleton & Co., 1915).

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could result in physical damage as necessary growth and wound repair would not take place, and excess levels of fatty acids in the blood would be converted into cholesterol, impeding cardiovascular circulation. In this way, a healthy adaptive response could inadvertently contribute to disease.

At the time, Cannon’s theory offered revolutionary evidence that emotions bore a direct relationship to endocrinological mechanisms of self-preservation. By demonstrating that emotional excitement stimulated the release of the adrenal hormone adrenaline and that adrenaline activates impulses in the sympathetic nervous system, Cannon created a scientific basis to support the pursuit of further psychosomatic research.31 His subsequent work on the prolonged effects of emotional stimulation on physiological functions expanded this field to examine how normal physiological behavior can become harmful when prolonged or in excess.

Cannon further contributed to the conceptualization of biological stress with his research on the psychological catalyzation of physiological states of shock. Two years after Cannon’s germinal monograph, he embarked on a new investigation of psychosomatic health when he served as Chairman of the Red Cross’s Medical Research Committee, and visited field hospitals in military laboratories throughout Europe as a medical volunteer for the American Expeditionary Forces in World War I. Working in an ambulance unit in the field, he investigated wound shock and blood volume among the infirmed, and had the opportunity to study the phenomenon of “shell-shock” first hand. The transformation of warfare during the First World War—invoking the introduction of chemical weapons, machine guns, tanks, aerial bombings, submarines, and trench warfare—created a scale of destruction that exacerbated the prevalence

of neuropsychiatric disorders amongst servicemen. Characterized by symptoms such as catatonia, mania, fits and night terrors, as well as migraines, amnesia, nervous tics, dyspepsia, gastrointestinal ulcers, and even incontinence, shell-shock offered a medical diagnosis to justify behavior that otherwise would have been interpreted as malingering and warrant court martial or execution. However, shell-shock was also a bleak diagnosis which presumed that patients’ symptoms arose from irreparable neurological damages, and as such held out little hope for rehabilitation. A shell-shocked patient warranted sympathy for incurring their illness through patriotic service, but they did not escape the stigma of mental illness.

Cannon helped to legitimate the medical nature of shell-shock in his post-war civilian research. He theorized that the unbearable stress of war weakened the sympathetic nervous system so that the heart became hyper-sensitized to even mild stimuli, incapacitating the afflicted soldier. Cannon supported his theory with clinical evidence showing that even in spite of severed cardiac nerves, adrenal stimulation of the remaining sympathetic nerves could increase the heartbeat from 70 to 90 beats in one minute, and if the adrenal glands were also denervated, the heart rate could still be affected by stimulation of the sympathetic nervous system.

Perhaps inspired by his familiarity with shell-shock, during the 1920s Cannon’s research focused on identifying neurological and endocrinological mechanisms of the autonomic nervous system, which led him to investigate the role of what would later become known as neurotransmitters in triggering adrenal responses. He followed-up on his WWI neuro-cardiac


research with a study of how adrenal stimulation could release sugar from the liver despite
denervation of the hepatic nerves regulating liver function, and later examined how nutritional
and hydration deficiencies were regulated through a neuro-endocrine mechanism by which
hormones sent signals informing the brain of the body’s need to eat or drink. 34 In 1928, in
collaboration with Philip Bard, he identified the hippocampal center for rage below the thalamus,
and showed that while the cerebral cortex controlled voluntary emotional expressions, this
subcortical center in the brain controlled the involuntary expression of emotions. In his revised
edition of Bodily Changes in Pain Hunger Fear and Rage published in 1927, Cannon added a
chapter on “Emotional Derangement of Bodily Functions,” which refuted the orthodox theory
that pathological states necessarily correlated with specific anatomical lesions. Cannon
persuasively argued that emotional states could profoundly alter organ function without affecting
morphological construction, as was evident in the disruption of digestive processes during
periods of excitement and the chronic elevation of blood pressure induced by repeated exposure
to strong emotional stimulants.35

Cannon’s greatest contribution to Selye’s theory of biological stress was his theory of
homeostasis, which he first presented in his monograph, The Wisdom of the Body, published in
1932. Building on French physiologist Claude Bernard’s theory of the internal milieu, Cannon
offered a detailed analysis of the regulatory functions of the body’s “fluid matrix,” examining
water, mineral, fat and sugar content of the blood, as well oxygen supply and body temperature.
Based on clinical, physiological research, he evaluated natural sensations of hunger and thirst as
a means of maintaining relative constancy of hydration and nutrients, and examined the


35 Ibid., 620-621.
deterioration of all of these natural mechanisms of regulation over time. Cannon argued that while the autonomic nervous system is responsible for maintaining internal stability in non-threatening conditions, the sympathetic nervous system was frequently called upon to regain stability in the face of constant pressure from external and internal forces that cause perpetual damage by wear and tear. According to Cannon, the body is only able to maintain equilibrium through “coordinated physiological processes …involving, as they may, the brain and nerves, the heart, lungs, kidneys and spleen, all working cooperatively,” to which Cannon applied the term homeostasis to emphasize an active and variable condition that remains relatively constant.36 Cannon described homeostasis as an economy of internal preservation, resulting from an evolutionary process that increases an organism’s self-control, or agency, and therefore, frees higher-level organisms to undertake more “complicated and socially important tasks.”37

As a widely respected pioneer in endocrinology, Cannon enjoyed a position of exceptional prestige within the scientific community (even in spite of his interest in psychosomatic research). As a testament to his professional esteem, in 1930, Cannon received a grant from the Rockefeller Foundation for $175,000 (approximately $2.5 million in 2015 dollars) for general research on physiology.38 The Rockefeller grant did not require him to commit to a specific research program, and as such, was the first grant to support basic research by one scientist that Rockefeller Foundation ever issued. With this substantial funding, Cannon gained greater independence in his research, and was able to devote more time to professional service.


Cannon had always been active in the scientific community, belonging to dozens of scientific societies, volunteering service during the First World War, spearheading an antivivisectionist movement in the 1910s as President of the American Physiological Society, and serving on various USNRC committees, including the Committee for Research in Problems of Sex, the Committee on Research in Endocrinology, and the Committee on Shock, Transfusion and Blood Substitutes. But, in the 1930s, thanks to his financial autonomy, Cannon’s activity as a scientist statesman escalated. By the mid-1930s, his distinguished record of professional service included senior statesmanship through his work with USNRC committees, over three decades as chairman of Harvard’s Department of Physiology, and the appointment of fellowships in the National Academy of Sciences and the American Association for the Advancement of Science.

As a result of his professional reputation and connections, Cannon wielded great influence throughout the scientific community—in the academy, government, and the private sector. Cannon provided expert scientific advice and academic references to officers of the Rockefeller Foundation and the Josiah Macy, Jr. Foundation, as well as executives in the private sector. He was a friend and advisor to Alan Gregg and Robert Lambert of the Rockefeller Foundation, frequently corresponding with both men regarding academic references and scientific questions. Similarly, professional researchers from Metropolitan Life Insurance Company, the Eugenics Records Office, and industrial researchers and executives from pharmaceutical companies, such as Eli Lilly, Burroughs Wellcome & Co., Lederle, Merck, E.R. Squibb, Ciba, frequently wrote to Cannon for advice on scientific questions.

39 Box 92-93, WBC.

40 Box 102-103, WBC.
Cannon’s opinion carried a great deal of weight both within and beyond the academy, and affected national science policy, as well as the careers of individual researchers. Thus, his own interest in psychosomatic medicine and endocrinology boded well for the development of both of these fields. Thanks in no small part to Cannon, by the mid-1930s, a field of psychosomatic medicine was emerging within the biomedical academy and professional health sciences—however, it was still regarded warily by most mainstream scientists who tacitly accepted Cartesian mind-body dualism as a fundamental tenet of biomedicine. In this atmosphere of skepticism, Cannon stood out as a conspicuous exception to the status quo, whose professional reputation lent a great deal of credence to this heterodox field.

While Cannon laid the foundation of physiologically-oriented psychosomatic medicine, progress in industrial hygiene research contributed to the scientific analysis of environmental factors affecting physical endurance and fatigue. Growing, in part, out of the field of scientific management that developed in the Progressive Era to rationalize the industrial workforce and improve worker efficiency—and catalyzed by the tragically high rate of occupational accidents and chemically-induced illness caused by poorly regulated industrial production—the field of industrial hygiene sought to improve workplace conditions and the health of workers by, among other strategies, better managing industrial human resources based on the scientific analysis of factors that affected workers’ motivation and performance. By the mid-1920s, industrial hygiene and human resource management had become mainstays of America’s welfare capitalist economy, leading management to voluntarily provide fringe benefits such as sick leave and paid breaks in order to improve workers’ satisfaction, discourage disruptive work actions, and maintain a steady workforce. Professional industrial hygienists advised management on various incentive strategies to improve productivity and reduce fatigue.
It is no coincidence that Cannon’s alma mater was also home to a pioneer in the investigation of physiological causes of fatigue, Harvard professor of industrial hygiene, Elton Mayo. While Cannon conducted animal experiments to observe physiological changes within organs and tissues, Mayo conducted field research that examined human beings’ reactions to various environmental and psychological influences on their productive capacity as laborers. His studies on worker performance at the Western Electric Hawthorne plant outside of Chicago from 1924-1932, are to this day an emblem of early research in human resource management. Mayo found that workers were more productive in orderly, well-lit environments, that sympathetic and receptive managers contributed to worker satisfaction and motivated productivity, and that pay incentives did not necessarily motivate communities of workers who feared that improvement in their own productivity might jeopardize less productive co-workers. (The Hawthorne Works experiments were later interpreted to indicate that experimental subjects might adjust their behavior when aware that they were being observed, known as the “Hawthorne Effect”).

In 1927, Mayo, his colleague at the Harvard Business School, Professor Lawrence J. Henderson, and Harvard Dean David Edsell, founded a new Laboratory of Industrial Research to understand ways of increasing the efficiency of the industrial workforce. The Fatigue Laboratory, as it was commonly known, was initially funded with grants from the Rockefeller Foundation, and collaborated closely with the Massachusetts General Hospital for research on human subjects. Distinct in its multidisciplinarity in an era of disciplinary isolation, the

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41 [untitled], memo re: History of the Fatigue Lab, Box 26, folder 37, RG M-CE03, Harvard Fatigue Laboratory Records, Center for the History of Medicine, Francis A. Countway Library of Medicine, Harvard University, Boston, M.A. (hereafter HFL).

42 [untitled], Box 26, folder 17, HFL. On the institutional history of the Fatigue Lab, see Steven M. Horvath and Elizabeth Horvath, The Harvard Fatigue Laboratory: Its History and Contributions (Englewood Cliffs, N.J.: Prentice Hall, 1973); Carleton B. Chapman, “The Long
Fatigue Laboratory pursued truly innovative research on the psychiatric, social and physical dimensions of exhaustion and endurance. From its inception, the Fatigue Laboratory was “concerned principally with the physiological rather than the psychological problems” of fatigue, focusing on “what makes men get tired in various environmental circumstances and what can be done to relive this fatigue?” While they focused both on external (environmental) and internal (physiological) factors contributing to fatigue, the vast majority of the more than 300 papers produced by the lab over the next two decades centered on environmental influences.

Very early in their research, the Fatigue Laboratory researchers were compelled to develop an effective means of detecting and measuring changes caused by fatigue. From 1927 to the early-1930s, the Fatigue Laboratory’s research focused on “establishing normal values for physiological variables in the healthy young working adult,” which were used in later years to measure effects of “unusual environments,” especially those of extreme heat, cold and high altitude. In the first five or six years of its existence, the Fatigue Laboratory focused on establishing standards for evaluating physiological variables in young, healthy working adults. They examined the effects of unusual environments, such as those characterized by extreme dry or moist heat, and of high altitude. They studied working conditions among laborers constructing the Boulder Dam and working in the steel mills of Youngstown, Ohio, and found that an adequate night’s rest, as well as sufficient water and salt were essential to maintain workers’ productivity in such sweltering heat. They further confirmed these findings through


43 “The Laboratory of Industrial Research, Harvard Business School,” Box 26, folder 17, HFL.

subsequent studies of the effects of humid heat among workers in Panama in 1931, and in the Mississippi delta in 1939.\textsuperscript{45} In 1935, the Fatigue Laboratory began a study of the effects of high altitude among miners in the Chilean and Bolivian Andes, which would help to guide research during World War II to diminish Air Force pilots’ susceptibility to altitude sickness.\textsuperscript{46}

The Fatigue Laboratory emblemized scientific interest in environmental influences on human endurance, signifying a dawning ecological understanding of health, embraced by sociologists, psychologists and a growing number of physiologists in the 1930s. Consequently, it is possible that Selye might have taken such factors into consideration in his own research. However, his training as a bench scientist guided him to investigate individual, not population health, and to utilize clinical techniques that examined biochemical, not social or psychological processes. Thus, even as he sought to develop a more holistic model of disease, he remained firmly oriented in a reductionist endocrinological perspective.

\textbf{IV. The Philanthropic Shaping of Early-Twentieth Century Biomedical Research}

While Cannon and the researchers at the Fatigue Laboratory contributed to a growing recognition of the biomedical legitimacy of psychosomatic health—a critical development in the conceptualization of biological stress—Selye’s research avoided the mind-body problem. Selye himself was not especially concerned with the psychosomatic implications of his theory at first, and did not address these questions in his own research. His primary focus was on correcting

\textsuperscript{45} Harvard University News Office Press Release, December 30, 1945, Box 26, folder 17, HFL.

what he perceived to be a fatal flaw of biomedicine—it’s dogmatic adherence to the doctrine of specific etiology. In doing so, he employed strictly orthodox research methods to document the biochemical mechanisms of the GAS. The premium that biomedical research placed on such reductionist methods was on the one hand a reaction to the revolutionary benefits of microbiological science (which bore the doctrine of specific etiology), and on the other, a reflection of the ways in which philanthropic and pharmaceutical interests profoundly shaped the academic culture and funding opportunities for North American scientists.

In the early-twentieth century, given a lack of state funding, philanthropic organizations offered the primary means of support for academic research. In so doing, they exerted a powerful influence on the design of newly developing North American academic medical and public health institutions. Large philanthropies, like the Carnegie Foundation, the Josiah Macy, Jr., Foundation, the Russel Sage Foundation and the Commonwealth Fund, to name only a few, were critical to the development of biomedical science in both the United States and Canada. Among them, the Rockefeller Foundation arguably exerted the greatest formative influence on the development of biomedical research in North America. From its founding in 1914 until 1930, the Rockefeller Foundation’s General Education Board donated more than $82 million to medical education in the United States and Canada (approximately $1.2 billion in 2015 dollars). Through large grants to universities strategically chosen to enhance North American regional centers of medicine, the GEB promoted the standardization of scientific medicine, in accordance with clinical, biomedical principles.

47 Ben-David, The Scientist’s Role in Society; Brown, Rockefeller Medicine Men; Fundamental Development of the Social Sciences, edited by Richardson and Fisher; Fee, Disease and Discovery; Kohler, From Medical Chemistry to Biochemistry; Kohler, Partners In Science.

48 Brown, Rockefeller Medicine Men, 193.
The Rockefeller Foundation was inspired by the Gospel of Wealth philosophy that elites bore a responsibility to invest their fortunes for the betterment of society, as well as a Progressive faith in the promise of science and efficiency to rationalize social problems, and the emerging associationalist formula which delegated responsibility for social and economic regulation to private charity and welfare capitalism. The Rockefeller Foundation viewed their support for the improvement of the university system in North America as an investment that would provide vital social resources through the development of a professional base of scientifically-grounded disciplines to advance “pure” knowledge and “apply” this advanced research to the resolution of modern problems. In so doing, universities would act as a socially-stabilizing force against the disruptions caused by industrial capitalism. \(^{49}\) Frederick T. Gates, the chief advisor to Rockefeller Foundation President, John D. Rockefeller, Jr., developed a passionate faith in scientific positivism after reading William Osler’s *Principles and Practice of Medicine*. Osler, the first physician-in-chief at Johns Hopkins, insisted on the importance of laboratory investigation in medical education. With the Rockefeller Foundation’s proselytizing endorsement, Osler’s principles and the Johns Hopkins research program became the model for medical education.

By promoting the creation of an institutionally-based professional class intended to guide social improvement, the Rockefeller Foundation helped to generate new methods of legitimating knowledge and conferring credibility through the development of a new social structure predicated on the expertise of academics. That the Rockefeller Foundation’s philanthropic principles were strongly informed by the corporate background of its benefactors, likely shaped

\(^{49}\) Richardson and Fisher, introduction to *The Development of the Social Sciences in the United States and Canada*, 8.
its perception of institutional progress as contingent on the functional division of labor. This involved the separation of teaching and research responsibilities, but it also promoted the disciplinary demarcation of different fields of research, which in turn promoted specialization within the sciences that established ideological and cultural boundaries between researchers of different specialties. In their study of the Rockefeller Foundation’s influence on the development of social sciences in North America, Donald Fischer and Theresa Richardson have emphasized the Rockefeller Foundation’s involvement in disciplinary “boundary work.” They argue that “power penetrates knowledge systems,” through the creation of disciplinary boundaries which come to govern “the process whereby legitimacy and cognitive authority are attached to ideas.” As a consequence, the development of specialized fields of research generates mechanisms of validation, credibility and prestige in which, “the distinction between science and nonscience is a critical element.” In establishing legitimate fields of science, the Rockefeller Foundation also participated in the promotion of certain methods and fields of knowledge above others—perhaps most conspicuously in their advocacy of allopathic biomedicine following the 1910 publication of Abraham Flexner’s Report on Medical Education in the United States and Canada, which exposed the disgraceful lack of scientific rigor in North American medical schools.

50 Richardson and Fisher, introduction to The Development of the Social Sciences in the United States and Canada, 8.

The publication of the Flexner Report attracted the Rockefeller Foundation’s General Education Board (GEB) to become involved in supporting medical education and research.\textsuperscript{52} The Rockefeller Foundation appointed Flexner as Secretary of the GEB, and gave him primary responsibility for determining how an allocated $50 million (approximately $1.2 billion in 2015 dollars) in Rockefeller Funds would contribute to the reform of medical education. He determined that grants would be distributed on the condition that the recipient would match or exceed the amount through other sources of funding and use the funds to improve facilities and instruction. The institutional grant system was intended to encourage the independence and self-sufficiency of each institution, and to discourage continued reliance on Rockefeller (or any other philanthropic) funding. The grants also carried caveats requiring that schools use the funds to improve their research facilities—laboratories and teaching hospitals—and prohibiting faculty from private medical practice.\textsuperscript{53} By 1920, the GEB had granted approximately $15 million for improvements in medical education, and by 1929 their total donations exceeded $78 million (more than half of the $150 million donated by all philanthropic foundations by 1938).\textsuperscript{54}

Under the direction of Wickliffe Rose in the 1920s, the GEB pursued a program of institutional system-building, to strengthen regional centers of academic excellence by providing large institutional grants to major universities for the purpose of endowing faculty chairs or specific departments or to improve the quality of research facilities. In doing so, the Rockefeller


\textsuperscript{54} Brown, \textit{Rockefeller Medicine Men}, 155.
Foundation viewed Canada as an extension of the United States. In December of 1919, John Rockefeller, Sr. gifted $50 million to the Foundation, $5 million of which was set aside to honor Rockefeller, Sr.’s request that at least some of the money be used “in promoting medical education in Canada.”

Richard Pearce, who had recently been appointed Director of the GEB’s Medical Education Division, organized a study to determine how best to use the funds. By February 25, 1920 Pearce and Rockefeller Foundation President George Vincent issued a report recommending that they issue two grants of $1 million each (approximately $12 million in 2015 dollars), to the University of McGill and the University of Toronto, each to be matched by a $900,000 grant from the Canadian government. The grants were intended to be used for the improvement of clinical research facilities and for the construction of buildings for departments of physiology, pathology, and psychiatry to increase “the closer union of hospital and school in the true university clinic … [and] the importance of this medical school as the national school of Canada.” By providing an additional $1 million endowment to support the McGill Faculty of Medicine, the Rockefeller Foundation also hoped to alleviate the burden of teaching responsibilities for researchers, as well as the distraction of private practice for medical faculty. By thus promoting the professionalization of academic research and medical education, the Rockefeller Foundation intended to “strengthen this system of teaching in the British Empire,”

55 Richardson and Fisher, introduction to The Development of the Social Sciences in the United States and Canada, 8.


57 Additional grants of $500,000 each were also issued to the Universities of Manitoba and Dalhousie, and even smaller sums to the Universities of Montreal and Alberta. Schneider, “The Men Who Followed Flexner,” 13-14.
and to inspire other medical schools to develop full-time, scientifically-based medical programs.  

Through the Rockefeller Foundation’s influence, McGill’s School of Medicine was designed to emulate the research-oriented program in scientific medicine implemented at Johns Hopkins by William Osler, a graduate and former professor of medicine at McGill. In addition to the construction of new buildings for physiology, pathology and psychiatry, Charles Martin, dean of McGill’s School of Medicine, used the Rockefeller Foundation’s funding to construct modern laboratory facilities and appoint a number of acclaimed scientists to professorships. The Foundation continued to impact the cultural and curricular development of the department through its continued financial support, in the form of research fellowships and research grants. In 1924 it endowed $500,000 (approximately $7 million in 2015 dollars) and for a university medical clinic and in 1929 it allocated $85,000 (approximately $1.8 million in 2015 dollars) for research and experimental surgery.  

Thanks to the Rockefeller Foundation’s support, by the 1930s McGill’s Biochemistry Department was an icon of modern endocrinological research, employing biomedical principles of falsifiable empirical evidence and specific etiology in the clinical investigation of reproductive biochemistry and physiology. Working in Collip’s lab, Selye was at the precipice of innovative endocrinological research. He also had direct access to Collip’s matchless expertise, learning essential methods of hormonal extract preparation from a master, and he worked with an interdisciplinary team of notable researchers that included J.S.L. Browne, David Landsborough Thomson, Evelyn Anderson and Eleanor Venning, all of whom would make profound

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59 Li, *J.B. Collip and the Evolution of Medical Research in Canada*, 62.
contributions to the endocrinological investigation of stress, as well. With the help of a rotating staff of three or four graduate students and never more than six post-graduate workers, the group was extraordinarily productive, publishing nearly two hundred papers from 1934 to 1941.\footnote{Li, \textit{J.B. Collip and the Evolution of Medical Research in Canada}, 92-95.}

Under Collip’s leadership, this prolific and talented team of scientists contributed immensely to what historian of medicine Alison Li has described as an “endocrine gold rush” of the 1930s.\footnote{Ibid., 96.}

Selye contributed to the McGill Biochemistry team as an expert histologist. He dissected placental and ovarian tissues treated with biochemical extracts prepared by Collip for biological assay, and scrutinize them for microscopic anatomical and physiological morphology. In her biography of Collip, Li has argued that “the team was particularly successful when it was anchored by the ideal configuration of Collip and Selye with their complementary skills in biochemistry and histology… Selye’s subsequent departure was a grave loss to Collip’s work.”\footnote{Ibid., 111-112.}

Selye’s early research was very much influenced by the environment of McGill’s Biochemistry department—particularly by its emphasis on reductionist methods and encouragement for researchers to compete for private funding. He thoroughly assimilated the premium placed on biomedical positivism and the centrality of clinical research to scientific investigation, while also becoming acclimated to dependency on research grants from private sources. In addition to the fact that Selye’s career as a North American scientist began with a Rockefeller Foundation fellowship to study at Johns Hopkins and McGill, Selye continued to depend on support from the Rockefeller Foundation over the course of his tenure at McGill. He benefitted both directly and indirectly from Rockefeller grants, collaborating with fellow researchers on projects for which
they received funding. In the late-1930s, Selye also secured funding from the Josiah Macy Jr. Foundation, the John and Mary R. Markle Foundation, the Commonwealth Fund, and the Banting Fund.

In addition to philanthropic support, Selye also learned to acquire laboratory materials and research grants from pharmaceutical companies. Through this education on scientific patronage, Selye, like other successful bench scientists, acclimated to the professional pressure to cater the design of his projects to appeal to funders by emphasizing the scientific-grounding and cutting-edge nature of his methods, the potential benefit of his work to medical knowledge and society, and potential commercial appeal of his research. His initial research on the endocrinological regulation of reproduction was a major focus not only of the McGill Biochemistry Department, but of pharmaceutical and philanthropic patrons, as well. In the late-1930s and early-1940s, Selye received funding and materials from a number of pharmaceutical firms, including Ciba, Des Bergers-Bismol, Merck, Frank W. Horner, Smith, Kline & French, Pfizer, Hoffman-LaRoche, and others.

In 1928, the Rockefeller Foundation began an internal reorganization in which its scientific activities were consolidated into four new divisions: natural sciences, medical sciences, social sciences, and arts and humanities. The Foundation’s structural transformation was accompanied by a new ethos of grant distribution that replaced the old practice of issuing large institutional grants with a new emphasis on smaller grants to individual faculty members for specific research projects. Until the late 1920s, the Foundation had been principally involved in supporting the development of research laboratories, faculties, and fellowships, however, following the restructuring, its focus shifted to the direct funding of researchers. On January 3, 1929, the Special Committee on the Work and Organization of the Division of Medical
Education resolved that “concern with the development of medical schools as institutions be lessened and the principle of aid to individuals, groups, and departments in relation to research and advance of medical knowledge be emphasized.” The onset of the Great Depression later the same year expedited this programmatic transition as depleted financial resources and new social problems took precedence over the grandiose systems-building of the previous decade.

The structural reorganization brought new program leaders into positions of power within the organization. After George Vincent retired in 1929, the Foundation’s new president, Max Mason and his colleague, Raymond Fosdick who succeeded Mason in 1936, conscientiously sought to depart from Rose’s system of patronage, in favor of one that fostered specialization. Alan Gregg took over administration of the Medical Sciences Division, and in 1932, Warren Weaver was brought in as the head of the Natural Sciences Division. Together, Gregg and Weaver had an immense impact on the curricular development of the medical and natural sciences, respectively. Each man targeted specific departments to receive funding, and while Weaver privileged biological research above all other disciplines—establishing the Foundation’s recognition of biology as a natural and not a medical science—Gregg emphasized the importance of allocating funding to psychiatric research. This created a formidable barrier between biochemists and psychiatrists and diminished biochemists’ access to philanthropic funding. As a result, in 1934 and 1935 Collip’s Biochemistry Department lost a bid for a $60,000 grant (slightly more than $1 million in 2015 dollars) from the Rockefeller Foundation to endow an

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65 Ibid., 396.

Endocrinological Institute, while his colleague at McGill, Psychiatrist Wilder Penfield won an astounding $1.28 million endowment (approximately $22.7 million in 2015 dollars) for his Neurological Institute.\(^{67}\)

The Rockefeller Foundation restructuring had a profound effect on the professional culture of academic scientific research. As individual researchers were forced to compete for grants, they became more self-conscious of their own careers, talents and distinction from other fields of research. They also were forced to be more efficient in their use of resources, and to cater their research to attract funding. Because the Rockefeller Foundation placed great importance on innovation in laboratory research questions and methods, researchers’ honed a competitive edge by designing projects that embraced new techniques and pursued unchartered scientific territories.\(^{68}\) Selye internalized this ethos in the design of his own research, innovating new surgical techniques to improve the accuracy and efficiency of histological examinations. Yet, more importantly it forced him to seek alternative sources of funding at a time when the growing field of endocrinology was producing marketable organotherapies that drew academic scientists into relationships with private pharmaceutical firms.

The Rockefeller Foundation’s requirement that faculty renounced their private practices separated medical practice from academic research and training, and contributed to the creation of a new, viable professional medical field immersed in a clinical, biomedically-oriented, positivist and reductionist culture. At the same time, American academic culture emphasized that scientific research be useful, and not purely for the sake of advancing knowledge—giving rise to what historian Robert Kohler describes as “basic applied sciences, infused with academic

\(^{67}\) Li, *J.B. Collip and the Evolution of Medical Research in Canada*, 116-128.

\(^{68}\) Kohler, *Partners in Science*, 402.
ideals but firmly rooted in the medical market.” The medical reform movement instigated by the Flexner Report also promoted the institutional isolation of distinct disciplines within independent departments of medical schools. One of many fields that gained formal distinction as a result of this process of disciplinary demarcation was biochemistry, which broadly involved research on the chemical processes that regulate organic life. As biochemistry developed its own unique authority, it provided essential training to future doctors and medical researchers and thereby creating what Kohler calls an essential “medical service role,” that justified its disciplinary autonomy and importance within the academy. Kohler claims that biochemistry earned this prestige and autonomy due to its isolation in an independent department, which enabled it to develop a systematic, clinical method and intellectual orientation.

Because American biochemistry developed in independent departments of medical schools, it had the autonomy to develop its own systematic design, rather than develop piecemeal in response to methodological or contextual problems. Kohler argues that as a consequence, “clinical biochemistry was accorded the intellectual prestige of an independent discipline.” This clinical orientation of biochemistry was paramount to the establishment of a network of institutions with access to political and economic resources, which in turn, influenced its orientation towards applied, rather than a basic research. Research in biochemistry grew significantly following the First World War, as the American Chemical Society and the Chemical Foundation undertook a public relations campaign to promote public recognition of the

69 Kohler, From Medical Chemistry to Biochemistry, 157.

70 Ibid., 6.

71 Ibid., 251.

72 Ibid., 251, 252.
importance of chemistry to modern health and to attract students to the study of chemistry to fill the growing pharmaceutical and medicinal industries.\footnote{Kohler, \textit{From Medical Chemistry to Biochemistry}, 273. There was a protectionist and distinctly anti-German ethos to these campaigns, as American pharmaceutical companies sought to prove they were on par if not better than their German rivals, who had up to that point dominated the industry. The Chemical Foundation gained political and economic clout when it was created to hold confiscated German pharmaceutical patents and administer licensing rights.}

Biochemistry grew as a discipline in the 1920s, when it began to attract large numbers of students. Following World War I, the American Chemical Society began a public relations campaign to promote awareness of the growing pharmaceutical and medicinal branches of the chemical industry (spurred by wartime emergency production) and to defend the quality of American pharmaceuticals against high-grade German competitors. The recently formed Chemical Foundation expanded the ACS’s publicity campaign with advertisements emphasizing chemists’ vital importance to protecting national security and improving public health.\footnote{Ibid., 272-273.}

The ACS and the Chemical Foundation performed important lobbying and publicity functions, but they also helped to foment a professional identity for biochemists, forging communities of professional researchers, and consolidating this specialized field of knowledge into a formal discipline. As historians Hugh Davis Graham and Nancy Diamond have argued, these professional sinews helped to generate and sustain professional cultures, while also enhancing “the cohesion of the academic marketplace.”\footnote{Hugh Davis Graham and Nancy Diamond, \textit{The Rise of American Research Universities: Elites and Challengers in the Postwar Era} (Baltimore and London: Johns Hopkins University Press, 1997), 22-23.} While there yet remained a taboo against academic-industrial alliances for commercial profit, the cross-sector professionalization of
biochemistry offered crucial financial support to academic researchers and encouraged them to pursue research in applied sciences.

IV. The Development of Endocrinology in the Early-Twentieth Century

Closely related to the discipline of biochemistry, the field of endocrinology entranced researchers and the public alike in the first half of the twentieth-century. Historian of endocrinology, Victor Medvei has argued that endocrinology is properly described as a field and not a discipline because “it is not unified by common techniques (like biochemistry or genetics) and “has drawn on the labour of researchers from various disciplines and – at varied periods – the field has been dominated by one or more individual disciplines,” which since the mid-twentieth-century have included physiology, biochemistry, immunology and molecular biology.76 As early as 1936, a pioneer in biochemical endocrinological research, Edward Doisy—who in 1924 co-discovered the known first estrus-stimulating hormone, estrin, and who won the Nobel Prize in Physiology or Medicine for his co-discovery of Vitamin K—argued that biochemistry facilitated four basic stages of endocrinological investigation: “1) recognition of the gland or organ as one producing internal secretion, 2) [the development of] methods of detecting internal secretion, 3) preparation of extracts leading to a purified hormone, and 4) isolation of the pure hormone, determination of its structure and synthesis.”77 However, according to a survey of major trends in endocrinological research, from the 1920s to the 1940s a


physiological paradigm of endocrinology prevailed, while from the 1940s to the 1950s biochemical endocrinology was most dominant.\textsuperscript{78} According to a study conducted by Case Western endocrinologist Arthur F. W. Hughes, the annual level of published endocrinological laboratory studies averaged 300 until well into the 1930s, and it was not until after the Second World War that it rose significantly, reaching a peak of 1,800 in 1951.\textsuperscript{79}

Major advancements in endocrinology generated great excitement about its potential benefit to human health. Since the late-1880s, scientists had become increasingly attracted to the study of biochemical regulatory mechanisms of the endocrine system. Following the “Father of Endocrinology,” French neurologist Charles Brown-Sequard’s germinal experiments with adrenal and testicular extractions, and French physiologist Claude Bernard’s investigations on determine the effects of pancreatic secretions on digestion, as well as glycogenesis in the liver. Bernard, the first chair of Physiology at the Sorbonne, revolutionized endocrinological research by promoting standards of investigation through his insistence on the universal use of the scientific method and the importance of blind testing and falsifiable results.\textsuperscript{80} At the same time, Bernard famously challenged Pasteur to admit that environmental influences are more important than germs in the propagation of disease, offering a refreshing counterpoint to orthodoxy of specific etiology and a critical insight that would undergird future stress research. He theorized that the human body was driven to maintain a constant \textit{milieu intérieur}, a stable fluid matrix that regulated essential bodily functions, so that whenever this state was disrupted, by disease,
temperature, shock, and other adverse agents, the body would initiate repair processes to retain
its prime steady state. This concept of biological equilibrium equipped biomedical researchers
with a framework for understanding how organ secretions conveyed chemical messages between
different tissues, organs and glands in order to combat disease and maintain optimum organ
function.

As previously noted, Bernard’s theory of the “internal milieu” intrigued Harvard
physiologist Walter Cannon, leading to his interest in the role of digestive and metabolic
hormones in regulating psychosomatic health, and in maintaining an optimum state of internal
balance, which he called homeostasis. Bernard and Cannon were at the forefront of a
burgeoning field of endocrinological research that gained apace following British scientists
William Bayliss and Ernest Starling’s 1902 discovery of the gastro-peptide secretin, which when
released from the intestines, stimulates the pancreatic secretion of digestive enzymes, the
scientific investigation of “internal secretions” gained cultural prominence as a potential means
of decoding innate biochemistry. 81 The ascendance of an endocrinological paradigm is marked
by Bayliss’s 1904 introduction of the term “hormone” to describe chemical substances that
communicate signals to regulate the functions of organs and tissues.

In the first two decades of the twentieth-century, hormones were detected in the adrenal,
thyroid and pituitary glands, the ovaries and testes, and the pancreas, and were found to regulate
such diverse bodily functions as heart rate; mineral absorption; perspiration; protein, fat and
mineral metabolism, bone and tissue growth; and reproduction. In order to conduct these
investigations, scientists performed vivisection on experimental animals. While experiments had
been performed on animals since the Ancient Greeks and Egyptians, the formal practice of

81 Michael Pettit, “Becoming Glandular: Endocrinology, Mass Culture, and Experimental
vivisection gained scientific credence with Ivan Pavlov’s use of animals to measure conditioned reflexes and Emil von Behring’s animal experiments to test the effectiveness of diphtheria antitoxin in the 1890s. Yet, there was a sizable contingency of the scientific community who questioned the ethical implications and scientific applicability of vivisection. Not only was the practice of experimenting on animals uncivil and uncompassionate, argued the antivivisectionists, there was also insufficient proof that lower-ordered animals shared the same physiological responses as human beings. In the late-19th century, Bernard emerged as an outspoken defender of the usefulness and moral justification of animals in laboratory research. He insisted that animal dissection provided scientific insight into fundamental medical questions that would not otherwise be possible, given the much greater ethical offense of conducting similar experiments on human beings.

Many scientists agreed with Bernard, that vivisection was an invaluable expedient in the advancement of modern science, and in the 1910s, the antivivisection movement provoked the backlash formation of a vivisectionist protection constituency within the academy, spearheaded by the American Physiology Society.82 As President of the American Physiology Society from 1914-1916, Cannon was a persuasive defender of the utility and very necessity of animal experimentation, and proved to be remarkably successful in opposing antivivisectionist legislation. As a physiologist, Cannon’s research depended upon the clinical examination of experimental animals, and through his own research had documented the immense value offered by vivisection.

Cannon innovated the use of x-rays to study glandular secretion by tagging them with radioactive chemicals, which facilitated a number of other breakthroughs in the understanding of

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endocrinological physiology. Much early endocrine research focused on the regulatory actions of digestive enzymes, adrenal hormones and reproductive steroids.\textsuperscript{83} John Abel and Jokichi Takamine’s 1901 discovery that epinephrine produced by the adrenal medulla that affected heart and blood pressure, led to further investigations—most notably, those of Walter Cannon—on the effects of epinephrine in regulating other biological functions, which contributed to a disproportionate interest in the adrenal medulla, rather than its cortex. Cannon’s research on emotional influences on digestion also aroused investigation of endocrine regulation of digestion, which was further catalyzed by Banting, Best, Collip and Macleod’s discovery of insulin in 1921. In 1921, the German pharmacologist Otto Loewi demonstrated that internal secretions regulated the heart rate by electrically stimulating a frog’s heart to beat slower, extracting the fluids that bathed the heart and applying them to another frog’s heart, forcing the second frog’s heart to beat slower, as well. The same year, Frederick Banting and Charles Best demonstrated the role of insulin in diabetes by removing the pancreases of dozens of dogs. In 1921, the Nobel Prize winning discovery by four Canadian researchers—Frederick Banting, Charles Best, John J.R. Macleod, and James Bertram Collip—that blood sugar levels are regulated by the pancreas’ secretion of insulin, revolutionized the treatment of diabetes through pharmaceutical hormone preparations, and generated widespread excitement in the promise of hormonal research.

The therapeutic successes achieved through vivisection attracted more and more proponents for its use. Over the course of the 1920s, the antivivisectionist camp withered as their meager efforts to legislate against vivisection proved futile. By the early-1930s, animal vivisection had become a fundamental method of endocrinological investigation, as endocrinology became an increasingly popular field of biochemical research. Vivisection may

\textsuperscript{83} For a thorough overview of the development of endocrinological science see Medvei, \textit{The History of Clinical Endocrinology}. 
also have gained acceptance as organotherpaies, such as insulin and thyroxin required the harvesting of pulverized glandular tissues from cows, horses and sheep. The mainstream acceptance of organotherpaies, as well as their commercial profitability may have helped to diminish antivivisectionists’ rebuke of the scientific use of live animals.

Epinephrine and insulin proved to be phenomenally commercially successful, demonstrating the lucrative potential of hormonal research to the pharmaceutical industry. A taboo inhibiting academic-industrial collaboration had existed since the mid-nineteenth century, when the American Medical Association (AMA) adopted its 1847 Code of Ethics denouncing medicinal patenting (as a means of distinguishing allopathic medicine from disreputable quack doctors and proprietary medicines of dubious quality. Moreover, the assimilation of the German University research model in late-nineteenth-century American higher education promoted basic research—wissenshacft—for the development of scientific knowledge rather than practical utility. Yet, in the early decades of the twentieth century, as antitrust reform increased competition between pharmaceutical firms and new federal regulations required food and drugs to meet standards for purity, the use of scientific authentication became a means of establishing a competitive edge by improving quality control and standardizing medicinal strength and efficacy. Parke, Davis & Co. became an industry leader after their 1902 creation of an in-house research laboratory for product development and improvement.

World War I was a major catalyst for industrial-academic collaboration, with the newly created National Research Council coordinating scientific research in both sectors for the war effort. The urgency of military mobilization enabled academics to transgress their prioritization for basic research, as well as their ethical proscription of commercial alliances. As historian of

medicine, John P. Swann has argued, following World War I the pharmaceutical industry took several steps that helped to erode the barrier between industry and academia: They began to 1) prioritize research in drug development, 2) hire respected scientists to direct industrial research programs, and 3) create in-house research laboratories and institutes. In the interwar period, the number of industrial research laboratories in the United States more than doubled—increasing from 1,000 labs in 1927 to 2,264 labs in 1940—while the number of research staff more than tripled—increasing from 19,000 to 58,000 employees in the same period. By the end of the 1930s, Abbot, Merck, and Squibb had joined Parke, Davis & Co. in prominence in the pharmaceutical industry thanks to their development of research units.85

As pharmaceutical companies began to embrace scientific research as a means of developing new drugs and endorsing the therapeutic value of their products, academic scientists felt more comfortable transgressing the ethical taboo against collaborating with industry. As the discovery of insulin proved, the commercialization of hormones offered a valuable method of making much needed drugs available to patients. In this context, academic-industrial collaboration could be seen as a noble venture, rather than avaricious and unscrupulous professional conduct. Moreover, by allying with pharmaceutical companies academic scientists were able to transfer the responsibility for developing practical uses for their research, while at the same time gaining financial support that enabled them to pursue basic research.

Gradually, during the interwar period, pharmaceutical companies and academic scientists began to forge alliances that would transform the political economy of biomedical research, and produce new pharmaceutical therapies that would drastically improve the quality of life for North American patients. In 1940, at the annual meeting of the Pharmaceutical Manufacturer’s

85 Swann, Academic Scientists and the Pharmaceutical Industry, 35, 15, 41.
Association, Howard B. Lewis, the Chairman of the University of Michigan’s Department of Biochemistry proclaimed that “the day of the individualist in scientific work is past,” as the complicated nature of modern scientific investigation dictated that “the most notable achievements have been those of groups, the results of teamwork.” Lewis celebrated the collaboration between academic and industrial scientists, noting that the availability of generous grants, fellowships and assistantships offered by the pharmaceutical industry, and the incorporation of academic scientists into new pharmaceutical research programs, created professional opportunities that would not otherwise be available to academic researchers.86

Estrogenic compounds proved to be a particularly lucrative market for pharmaceutical companies. Merck & Co.’s 1890 development of Ovarriin, a compound derived from pulverized cow ovaries and marketed for the treatment of menopausal symptoms, quickly emerged as one of the most popular and profitable pharmaceutical products in North America. After Edward Doisy isolated and purified estrogen in the late 1920s, the development of menopause supplements vastly improved. In the early-1930s, Ayerst, McKenna and Harrison, Ltd. began marketing Collip’s Emmenin, which was derived from the urine of pregnant women and could be taken orally (instead of dissolved in a substrate of oil and injected intravenously). By the end of the 1930s, two new products improved on Emmenin’s basic design. In 1938 A.G. Schering developed Progynon II, and in 1942 Ayerst-Wyeth Laboratories began selling Premarin, both of which were more cheaply produced using urine from pregnant mares instead of human beings.

Estrogen compounds enjoyed great commercial success partially due to gender bias in Progressive and Depression Era medicine which in many ways retained the Victorian penchant

for medicalizing female sexuality. Yet, alongside the popularity of women’s hormonal medications stood a smaller yet still very lucrative market for male reproductive pharmaceuticals. Since Brown-Sequard first injected himself with extracts from pig and dog testes in 1889, researchers had searched for methods of developing testosterone extracts for their purported invigorating properties. In 1935, Coroli David and Ernst Laqueur isolated crystalline testosterone from testicles, and Schering and Ciba began preparing commercial testosterone products, which were marketed for their rejuvenating properties. And in 1939, Butenandt and Leopold Ruzicka shared the Nobel Prize for their independent synthesis of testosterone from cholesterol.

Research on reproductive hormones was not only commercially profitable and professionally esteemed, it was also popularly appealing. Historian Michael Pettit has argued that innovations in hormone therapy (both pharmaceutical and surgical) in the 1910s and 1920s, particularly in the field of hormonal “rejuvenation” aroused a public fascination with “glandular psychology,” which promoted the conception of individuality and health as products of hormonal determinism, exemplified by the gland-based personality typing. “Gland talk” made endocrinology public knowledge and inspired widespread belief in the potential of hormones to cure degenerative diseases and prolong youth.\(^{87}\) Popular interest in hormonal therapies enhanced the marketability of pharmaceutical preparations and increased pharmaceutical funding for endocrinological research. This forged collaborative and financial alliances between researchers in academia and the pharmaceutical industry that slowly began to challenge the stigma against academic scientists participating in the patenting or commercialization of their research.

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\(^{87}\) Pettit, “Becoming Glandular,” 1052-1076.
The professional and economic incentives offered by reproductive endocrinological research profoundly influenced Selye’s early career, guiding him to concentrate on reproductive hormone research, and in doing so, hone skills in endocrinological research methods and acclimate to the culture of competitive pharmaceutical and philanthropic funding. McGill’s Department of Biochemistry received substantial funding from the Banting Memorial Fund, as well as royalties from Collip’s share in the patents on insulin, Emmenin and Premarin. By 1940, Collip’s royalties from Emmenin alone totaled nearly $78,000 (approximately $1.2 million in 2015 Canadian dollars), while the insulin royalties that he shared with Frederick Banting, Charles Best, and the University of Toronto brought in $180,000 annually during the 1930s. These reliable financial resources enabled Collip to undertake ambitious research programs without fear of interruption for lack of funding (however, when his insulin royalties expired in 1940, he became acutely concerned with his impending financial uncertainty, and began courting large philanthropic endowments, such as the grant he sought from the Rockefeller Foundation). This financial security also empowered Collip to pursue basic research that led to his momentous discovery of parathyroid hormone in 1924, and of somatotropic hormone, also known as human growth hormone, in 1933. Collip’s revolutionary discoveries enhanced his own professional reputation and garnered international prestige for Canada’s expanding research of life sciences. It is important to note that though Collip’s reputation derived from discoveries

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88 Li, J.B. Collip and the Development of Medical Research in Canada, 115.


90 Li, J.B. Collip and the Development of Medical Research in Canada, 150.
produced from basic research, it was the extensive therapeutic value of the pharmaceutical drugs he helped to develop that safeguarded his worth as a scientist and national icon.

V. Honing the GAS

Selye left Collip’s Department in 1938 following a dispute over the nature of hormonal resistance. In 1935 Collip was beginning to develop a theory of antihormonal balance based on his observations that hormone therapy increased experimental animals’ resistance to the specific hormone with which they were injected. He deduced that this likely indicated that the repeated injections stimulated the release of an antigen that was naturally present in the blood. While Collip’s theory was later proven wrong (hormone resistance is an immunological reaction in which antibodies in the blood combat the injected hormone), over the next several years he devoted a considerable amount of time to investigating his antihormone theory. By 1936, Selye’s developing theory of the GAS led him to believe that hormonal resistance was a symptom of a larger reaction to the stress caused by the toxicity of the hormone injections. As Collip became increasingly absorbed with antihormonal research, Selye moved to a small laboratory space in the anatomy department where he was able to focus his research on elaborating the GAS. He did, however, continue to perform histological research for Collip even after his departure.91

Despite their different perspectives on hormonal resistance, Selye emulated Collip’s research strategies and business savvy in his own professional conduct. He employed the same reductionist methods of proof by substitution and deficiency, vivisection and bioassay to isolate and assess the actions of various hormones. Selye’s principal method of investigation involved

91 Li, J.B. Collip and the Development of Medical Research in Canada, 104-107.
the histological analysis of animal tissues harvested from vivisection. From 1932 to 1950 he reportedly experimented on over 15,000 rats, in addition to numerous monkeys, rabbits, and guinea pigs. At the same time, he also sought to design his research to attract philanthropic and pharmaceutical funders by emphasizing its applicability and marketability. Perhaps ironically, even as Selye strove to challenge one of the most sacred tenets of biomedical science, he otherwise ascetically conformed to the culture and political economy of biomedical in all other respects.

Selye was sensitive to the professional attacks on the validity of his theory of nonspecificity. He dedicated himself to designing further research in strict accordance with biomedical standards in order to persuasively defend the legitimacy of the GAS. Realizing that one of the greatest flaws of his theory was an imprecise understanding of the mechanisms through which the GAS operated, he was determined to “elucidate the dynamics of the adaptation syndrome,” and to specifically identify the ways in which a damaging agent, “could find its way to the adrenals or the thymus and induce characteristic alarm-reaction changes in them.” Since one of the primary characteristics of the GAS was adrenal enlargement, this second phase of investigation largely focused on identifying the functions of the adrenal gland in the GAS, and specifically emphasized the regulatory actions of adrenal cortical steroids.

Whereas Cannon’s research of adrenaline had unveiled the critical importance of hormones produced by the adrenal medulla, Selye’s work on the GAS was focused on those produced by the adrenal cortex. At the time, many scientists adhered to a “unitarian” theory that


93 Selye, The Story of the Adaptation Syndrome, 51.
the adrenal cortex produced only a single hormone, “cortin.” However, Selye’s research indicated that adrenocortical secretions caused diverse and even contradictory actions, indicating that the cortex in fact produced a number of different hormones. By the mid-1930s, Mayo Clinic endocrinologist Edward Kendall had also produced research indicating that there were several different adrenocortical hormones that performed different actions, and employed a classification system naming the compounds by letter (discussed on p. 90). From 1936 to 1942, Selye identified for the first time many of the hormones produced by the adrenal cortex, including cortisol, aldosterone, lutoids, folliculoids, and testoids, and recognized that certain cortical secretions were found to induce glucose formation, providing energy for an emergency response, while others primarily regulated mineral metabolism—causing salt and water retention, and decreased potassium availability.94 Selye introduced new nomenclature to describe these groups—the glucose-generating hormones he called “gluco-corticoids,” and the mineral-regulating hormones he called “mineralo-corticoids.”95 But perhaps more importantly, Selye realized that these two different classes of corticoids each affected immune response differently: mineralo-corticoids induced inflammation, and gluco-corticoids reduced it. (In the late-1940s, he would realize that these antagonistic actions acted as natural checks on each other—if mineralocorticoids induced an excess of inflammation, the release of glucocorticoids could alleviate it).

By 1937, Selye noted that an excess of either kind of corticoid for an extended time would result in physiological damage. This recognition of the adrenal cortex’s mediation of


95 Selye, The Story of the Adaptation Syndrome, 58.
immunity offered finer insight into the ways in which the GAS could actually cause physical damage. In March of 1937 Selye published an article in *Science* reporting the results of a study in which he exposed normal and adrenalectomized rats to excessive exercise, cold, and sub-lethal dosages of drugs. He found that when the animals were sensitized to these stressors by the removal of the adrenal glands, their symptoms of adrenal deficiency—decreased blood pressure, water retention, decreased blood sugar, decreased body temperature, muscular weakness, gastric and intestinal ulcers—were “almost identical with those observed in non-adrenalectomized animals after exposure to serious damage.” However, exposure to alarming stimuli caused “much more pronounced changes in adrenalectomized animals than these same stimuli would be able to produce in the normal.” The variable group was better able to withstand exposure to the harmful stimuli, while the control group lacked the same resilience because they had neither the benefit of previous adaptation, nor the capacity to mount a new adrenal defense. Selye deduced that “the most important function of the adrenals is to increase resistance to alarming stimuli.”

Selye’s work on the mechanisms of the GAS led him to realize that over time animals exposed to a specific stimulus also developed a heightened resistance to all other noxious stimuli. For example, a rat that was forced to endure freezing temperatures would also become resistant to toxic chemicals, extreme exercise or starvation. Selye, deduced that this phenomenon, which he called “crossed-resistance,” indicated a heightened capacity for self-defense that enabled the body to protect itself against multiple antagonists at once. However, he soon realized that this crossed-resistance was unique to the Alarm Reaction, and would diminish with the onset of the Stage of Resistance. As the animal became inured to a particular stimulus, it would begin to exhibit increased sensitivity to other stimuli. Thus, a rat that adjusted to tolerate extreme cold

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might become more susceptible to damage caused by intoxication or muscular distress. Selye called this differentiation in susceptibility “crossed sensitization.”

At the core of the concepts of “crossed-resistance” and “crossed sensitization” is a realization that an animal’s capacity for adaptation is progressively attenuated. Not only does the response to antagonistic stimuli occur in a three-stage pattern, but overtime they lose their capacity to resist the damaging agents—first losing their universal “crossed-resistance,” and eventually succumbing to the fatigue of constant resistance in the final stage of the GAS, the Stage of Exhaustion. This gradual deterioration of an animal’s capacity to resist damage led Selye to develop the concept of “adaptation energy.” He theorized that all animals have a finite amount of energy that enables them to endure and adapt to harmful stimuli. However, overtime, as these stores of adaptation energy are depleted, an animal loses its capacity for adaptation and more easily succumbs to damage. Thus, over the course of one’s lifetime, as their adaptation energy is gradually lost, they lose their youthful capacity to resist harmful agents, and are more susceptible to a breadth of injuries.

Selye was beginning to explain how although the primary purpose of the GAS was to protect against potentially harmful agents, when prolonged, excess levels of adrenocorticoids could induce damage overtime. He likened this phenomenon to that of an allergic, inflammatory or shock response, all of which were meant to protect against further bodily damage by inhibiting certain normal biological processes. Selye later reflected that, “by the end of 1937, it had

98 Selye proposed the theory that the symptoms of the Alarm Reaction may likely be directly caused by “the liberation from the tissues of some toxic metabolite,” similar to a histamine released in response to an allergen, and that the activation of adrenal secretion served to detoxify this substance. He noted that the Alarm Reaction exhibits many symptoms also characteristic of histamine toxicosis or anaphylactic shock, and that therefore perhaps adrenal stimulation signals the liberation of a histamine-like substance (“H-substance”), which he
become evident that the stress-response consists of two parts: damage and defense,” which led to his recognition that adrenocorticoid secretions “can be the cause of naturally occurring pathologic organ changes.” Though he had yet to uncover the specific mechanisms through which local tissue damage produced systemic damage and disease, he was beginning to identify yet-undiscovered adrenocortical hormonal secretions that played a vital role in this process.99

The Development of Synthetic Adrenocorticoids

Selye was initially quite surprised to realize that the adrenal cortex played such a large role in the GAS. The theory that the adrenal glands were instrumental in initiating an emergency physiological response was not new to medical science. Selye extended Cannon’s research on the adrenal regulation of adaptive responses by documenting the vital role of hormones released from the adrenal cortex, in addition to those of the adrenal medulla. Selye was drawn to focus on the adrenal cortex by the simple observation of its consistent enlargement during the Alarm Reaction. However, in order to convincingly demonstrate the primary role of the adrenal cortex in accordance with Koch’s Postulates, he had to prove that adrenal cortical enlargement would be present in every case, and that the Alarm Reaction would never occur without it. While Selye’s experiments to test the extent of the nonspecific nature of the GAS had satisfied the first standard (to prove that the germ was present only in diseased and not in healthy organisms), in order to meet the second standard (to isolate the germ in pure culture) Selye had to remove the target glands and document the effects of stimulating agents.

In the mid-1930s, the two primary endocrinological methods of evaluating mechanisms governing glandular secretion were “proof by deficiency” and “proof by hormone substitution or overdosage.”100 Proof by deficiency involved removing a gland to evaluate how its absence altered a known bodily process. This invariably required surgical removal of the gland. Proof by substitution was more difficult as it required the removal of the gland that was thought to govern a reaction, and the administration of extracts of the gland to the experimental animal. This enabled the controlled observation of the actions of a glandular secretion. In the late-1930s, pure adrenocortical hormones had not yet been isolated for reproduction. Therefore, his efforts to establish the actions of adrenocorticoids using proof by substitution were necessarily limited to the use of synthetic corticoids, which exposed him to the criticism that he could not obtain proof that the adrenal cortex naturally produced the same results that he found in his experiments.

Selye was fortunate to work under a pioneer of proof by substitution. In the early 1920s, Collip contributed to Banting and Best’s insulin research by preparing pancreatic extracts to be administered to pancreatectomized dogs. At the time, this was a revolutionary technique that provided indisputable evidence that insulin, secreted from the pancreas, was principally involved in the regulation of blood sugar levels, and therefore deficient production of insulin induced diabetes. This medical revelation led to the widespread practice of the proof by substitution technique when possible. Yet, such experiments required the administration of glandular extracts, and while it was possible to create a crude extract using the techniques with which Selye prepared the contaminated ovarian preparations, the precise content of such extracts was difficult to determine.

100 Selye, The Story of the Adaptation Syndrome, 55.
By the late-1930s, several researchers, including Wilbur W. Swingle and J.J. Pfiffner at Princeton and Frank Harman at the University of Buffalo, had successfully developed methods for producing a crude cortical extract. Despite mounting evidence to the contrary, many scientists still subscribed to a “unitarian theory” that the adrenal cortex only produced a single hormone, or “cortical principle,” which had yet to be isolated and synthesized. However, the preparation of “cortin,” which contained this unknown hormone, was sufficient to measure the effects of hormone substitution on adrenalectomized experimental animals. Selye’s research on the actions of cortical hormones was made possible by a transcontinental competition to isolate the mysterious cortical principle in cortin. In North America, the primary actor in this drama was Mayo Clinic endocrinologist, Edward C. Kendall, who first gained scientific notoriety in 1914 for his isolation of the thyroid hormone thyroxine.

By 1934, with the help of a new method of assay innovated by his lab assistant Dwight Ingle, Kendall had isolated a total of five different hormones secreted from the adrenal cortex, which he identified as compounds A-E (he would discover a sixth compound F within the next two years), of which compound E was determined to be the most similar to cortin in physiological behavior. In spite of the seemingly clear evidence that the adrenal cortex produced a number of hormonal compounds, many scientists, Kendall included, held fast to the search for the single hormone, cortin. As Kendall later observed,

There were two reasons why belief in the unitary nature of cortin was so widespread and so firmly fixed. The first was the result of the original concept that ‘the hormone’ of an endocrine gland must possess the physiologic properties of an extract of that gland. After that idea had been fixed

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in the minds of biologists, physiologists, biochemists, and clinicians, it became deep-rooted and immovable. The second reason was that the only method of assay for the active crystalline compounds separated from the adrenal cortex was the one devised by Dwight Ingle and used in our laboratory. No other laboratory had adopted the method, and perhaps it was just as well. Within a short period Dwight had determined the relative activity of all crystalline compounds that were available. What was then needed was an independent criterion that could be used to prove or disprove these results.103

In 1934, Kendall contracted with Parke Davis & Company of Detroit and Wilson Laboratories of Chicago to supply his lab with bovine adrenal glands. In exchange, Kendall extracted epinephrine for Parke Davis’s commercial production,104 and supply Wilson Labs with a standardized cortical extract. To meet the production demand, Kendall created a veritable gland factory, hiring three times as many assistants in order to run the process in 8-hr shifts for 24 hours per day.105 Despite their manufacturing and financing prowess, the Mayo group failed in their quest to become the first to isolate and replicate cortin.

In 1937, Kendall’s foremost rival in the quest to isolate cortin, Swiss scientist Tadeus Reichstein published a paper describing his isolation of the adrenocortical hormone, substance H, which he gave the formal name of “desoxycorticosterone” (often shortened to “corticosterone” or “DOC”).106 At the time, it was widely believed that Reichstein had discovered cortin, when in fact he had only discovered one of many adreno-cortical steroids. Despite the revolutionary nature of his discovery, the method that Reichstein used to prepare corticosterone was woefully inefficient. It required approximately 1,000 kilograms of bovine adrenal glands taken from

103 Kendall, *Cortisone*, 74-75.

104 Kendall, *Cortisone*, 59.

105 Kendall, *Cortisone*, 62.

about 20,000 cattle to produce only a few grams of the steroid.\textsuperscript{107} Furthermore, because Reichstein contracted out the preparation of corticosterone to the Dutch pharmaceutical company Organon, there was an extremely limited supply, and in many ways contingent upon whether Organon continued to find corticosterone preparation profitable.\textsuperscript{108} In fact, by the end of the year, Reichstein wrote to Kendall that he would have to suspend research on the adrenal cortex for several months, leaving the Mayo group to be the only lab continuing research on cortin.\textsuperscript{109} The same year, two members of Kendall’s lab, Harold Mason and William Hoehn began an investigation of the structure of compounds A and B, using a process that degraded a bile acid. While they initially anticipated that the project would be easily accomplished, it ultimately took a year to complete, but bore exciting results, and proved the bile acid preparation to be an extremely effective method of synthesizing cortical compounds.\textsuperscript{110}

Though it failed to prove the existence of a single cortical hormone, the discovery of DOC was a watershed moment in the history of adrenocortical research as it enabled more precise measurement of the effects of cortical hormones in the body. For Selye, it was absolutely essential to establishing a sound scientific basis for his theory that the adrenal cortex was fundamentally responsible for regulating all adaptive responses. Selye obtained DOC acetate (DOCA) extracts from both Kendall and Reichstein, which he administered to his experimental animals before exposing them to various antagonistic stimuli. He found that DOCA extracts, in contrast to adrenaline extracts, produced the same thymic and lymphatic shrinkage that surgical

\textsuperscript{107} Thom Rooke, \textit{The Quest for Cortisone} (East Lansing, M.I.: Michigan State University Press, 2012), 78.

\textsuperscript{108} Kendall, \textit{Cortisone}, 69, 70.

\textsuperscript{109} Ibid., 79.

\textsuperscript{110} Ibid., 76.
shock, spinal shock, extreme cold, and excessive muscular exercise induced in normal animals, but not in adrenalectomized animals. However, he also found that adrenalectomized rats treated with DOCA produced even more pronounced ulcers and decreased body temperature and blood pressure, suggesting that DOCA might exacerbate tissue damage caused by noxious stimuli.  

DOCA proved to be indispensable to Selye’s adrenocorticoid research over the next decade. In order to evaluate the conditions under which adrenocortical secretion could become harmful, Selye needed to administer cortical extracts to adrenalectomized animals and measure their responses. By 1941, DOCA was commercially produced by several pharmaceutical companies in the United States and Canada, and Selye was able to acquire ample amounts of DOCA from the Schering Corporation of Bloomfield, New Jersey, the American subsidiary of the German pharmaceutical conglomerate, A.G. Schering (whose American assets had recently been seized by the US Department of State). In the late-1930s, Selye developed a relationship with two chemists at Schering Corp., Erwin Schwenk and Gregory Stragnell after having aided J.B. Collip on experiments using estrogen extracts prepared by Schering. Through Schwenk and Stragnell, Selye was able to secure several grants from Schering for DOCA-related research. Yet, even as DOCA became increasingly prevalent in endocrinological research, Selye remained vulnerable to the criticism that he used a synthetic drug in his research (and may have administered a toxically-high dosage) and therefore could not conclusively prove that the adrenal cortex would naturally produce this hormone, or even if it did, could produce it in the same abundance that Selye used to produce lesions in his experimental animals.  


The First Mediator

In addition to the allegations that he failed to use a pure cortical substance, Selye was criticized for failing to explain what initiated the adrenocortical activity in the GAS. Despite the fundamental significance of adrenocorticoids, Selye also recognized that adrenal stimulation must be initiated by hormones produced by another gland, for when he removed the adrenal cortexes from his rats, he found that the animals failed to initiate many of the characteristic symptoms of the GAS, including thymico-lymphatic atrophy. However, he noted that in many cases they still exhibited gastrointestinal ulceration, decreased body temperature, lowered blood pressure and reduced blood chloride content. Evidently some aspects of the animals’ responses were controlled by the adrenal cortex, yet other aspects were not. The question was, if the adrenal cortex did not induce these other symptoms, what other gland, and what other hormones stimulated their presentation?

By early-1937, Selye began to look for the “first mediator” that triggered hormones to be released from the adrenal cortex. He would later admit that at first, his experiments were “strongly influenced by the investigations of Cannon who had found that, during emergencies, the secretion of the adrenal medulla is regulated by its secretory nerves,” leading Selye to believe that when exposed to an adverse stimulus, corticoid secretion was initiated by nervous impulses. However, he was disappointed to find that all his attempts of nervous enervation—including, severance of the nervous connections to the adrenal cortex and to the site of injury, as well as nervous inhibition of vegetative regions of the brain—failed to halt the GAS. Then he

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113 Selye, “Thymus and Adrenals in the Response of the Organism to Injuries and Intoxications.”


115 Selye, The Story of the Adaptation Syndrome, 64.
theorized that another endocrine gland might secrete hormones that signaled cortical stimulation. He experimented with removing both the thymus and the liver, but found that removal of neither of these organs inhibited the hormonal secretion from the adrenal cortex.

It was not until the spring of 1937 that it occurred to Selye that the pituitary gland might be involved. He suddenly remembered his experiments with the ovarian and placental extracts in 1935 that had failed to initiate adrenal stimulation in hypophysectomized rats. Other scientists—most notably, Herbert McLean Evans, Collip’s professional rival at the University of California, Berkeley—had also recently found that removal of the pituitary reduced the size and functional capacity of the adrenal cortex, which could then be regenerated with extractions from the pituitary. In fact, that same year Selye had contributed to experiments performed by Collip and Evelyn Anderson which ultimately produced a crude form of the pituitary hormone ACTH (adrenocortiotropic hormone), which stimulated the release of adrenocorticoïds.

Turning his focus to the possible role of the pituitary, Selye’s earlier practice with hypophysectomizing rats proved to be an asset. The method for hypophysectomy that he had developed in 1932-33, “necessitated a minimum amount of trauma and made it possible to remove the pituitary rapidly, without much damage,” enabling hypophysectomized rats to withstand exposure to damaging agents. Immediately, this line of experimentation bore encouraging results. He subjected the hypophysectomized rats to extreme cold, physical trauma, physical trauma,


and sub-lethal intoxicification, and found that they showed absolutely no stimulation of adrenocortical production. This led Selye to conclude that removal of the pituitary blocks the pathway of adrenal cortical response during the GAS.\(^{119}\) In the late-1940s, subsequent experiments would demonstrate that when the animals were exposed to stimulating agents, the anterior lobe of the pituitary gland secretes the adrenocorticotropic hormone, ACTH.

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Selye had discovered that the pituitary-adrenal-axis governs the stress response, but he had not yet identified the “first mediator” of the GAS. He knew that there must be a mechanism that mediates the pituitary’s response to a stimulating agent that signals it to release ACTH.

\(^{119}\) Selye, \textit{The Story of the Adaptation Syndrome}, 66.
However, Selye remained stubbornly fixated on the endocrine system as the primary regulator of the GAS, so he never seriously explored the extent to which the brain controlled the pituitary. Four decades after Selye’s initial discovery of the GAS, one of his own students, Roger Guillemin, would participate in the momentous discovery of neurohormones—peptides produced in the brain that stimulate activity in endocrine glands. For this discovery, Guillemin and his rival co-discoverers, Andrew Schally and Rosalyn Yalow would be awarded the 1977 Nobel Prize in Physiology, an honor for which Selye was repeatedly nominated, but never achieved, partially because he mistakenly dismissed the possibility that the brain may be the originator of the elusive “first mediator.”

Conclusion

Selye embraced the reductionist methods of laboratory investigation and remained fervently committed to the biomedical principles of empiricism and induction. By retaining these attributes of biomedical orthodoxy as he documented the biochemical mechanisms of the GAS, he was able to eventually mount a successful challenge to the limitations of exclusive specificity. In doing so, he ushered in a new framework of medical inquiry perfectly suited to the epidemiological challenges of the mid-twentieth century. By helping to legitimate the concepts of multicausation and risk, he empowered researchers to more comprehensively examine the causes of chronic, degenerative diseases—such as cancer, chronic heart disease, hypertension,

\[120\] John W. Mason has argued that Selye’s obsession with the search for the first-mediator of the stress response indicated that even in his awareness of multicausation, he retained a mind-set predisposed to searching for singular causes. Current endocrinological theory accepts that many hormones respond to multiple forms of neuro-endocrine messages. See Mason, “A Historical View of the Stress Field, Part II,” *Journal of Human Stress* 1, no. 12 (June 1975): 25-26.
and arthritis—that had become increasingly prevalent as bacteriological interventions extended life expectancy (discussed in Chapter Three).

Selye’s research did not win validation simply based on his perseverance in the laboratory. Rather, his ability to prove its relevance to emerging public health concerns won him crucial funding from state and corporate funders that became available during the Second World War. Selye did not only benefit directly from state funding for military research, but also from collateral neuropsychiatric research on combat stress. While Selye’s research failed to evaluate the relationship between the mind and the body, a growing field of psychosomatic and psychoanalytic researchers undergirded the US Army’s efforts to improve neuropsychiatric casualty rates. Following the medical recognition of combat stress during the war, Selye was able to appropriate the medical valence of the term stress to win acceptance for his theory of the GAS.
Chapter 2: World War II and the Transformation of Stress Research

Introduction

The radical transformation of the political economy of medical research during World War II had a profound effect on Selye’s conceptualization of stress. The US and Canadian Armed Forces and National Research Councils dedicated vast financial and administrative resources for medical research to support the war effort, enlisting the support of academic scientists and private business to develop new drugs, like penicillin and sodium pentathol to treat wounded soldiers, and adrenocortical steroids to alleviate shock and fatigue. Selye participated in the war’s research initiative to develop adrenocortical extracts in the hope that they would support soldiers’ endurance under the strain of combat. In the course of these studies, he refined his theory that despite their initial protective function, over time an imbalance of adrenocorticoids could induce degenerative “diseases of adaptation,” such as hypertension and arthritis. He further noted that certain “conditioning factors” could exacerbate the effects of adrenocorticoid overdosage, indicating that these increasingly prevalent diseases developed from multiple and dynamic causes. With these dual concepts of attributable risk and cumulative damage, Selye offered a unified etiological model of disease centered around adaptive endocrine function.

Despite the seemingly holistic nature of the GAS, Selye’s theory remained rooted in somatic physiology. Yet, at the same time that he was using funding from US and Canadian NRC grants to refine his theory, the war was also stimulating research on the neuropsychiatric disease model of stress. Even as Selye began using the term “stress” to describe the biological phenomenon of disease caused by wear and tear, he did so without acknowledging that he was appropriating a word that was popularized and legitimated by military psychological research on “combat stress.” However, the medical validation of Selye’s theory of biological stress very
much depended upon the parallel development of a medical theory of psychological stress, advanced by an increasingly organized field of psychosomatic medicine, and the growing influence of psychoanalysts within psychiatry. Indeed, the medicalization of stress was catalyzed by concurrent but independent research on shock and anxiety that was funded by the US and Canadian governments during the Second World War. Together, the biological and psychological pathologization of stress, which accepted that “everyman had his breaking point,” and held that certain lifestyle risk factors could exacerbate disease, coalesced to promote a popular perception of stress as a psychosomatic condition that affected every person to some degree.

### I. World War II Mobilizes Scientific Research

World War II transformed the political economy of medical research by introducing new state and corporate funding sources to augment the traditional reliance on philanthropic aid. The ethos of corporate liberalism that undergirded war mobilization efforts enlisted the financial support of government agencies and private enterprise, with pharmaceutical companies and governmental agencies emerging as major underwriters of academic scientific research. Prodigious sums of federal aid suddenly became available for war-related research projects, both in academia and the private sector. During the war, federal investment in research and development skyrocketed from $74.1 million in 1940 (approximately $1.26 billion in 2015 dollars) to $1,590.7 million in 1945 (approximately $21.02 billion in 2015 dollars).1 The United States and Canadian National

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Research Councils (USNRC and CNRC, respectively) enlisted university-based scientists as well as private industry to assist in wartime research projects through an extensive program of grants issued to individual researchers. The USNRC proved to be a much more powerful funder than the CNRC, with its Committee for Medical Research (CMR), organized under the Office for Scientific Research and Development (OSRD), alone contracting more than $24 million dollars for 593 research grants over the course of the war. The CNRC, in contrast, issued less than $100,000 in grants per year from 1940 to 1944, and just slightly more than $100,000 from 1944 to 1945 (an average of approximately $1.43 million in 2015 Canadian dollars). Yet, compared to its prewar activity, the CNRC grew substantially during the war, with its annual budget increasing to five times its prewar level by 1943. The CNRC also offered funding through the War Technical and Scientific Development Committee’s independent “Santa Clause Fund,” originally created with royalties from insulin production for which it was later renamed the Banting Fund, but by 1940 largely consisted of donations from corporations totaling over $1.3 million dollars (approximately $20.2 million in 2015 Canadian dollars).

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4 Li, *J.B. Collip and the Evolution of Medical Research in Canada*, 155.

J.B. Collip, head of the McGill Biochemistry Department, began working for the CNRC’s Associate Committee on Medical Research (ACMR) in 1938, and became its Chairman in 1941 after his predecessor, Frederick Banting’s unexpected death. The CNRC worked in close collaboration with the USNRC through the course of World War II to coordinate research to support war mobilization. While previous wars also saw increased support for medical and technological research—both NRCs were originally created for such purposes during World War I—World War II escalated the scale and expanded the breadth of research programs. The USNRC’s war research programs represented nothing less than a mass mobilization of North American civilian scientific resources, recruiting academic institutions and private industry for research, production and advisement in science policy for the war effort. Their joint efforts included research on radar, atomic weaponry, biochemical warfare and the physiological response to trauma, as well as psychological screening and treatment of servicemen. These research projects advanced medicine, science and technology, generating discoveries and strengthening institutions that would transform research in the postwar period. In Canada, the CNRC’s wartime research was transformative not only in the results it produced, but in the organizational empowerment of dominion agencies and the national pride derived from demonstrating the prowess of Canadian science.

With Hitler’s invasion of Poland on September 1, 1939, Frederick Banting began advocating for centralized mobilization of medical research to support the war effort. The very next day, Banting circulated a memorandum outlining the need to organize ACMR to develop resources for chemical warfare, bacteriological warfare, neurophysiological research and chemotherapy. Banting’s memo emphasized the superiority of German armaments and medical resources, and argued that in order to fairly compete against the Nazis, and even maintain
national autonomy, it was absolutely essential that Canada commit itself to the development of its own scientific resources. As Historian Terrie Romano has argued, the CNRC’s “role was to proselytize about research, not merely fund it.” The Associate Committee organized a number of subcommittees, including the Army Medical Research Committee headed by Deputy Director General, Brigadier Jonathan Campbell Meakins, the Dean of McGill’s Faculty of Medicine and Director of the Medical Clinic. The Research and Development branch of the Army Medical Research Committee was chaired by J.B. Collip. Collip was joined by Lieutenant Commander Charles H. Best, J.C. Meakins and J.S.L. Browne, among others.

At this point, many endocrinologists hoped that hormones from the adrenal cortex might be useful in treating traumatic and surgical shock, relieving or preventing fatigue, and discouraging altitude sickness resulting from hypoxia (the severe deprivation of oxygen). As American endocrinologist Dwight Ingle would later recall, by the beginning of the war “it was well established that adrenal insufficient animals and patients are abnormally sensitive to all forms of stress,” and therefore, “it seemed reasonable to expect that the cortical steroids would raise the resistance of combatants to the kinds of stressors encountered in war.” In correspondence with Walter Cannon regarding proposed USNRC research, Edwin Astwood of Johns Hopkins University proclaimed “the well known response of the adrenal cortex to conditions of stress, trauma, toxins, etc.,” indicating the extent to which the mainstream scientific community implicitly accepted that adrenocorticoids played a prominent role in regulating the


physiological response to acute exposure to harmful agents. Clearly, even before the war began, the term “stress” was casually invoked by medical researchers to describe an adverse stimulus, and the role of the adrenal cortex in regulating responses to stress was commonly recognized. However, “stress” was not yet understood to be a specific syndrome, as Selye would claim by the war’s end. Historian of medicine Elizabeth Siegel Watkins has shown that Index Medicus did not list the term “stress” as a subject heading until 1950, and the Reader’s Guide to Periodical Literature did not list “stress” until 1951—indicating that stress did not achieve medical legitimacy or popular acceptance until the postwar period.9

II. The Cortin Committee

Selye was only tangentially involved in military stress research during World War II, while several of his colleagues at McGill served in leadership roles in the bi-national effort to develop adrenocortical steroids. In October 1939, Meakins appealed to the ACMR to develop a research program exploring the synthesis of DOC believing that it might be useful in treating shock.10 In response, the ACMR formed the Subcommittee on Shock and Blood Substitutes (SSBS),11 comprised by Sir Frederick Banting, C.H. Best, J.S.L. Browne, and Meakins, among several

8 Edwin B. Astwood to Walter B. Cannon, February 21, 1940, Box 80, folder 1088, WBC.
10 G.H. Ettinger, "Medical Research in Canada During the War” manuscript, December 18, 1943, p. 22, Box 9, RG 128, Records of the Canadian National Research Council, Associate Committee on Medical Research, Library and Archives of Canada, Ottawa, Ontario (hereafter ACMR).
11 The SSBS was one of three main subcommittees of the ACMR. The other two oversaw research on infections and surgery, respectively. See Li, J.B. Collip and the Evolution of Medical Research in Canada, 156-57.
others, and instructed it to investigate the methods to mitigate the compounded harm caused by acute chemical and neurological reactions to physical injury. At the recommendation of Sir Frederick Banting and J.B. Collip, the project was divided into three branches with Meakins in charge of the investigation of surgical shock, Dr. R.A. Cleghorn in charge of research on electrolyte distribution and the role of the adrenal cortex in shock, and Dr. G.H.W. Lucas investigating the effect of anaesthetics on shock. Ultimately, by 1943 these investigations showed that adrenocortical steroids were ineffective in the treatment or prevention of shock. However, military interest in adrenocorticoid research continued in the hopes of developing a means of treating or preventing not shock, but fatigue. This was accomplished by a bi-national program to develop the mysterious adrenal hormone, cortin.

Even before the United States entered the war in December 1941, it began preparations for war mobilization that included the organization of a diverse array of scientific research campaigns. At a conference on the adrenal cortex sponsored by the Josiah Macy Jr., Foundation and held at Yale University in May 1941, it was reported that German scientists had developed an extract that counteracted hypoxemia (deficient arterial oxygen tension), enabling Luftwaffe pilots to fly at 40,000 feet. The devastation that the Luftwaffe’s aerial assaults had caused in England and France proved the very real threat of a Nazi monopoly on such information, however the allegation that German U-boats were at that moment en route to Argentina to obtain bovine adrenal glands to prepare the extract added a heightened sense of urgency to Allied corticoid research. While the rumor ultimately proved to be false, it was a catalyst for a major

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12 Ettinger, "Medical Research in Canada During the War,” 19-20.


14 Kendall, Cortisone, 99.
research initiative to subsidize the development of adrenocorticoid production in university and private laboratories.\textsuperscript{15}

In the summer of 1941, the National Academy of Sciences instructed the USNRC to organize committees to coordinate medical and technological research, recruiting academic and commercial scientists to support the war effort. Alfred Newton Richards of the University of Pennsylvania was appointed chairman of the committee in charge of medical research, Vannevar Bush of the Carnegie Institution for Science was appointed head of the committee of physics (and the head of the OSRD), and William Mansfield Clark of Johns Hopkins University was appointed head of the division of chemistry and chemical technology. Together, the committee chairs determined three top priorities for medical research: first, the development of cortin extracts; second, the mass-production of penicillin; third, improved anti-malarial drugs.\textsuperscript{16}

On October 7, 1941 in Washington, D.C., Dr. Clark chaired a meeting of approximately fifteen chemists prominently involved in adrenocortical research, with the intention of organizing a standing committee to coordinate the development of cortin between laboratories of different universities and pharmaceutical companies. After attending a semi-annual meeting of the ACMR in Ottawa on October 23, 1941, O.H. Perry Pepper, Chairman of the CMR, reported to Lewis H. Weed, Chairman of the USNRC that amongst the Canadians, “there was a constant expression of desire for closer exchange of information. For instance, Dr. H. Selye, Medical Building, McGill University, is working on cortin in shock and knows nothing of the Yale Conference or our


\textsuperscript{16} Kendall, \textit{Cortisone}, 100.
research plans.”17 In November 1941 J.B. Collip was appointed as the Medical Liaison to Washington and promoted to rank of Lieutenant Colonel. The Canadian-US alliance encompassed a broad range of medical research, including the development of synthetic corticosteroids. In 1942, R.D.H. Heard of the University of Toronto was assigned to represent the ACMR at meetings of steroid chemists in the United States and to act as a communiqué between the CMR and ACMR.18

Drawing on distinguished endocrinological experts in the academic and industrial sectors, the final committee consisted of the following members: Hans T. Clarke of Columbia University; Everett Wallis of Princeton University; Caesar Schola of Ciba, Inc.; Louis Fieser of Harvard University; Karl Folkers and Randolph T. Major of Merck & Co.; Edwin Schwenck of the Schering Corporation; R.D.H. Heard of McGill University; James B. Collip of McGill University and the Canadian NRC; Oskar Wintersteiner of E.R. Squibb & Co.; Thomas F. Gallagher of the University of Chicago; Werner Bergmann of Yale University and Edward C. Kendall of the Mayo Clinic. The Research Corporation of New York City secured a patent to cover any work produced by the committee.19 The Mayo Clinic took a leadership role in the committee’s efforts. Kendall served as a central node of communication between different committee members and was largely responsible for the committee’s adoption of his own system of nomenclature for compounds A-F. Though Kendall’s compound E was thought to be the most effective substance,


18 G.H. Ettinger, "A History of the Associate Committee on Medical Research," p. 39, Box 9, ACMR.

19 Kendall, Cortisone, 100-101.
it was feared that it would be too complicated, costly and time-consuming to develop. While compound A, was only slightly less complicated in structure, “compound E was regarded as a big brother of compound A,” therefore it was decided that for expediency’s sake, initial research efforts would focus on the development of the little brother with the hope that once that line of research was successful, it would segue into work on the more complicated sibling.20

Through his work on the Cortin Committee, Kendall developed a close professional relationship with Merck & Co. Within the first month of the committee’s existence (by November 1, 1941), Merck chemist Dr. Jacob van de Kamp joined Kendall’s lab to learn how to prepare an intermediate compound made from desoxycholic acid, which was used to make compound A. Van de Kamp transmitted this information to Merck, which took over production of this intermediate compound, freeing Mayo Clinic researchers to attend to more complicated aspects of Compound A production.21

Despite the Mayo Clinic’s dedication and seemingly tireless devotion to the cortin project, Kendall complained that their efforts were frustrated by decreased efficiency due to a loss of manpower as laboratory staff were drafted into military service. Perhaps as a consequence, though cortin was given top priority by the USNRC, both penicillin and the new antimalarial drug atabrine became widely available before any significant progress had been made on the development of cortin. Furthermore, by 1943 research into the usefulness of adrenocortical steroids in treating hypoxia, surgical and traumatic shock had failed to produce positive results.22

To make matters worse, in the fall of 1943, Caesar Schola, the committee member from Ciba

20 Kendall, *Cortisone*, 114.

21 Ibid., 102.

Pharmaceuticals, reported that Swiss chemist Tadeus Reichstein who had previously beaten Kendall to first synthesizing DOC, had now successfully synthesized compound A. Yet, while Reichstein’s discovery discouraged the committee members who had put so much time and energy into developing compound A, at the same time it also offered reassurance that the Cortin Committee was not wasting its time on compound E, as it confirmed that their hypothesized structure of compound A was indeed correct. However, the prospect of developing sufficient quantities of compound E in a timely manner was formidable. As a consequence, by June of 1944, every member of the Cortin Committee except for those at the Mayo Clinic and Merck had ceased work on compound A.  

**III. Military Support for Selye’s Stress Research**

In addition to the USNRC and NRC’s efforts to develop adrenocorticoids to treat hypoxia and fatigue, they were also interested in their potential use to treat shock. Traumatic shock (not emotional shock, or what is now known as Acute Stress Response) was a significant problem for the medical corps because it severely inhibited the process of rehabilitation for soldiers suffering from combat induced injury and surgical trauma. When a patient went into shock, the natural process of healing would halt and jeopardize their potential for recovery. The possibility that hormones might abate the onset of shock foretold a revolution in combat medicine and significant reduction in military casualties.

Collip’s staff in the McGill Biochemistry Department contributed immensely to the SSBS’s investigation of the role of the adrenal cortex in traumatic shock, developing a standard method of producing shock by revolving rats in a drum, that was widely adopted by other

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23 Kendall, *Cortisone*, 102, 105.
laboratories in the United States, and documenting some rats’ capacity to develop resistance to this form of shock by repeated exposure to mild trauma or by increased intake of dietary protein. Within Collip’s lab, J.S.L. Browne also directed research on the identification of cortin-like substances in urine after shock or damage and was primarily conducted at McGill and the Royal Victoria Hospital, drawing heavily on the assistance of Eleanor Venning.\textsuperscript{24} By the end of the war, Venning would demonstrate an increase in adrenocortical activity during fasting, trauma and disease, documenting an increase in the concentration of corticosteroids in the urine of adult men and women within 24 hours of fasting, and five to ten times great concentrations in the urine of patients suffering from burns, infections, Cushing’s syndrome or who were recovering from surgery.\textsuperscript{25}

Prior to the initiation of the SSBS’s shock research, Selye had become interested in shock physiology as it relates to the Alarm Reaction. In a chapter he contributed to the \textit{Cyclopedia of Medicine, Surgery and Specialties} in 1940, he explained that the Alarm Reaction consisted of two phases: an initial, acute phase of shock brought on by exposure to an “alarming stimulus,” and a subsequent phase of counter-shock that began within 24 hours following the onset of the shock phase. While the shock phase was characterized by general adrenal insufficiency and impaired immunological function (sometimes signified by the formation of ulcers, edema, loss of blood sugars and chlorides, decreased temperature or muscular tone), the counter-shock phase showed an increase in adrenocortical secretions, blood volume, blood sugar and chlorides, and body temperature, as well as decreased size and activity of the thymus and other lymphatic

\begin{footnotesize}
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\item \textsuperscript{24} “Proceedings of the First Meeting of the Subcommittee on Shock and Blood Substitutes of the Associate Committee on Medical Research,” January, 4, 1941, Section 5, “Reports on Shock,” Box 8, ACMR.
\item \textsuperscript{25} “Proceedings of the Ninth Meeting of the Subcommittee on Shock and Blood Substitutes,” October, 29, 1945, Box 8, ACMR.
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organs, and by a general “reversal of most of the characteristic signs of the shock phase.”26 The shock phase could be instigated by any “alarming stimulus, or nonspecific noxious agent which causes sudden general, systemic damage,” and may include traumatic, nervous or obstetrical shock, infection, hemorrhage, muscular exercise, extreme cold, burns, pharmaceutical drugs, x-rays, solar rays, fasting or nervous commotion.27 Selye noted that by the principle of crossed-resistance, the adrenal insufficiency of the shock phase could be prevented by high doses of cortin or DOCA, and that immediately following the counter-shock phase animals developed nonspecific resistance to all alarming stimuli. However, animals that had previously experienced an alarm reaction in response to a specific alarming stimulus developed resistance to that specific agent, but failed to develop nonspecific “crossed-resistance.”28 He suggested that this may be due to an exhaustion of “adaptation energy,” which ultimately contributed to cumulative wear and tear that forced the animal to succumb to chronic disease, diseases of senility or even mere aging.29

Selye participated in the SSBS’s shock studies at McGill by conducting research on shock resulting from physical injury and surgical trauma.30 At the second meeting of the SSBS in late-January of 1942, Selye presented his findings that pretreatment with DOCA made experimental rats less resistant to shock, due to depressed adrenal cortical function, and reported


28 Ibid., 25.

29 Ibid., 33.

30 “Proceedings of the First Meeting of the Subcommittee on Shock and Blood Substitutes of the Associate Committee on Medical Research,” January, 4, 1941, Section 5, “Reports on Shock,” Box 8, ACMR.
that he had detected cortin-like material in the urine of animals forced to undergo physical exercise (but not in the urine of non-exercised animals).\textsuperscript{31} Later that same year, Selye reported to the SSBS that he had detected a decrease in blood sugar in traumatized limbs.\textsuperscript{32} Based on these findings he hypothesized that shock occurs because essential compounds are drained from uninjured areas due to the active metabolic demands of a traumatized area. This challenged a competing theory that shock arose from the release of toxic materials produced by tissue damage.

Since the late-19\textsuperscript{th} century, physiologists and biochemists had made significant advancements in the medical understanding of shock, stemming from George Crile and Alfred Blalock’s independent findings that shock arose from a severe decrease in blood pressure. While some scientists endorsed a theory that the nervous system ultimately regulated this drastic decrease in blood pressure (often attributing the onset of shock to acute psychological attacks, or adverse personality profiles), an alternate camp (helmed by several pioneers of endocrinology, namely Bayliss, Starling and Cannon) advanced a theory that a loss of circulating blood volume was the main cause for the decrease in blood pressure.\textsuperscript{33} Selye’s theory that shock reaps systemic affects by draining necessary substances from uninjured areas to compensate for their loss in injured areas further advanced the circulating blood volume theory, and at the same time invoked Cannon’s concept of homeostasis.

\textsuperscript{31} “Proceedings of the (2nd) Meeting of the Subcommittee on Shock and Blood Substitutes of the Associate Committee on Medical Research,” January 29, 1942, Box 5, ACMR.

\textsuperscript{32} Report on a Meeting of the Associate Committee on Medical Research of the National Research Council of Canada, October 29, 1943, Drawer 1, folder “Canada, 1943-44,” ACSG.

The SSBS must have found Selye’s theory promising because in 1943 it issued him a $1,700 grant ($23,245 in 2015 Canadian dollars) for two studies on carbohydrate metabolism pulmonary edema during shock. Though he was denied an additional $700 for a study of the prevention and cure of acute gastro-intestinal ulcers, he did receive the largest of four grants awarded to researchers at McGill that year, and a significant sum considering that the total amount of grants distributed by the ACMR that year was $47,755. The following year, the ACMR granted Selye an additional $1,200 for research on lung edema and on the role of the adrenal cortex in shock. In addition to his research for the SSBS, Selye was awarded several grants from USNRC committees. From 1940 to 1943, the NRC Committee on Research in Endocrinology awarded Selye three grants totaling $3,200 (worth approximately $45,000 in 2015 dollars) for research on the effects of steroid hormones on the kidney, and the impact of DOCA on nitrogen and blood chloride metabolism. In addition to his research on shock, Selye

34 "Proceedings of the Third Meeting of the Subcommittee on Shock and Blood Substitutes," March 26, 1943, Box 8, ACMR.

35 E.S. Mills was given $1,000 for a study of "Plasma Proteins in Shock," J.S.L. Browne was awarded $1,200 for a "Study on Shock; Extraction of Cortin from Post-operative Urine," and R.L. Noble was given $1,500 for "Studies on Shock with Special Reference to Toxic Extracts." See also, "Proceedings of the Eleventh Meeting of the Associate Committee on Medical Research," March 27, 1943, Box 6, ACMR.

36 “Proceedings of the Thirteenth Meeting and a Special Meeting of the Associate Committee on Medical Research," March 17-18, 1944, Box 6, ACMR.


38 Walter B. Cannon to Hans Selye, April 29, 1941, and “Summary of the Work Performed With the Help of the Grant Given to Dr. H. Selye by the Committee on Research in Endocrinology of the National Research Council,” folder “MED: Com on Res in Endocrinology, 1940-1944, Grantee: Selye H,” Records of the Committee for Research in Endocrinology, 1936-1952, DMS.
participated in military endocrinological research by contributing studies on the anesthetic effects of steroids, the effect of nutritional “conditioning factors,” such as salt and protein on adrenal functions, and the adrenocortical regulation of cardiovascular, renal and gastrointestinal diseases. During the course of the war, Selye published a total of ten papers based on research funded by the CNRC, and another ten based on research funded by the USNRC.


In 1943, Selye published a letter to the editor of the *Lancet* offering an explanation of a recent debate in the journal about the reasons for the marked increase in gastro-intestinal ulcers among residents that survived Germany’s prolonged bombing campaigns of London, Bristol and Liverpool. He attributed the increase in ulcers to the pathological derailment of the Alarm Reaction. Selye argued that the increased secretion of adrenocorticoids during the shock phase


of the Alarm Reaction raises resistance, but in the subsequent counter-shock phase, excessive exposure to these hormones induces the development of ulcers that can be exacerbated by exposure to other stressors, such as starvation and cold which “greatly increase the ease with which such lesions are produced in animals by exposure to stress.”

In March of 1943, Selye submitted an “Annual Report on Shock” to the third meeting of the SSBS, reporting that he had established a standard method for producing peptic ulcers by nervous stimulation, similar to those prevalent amongst servicemen and air-raid survivors, and that he had successfully treated these experimentally induced ulcers through dietary modifications and the administration of pharmaceuticals, which he suggested “may prove of value in the prophylaxis and cure of neurogenic peptic ulcers in the armed forces as well as in the civilian population of communities subjected to prolonged air-raids.” Later that same year, Selye reported to the SSBS that he had prevented the development of shock-induced gastric ulcers by pre-treating experimental animals with glucose and aluminum hydroxide.

Selye depended heavily on military grants for the duration of the war, submitting multiple grant applications to multiple branches of the USNRC and CNRC at the same time. While the grant review boards generally recognized Selye as a dedicated researcher and a worthy candidate for funding, they also seemed wary that his overzealous pursuit of aid entailed a hazardous dependency on state funding. When Selye applied for a grant from the Committee on Problems in Sex Research in 1940, Cannon wrote to his fellow committee member, Harvard psychologist

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45 “Proceedings of the Third Meeting of the Subcommittee on Shock and Blood Substitutes,” March 26, 1943, Appendix I, Box 8, ACMR.

46 Report on a Meeting of the Associate Committee on Medical Research of the National Research Council of Canada, October 29, 1943, Drawer 1, folder “Canada, 1943-44,” ACSG.
Robert Yerkes, recommending Selye as “a good worker and active.” However, two years later, when Selye applied for three grants (from the Committee on Research in Endocrinology for a study of the pituitary regulation of blood chlorides, to the Committee on Research in Problems of Sex for a study of the role age in the pituitary regulation of reproductive hormones, and the Markle Foundation for research on the anesthetic properties of steroids), Cannon suggested that they “let Selye be satisfied with the Markle grant,” even though Archie Woods of the John and Mary R. Markle Foundation had advised Cannon that Selye was competent to handle three proposed research projects at the same time, as Woods considered Selye to be “a man of tremendous energy and enthusiasm, one who could keep a good many balls in the air at the same time.”

Unaware that his enthusiastic pursuit of state and philanthropic aid was actually undermining his success in receiving grants, Selye continued to submit numerous proposals at the same time. For the fiscal year 1943, Selye submitted a total of five proposals to the Committee on Research in Endocrinology and the Committee on Research in Problems of Sex, of which only one was approved—the Committee on Research in Endocrinology awarded him

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47 Walter B. Cannon to Robert M. Yerkes, December 13, 1940, Box 78, folder 1059, WBC.

48 Walter B. Cannon to Robert M. Yerkes, March 6, 1942, Box 78, folder 1060, WBC.

$1,200 for his proposed study of the effect of DOC-overdosage on the kidney.\textsuperscript{50} The following year, Selye’s request for the grant to be renewed was rejected.\textsuperscript{51}

Yet, Selye was resilient in his quest for state support. In the final year of the war, Selye sought further funding from CNRC to expand his research on adrenocortical secretions during the Alarm Reaction, proposing to investigate the role they played in shock-related tissue damage. In a March 17, 1944 meeting of the SSBS, Selye submitted additional proposals to study of the role of the adrenal cortex in regulating shock, however the committee determined such research would be a waste of its resources, given the fact that previous research along these lines had “been entirely negative in its conclusions as to the value of these hormones in the acute phases of shock.”\textsuperscript{52} Yet, while the CNRC chose to fund only a few of Selye’s proposed projects, the research he conducted under these grants led to his development of a coherent theory of adaptive biological stress. Selye’s wartime research helped him to explain how, by triggering adrenocortical secretions, prolonged stress can induce degenerative diseases, and by discovering that exposure to certain factors can sensitize tissues to the effects of adrenocorticoids, he was also able to explain why stress did not consistently produce the same conditions to the same degree in all people exposed to the same stressors.


\textsuperscript{52} “Summary of the Meeting of the Subcommittee on Shock and Blood Substitutes of the National Research Council of Canada,” Ottawa, March 17, 1944, Records of the National Research Council, “Canada, 1943-1944,” NRC.
Diseases of Adaptation

Selye’s participation in wartime research coordinated by the ACMR and the CMR profoundly affected his developing theory of the GAS. Even though his research on the adrenocortical regulation of shock proved to be ineffective, it nevertheless led him to develop a more nuanced understanding of the tendency of adrenocorticoids to exert either protective or harmful effects on the body, depending on their type, concentration, duration, and to what tissues they were exposed. He became more interested in the long-term consequences of adrenocortical activity, rather than the immediate adaptive response to shock. 53

As described in Chapter One, by the early-1940s, Selye had already revolutionized adrenocortical research by helping to verify and classify the existence of many different hormones produced by the adrenal cortex and their specific actions. He classified these hormones into two groups according to their primary action: glucocorticoids, which converted proteins and other compounds into glucose, and mineralo-corticoids, which regulated mineral metabolism. Selye found that while mineralocorticoids typically increased inflammation, glucocorticoids tended to reduce it. 54 During the GAS, both kinds of corticoids were released to regulate the body’s response to injury. However, prolonged exposure to a harmful agent could easily produce an excess of either kind of corticoid, which would result in tissue damage and could ultimately induce high blood pressure, hypertension (which arises when the accumulation of hyaline, a plaque-like substance, along the lining of the arteries, shrinks the arterial lumina, making it more difficult for blood to pass through, and increasing blood pressure), rheumatic


conditions (which are characterized by the accumulation of fluid in joints, tissues and organs), and nephrosclerosis (a hardening of the nephrons of the kidneys, which filter blood and regulate electrolyte, metabolite and water absorption). Though the GAS was initiated as a natural protective mechanism that helped to preserve life against fatal injury, in protracted cases, it could itself become pathological and contribute to the onset of what Selye called “diseases of adaptation.”

Throughout the 1940s, Selye’s research on diseases of adaptation centered around the administration of DOCA to experimental animals to induce hypertension, arthritis and nephrosclerosis. And as he grew more reliant on DOCA in his research, he developed a symbiotic relationship with Schering Corp., his main supplier of DOCA. From the beginning of their association in 1938 until the end of World War II, Selye published no less than twenty-five papers based on research conducted with grants from Schering, and no less than seventy-five—one-third of the total number of papers he published during that time—using complimentary hormone preparations supplied by Schering. As was customary, in return for their support Selye would acknowledge Schering’s donations in his publications, offering them a form of free advertising and professional endorsement. The dependability of funding that this relationship provided, no doubt attracted Selye to pursue further support from pharmaceutical firms to offset the capriciousness and uncertainty of competing for military grants and philanthropic aid. Yet, while Schering was by far his most consistent source of aid, Selye received support from numerous pharmaceutical, philanthropic and state funders during this time. Selye’s publications

also acknowledge aid from philanthropies including the Josiah Macy Jr. Foundation; the John and Mary R. Markle Foundation; the Commonwealth Fund; and the Banting Fund; as well as, the support of pharmaceutical firms including Ciba; Des Bergers-Bismol; Merck; Frank W. Horner; Smith, Kline & French; Pfizer; Hoffman-LaRoche; and others.

Selye began actively soliciting aid from pharmaceutical firms at a time when the industry was gaining financial strength and enhanced production capacity through its government-contracted work for the war effort, enabling firms to offer increased funding opportunities and complimentary lab materials. In 1942, Selye received a grant from Des Bergers-Bismol for the study of the pathological affects of DOCA overdosage. When Selye treated adrenalectomized animals with DOCA, he found that they did not display the thymico-lymphatic shrinkage and decreased immune response characteristic of the GAS. However, they did develop a marked increase in blood pressure, as well as nephrosclerosis, hypertension and rheumatic-allergic conditions.\(^{56}\) Because the nephrons participate in the regulation of blood pressure, the hardening of the nephrons and the production of renal lesions stimulated by DOCA overdosage can induce hypertension.\(^{57}\)

The following year, Selye received a grant from the Montreal pharmaceutical firm, Frank W. Horner, Ltd. for research on the inflammatory affects of DOCA. He found that DOCA produced rheumatic conditions due to what he described as an increased inflammatory potential

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\(^{57}\) Selye, “Production of Nephrosclerosis by Overdosage with Desoxycorticosterone Acetate”; Selye, *The Story of the Adaptation Syndrome*, 74.
of connective tissue, leading to the onset of cardiovascular disorders, including periarteritis nodosa, myocarditis, endocarditis and pericarditis, as well as polyserositis and joint lesions. Selye found further evidence that hyper-stimulation of the adrenal glands was linked with rheumatism when he discovered that DOCA overdosage induced polyarthritis in his rats. Horner’s grant, combined with support from the CNRC, funded experiments which found DOCA overdosage to induce the development of visible inflammatory lesions, particularly in the arteries and arterioles, the heart, the brain and the adrenals. Selye had discovered that mineralocorticoids caused inflammation of the connective tissue interwoven throughout the organs, muscles and blood vessels of the body, which in turn stimulated the onset of arthritis and cardiac dysfunction, indicating a “pathogenic relationship between the adrenocortical hormones and the rheumatic diseases.” He theorized that since the administration of exogenous, synthetic DOCA induced a rheumatic syndrome, the indogenous secretion of pure corticoids during the stress response would likely do the same. In 1944, further experimentation supported by the


59 Selye and Pentz, “Pathogenetic Correlations Between Periarteritis Nodosa, Renal Hypertension and Rheumatic Lesions.”

60 Selye, The Story of the Adaptation Syndrome, 74; Hans Selye and Charles E. Hall, “Pathologic Changes Induced in Various Species by Overdosage with Desoxycorticosterone.”

CNRC’s Banting Research Fund revealed that “under certain conditions, stressors caused lesions which simulated overdosage with cortical hormones,” demonstrating that “it was possible to reproduce by stress [alone] the manifestation of characteristics of overdosage with antiphlogistic (diminution of hyperergic inflammation, thymolysis) or prophlogistic corticoids (nephrosclerosis, hypertension, arteritis, arthritis, myocarditis).”

It was not particularly surprising that pro-inflammatory mineralo-corticoids would induce hypertension, rheumatic conditions, or nephrosclerosis, since each of these conditions were associated with increased blood pressure. However, what was remarkable about this triad of symptoms was that all three were regulated by the adrenal cortex. Yet, never having performed experiments with glucocorticoids, Selye had no evidence that they too would produce malignant changes, or counteract the effects of mineralocorticoids (as he would later discover). Nor had he proven that they necessarily contribute to the development of nephrosclerosis or rheumatic-allergic diseases since he had no evidence that these conditions could arise from stressors that stimulated endogenous corticoid secretion. Such verification was beyond Selye’s technical capacity until the late-1940s when pure glucocorticoid extracts became available for experimental research.

Selye’s theory that adrenocorticoids exacerbated cardiovascular, renal and inflammatory diseases provoked the criticism from a number of Selye’s colleagues that 1) since DOCA was an

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63 Selye, *The Story of the Adaptation Syndrome*, 77. In 1946, Selye developed a technique of converting the kidney into an exclusively endocrine organ, by which he was able to induce the same pathological conditions he showed with DOCA. See Hans Selye and Helen Stone, “Pathogenesis of the Cardiovascular and Renal Changes Which Usually Accompany Malignant Hypertension,” *Journal of Urology* 56 (1946): 399-419; Hans Selye, “Transformation of the Kidney into an Exclusively Endocrine Organ,” *Nature* 158 (1946): 131.
artificial synthetic corticoid which was not naturally produced by the adrenals, it was erroneous to deduce that endogenous adrenocorticoids would also induce systemic inflammation, 2) even if DOCA did closely resemble a pure corticoid, the quantities that Selye used to solicit these pathogenic responses far exceeded the productive capacity of the adrenals, and 3) that the adrenal cortex may not be the originator of the pathological changes Selye associated with the GAS. In order to refute these allegations, Selye needed to show that that naturally-stimulated adrenocortical hormones did in fact produce diseases of adaptation. He obtained a grant from the Josiah Macy Jr., Foundation to measure the exclusive influence of adrenocorticoids on these conditions. Knowing that adrenocorticoid secretion was mediated by the pituitary, Selye developed a crude preparation of lyophilized anterior pituitary extract (LAP) made with pulverized bovine anterior-pituitary glands. He found that LAP produced renal, cardio-vascular and joint lesions similar to those induced by DOCA overdosage, as well as nephrosclerosis, hypertension, joint lesions, and a marked rise in “inflammatory potential,” but only in the presence of adrenal tissue. Therefore, the pituitary could not be directly responsible for producing disease, but rather must only participate through the stimulation of adrenocorticoid secretion. Adrenocorticoids must be primarily responsible for inducing these diseases.64

Based on his finding that overdosage with DOCA or LAP can cause nephrosclerosis, hypertension and a systemic increase in inflammatory potential, Selye deduced that by acting on the adrenal cortex, “stress invariably stimulates the pituitary-adrenocortical system,” in two distinct and incompatible patterns. One form of reaction, likely mediated by ACTH was characterized by thymico-lymphatic shrinkage and decreased inflammatory potential, whereas

the second form of reaction increased inflammation, producing nephrosclerosis, hypertension and rheumatic-allergic manifestations. Selye surmised that this second form of stress response was mediated by mineralocorticoids, like DOCA, and some pituitary principles other than ACTH, or somatotropic hormones (STH), since LAP extracts were especially rich in this hormone. Yet, while DOCA typically produced adrenal shrinkage, LAP tended to enlarge the adrenals as it stimulated an increase in adrenocorticoid production. Selye concluded that this “adrenocortical stimulation was undoubtedly related to the development of nephrosclerosis,” since the anterior-pituitary extracts did not produce nephrosclerosis in adrenalectomized animals.

In demonstrating the differential effects of various pituitary and adrenocortical factors, Selye defended the primacy of the adrenal cortex in producing diseases of adaptation, though he did not conclusively demonstrate that it was the fulcrum of a non-specific unified response to all disease. Even as he advanced the scientific evidence to defend the concept of the GAS, he continued to receive criticism against the larger claims of his theory (discussed in greater detail in Chapter Three and Four). Yet, Selye’s research on the differential roles of pituitary and adrenal hormones in facilitating biochemical adaptation also began to clarify the reasons for extreme variation in the pathological manifestations of the stress response. Yet, this still failed to explain why it was that different diseases developed to different degrees in different patients at

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65 It was not until 1951, when Selye was able to obtain pure extracts of STH from Choh Hao Li at the University of California, Berkeley, that he was able to verify this hypothesis. See Hans Selye, “Role of Somatotrophic Hormone in the Production of Malignant Nephrosclerosis, Periarteritis Nodosa and Hypertensive Disease,” *British Medical Journal* (February 10, 1951): 263-270.

different times, even though they were exposed to the same stressors. Such variability indicated
that there were other co-factors which influenced the course of the stress response.

**Conditioning Factors**

By 1944 Selye had found evidence suggesting that adaptive hormones could contribute to
cardiovascular disease, arthritis and gastrointestinal disease, however he could not yet explain
why it was that DOCA overdosage failed to produce consistent, uniform inflammation in the
same joints, tissues and organs of all experimental animals. Nor did he understand why it was
that DOCA overdosage only began to generate an inflammatory response at a certain point over
the course of several weeks of daily administration. He realized early in his adrenocortical
research on diseases of adaptation that sodium chloride sensitized animals to DOCA,
exacerbating production of nephrosclerosis and inflammation. Selye also noticed that cold or
humidity (as well as other irritants) could increase the severity of arthritic symptoms induced by
DOCA overdosage and determined that such stressors can create “selective sensitization,” which
to some extent would account for the polymorphogenic nature of the inflammatory response.

He also found that sodium and protein rich (or potassium deficient) diets aggravated the onset of
hypertension, nephrosclerosis, myocardiac infarctions and rheumatism when experimental rats
were exposed to stress, while fasting predisposed animals to develop peptic ulcers, especially
when under stress. It seemed to him that such factors “do not cause manifest pathologic

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67 Selye, “On the Production of Malignant Hypertension by Chronic Exposure to Various
Damaging Agents”; Selye, Sylvester, Hall and Leblond, “Hormonal Production of Arthritis.”


69 Hans Selye and Helen Stone, “Role of Sodium Chloride in Production of
Nephrosclerosis by Steroids,” *Proceedings of the Society for Experimental Biology and
Medicine* 52 (1943): 190-193; Hans Selye, Helen Stone, Paola S. Timiras and C. Schaffenburg,
changes in themselves, but merely sensitize the tissues for the toxic effects of these hormone preparations,” indicating that each of these degenerative conditions arose from a multiplicity of causes, not any single, specific factor.

These observations led him to the realization that stress could be mitigated or exacerbated by certain “conditioning factors,” that sensitized tissues and organs to amplify or suppress the effects of adaptive hormones. Such factors were not directly responsible for producing physiological changes, but influenced these changes by affecting hormonal potency. By offering this etiological model of multi-causation Selye resolved the quandaries presented by the fact that patients exposed to the same stressors develop different diseases, and the inconsistent pathogenic expressions produced by the GAS. By analogy, Selye explained “the same electricity can create motion, light, sound, heat, cold and innumerable combinations of these effects, depending upon whether it is conducted, selectively or in combination, to an electric motor, a light bulb, a bell, a stove or a refrigerator,” just as the hormonal pathways of the GAS might induce different physiological effects depending upon the biochemical conditioning of tissues prior to its initiation.\(^70\) In practice, this meant that conditioning factors—diet, heredity, environmental pathogens, trauma, etc.—could selectively sensitize organs to resist or succumb to stress and adaptive hormones, and explained the highly individualized nature of diseases of adaptation.

Through his wartime research Selye produced evidence that the number one killer of the modern era, cardiovascular disease, and one of the most prevalent debilitating degenerative diseases, arthritis, were both regulated by adrenocorticoid secretion. In addition, he demonstrated that environmental and lifestyle factors could influence the development of these

\(^70\) Selye, *The Story of the Adaptation Syndrome*, 103-104.
diseases. These findings offered hope that such conditions could be treated by manipulating body chemistry—by adjusting levels of pro-inflammatory mineralocorticoids and anti-inflammatory glucocorticoids—and by avoiding harmful conditioning factors. In this way, science could potentially develop a means to naturally induce healing for a diverse range of degenerative disease by mimicking and modifying biological processes of adaptation. Selye mused that perhaps the reason that medical science had yet failed to identify the etiological foundation or effective preventive methods for such diseases “was precisely because they have no specific cause,” and that therefore “it proved impossible, despite centuries of research, to find the agents which elicit these particular diseases.” A more comprehensive, holistic and dynamic perspective of disease etiology was necessary to recognize the complex forces that combined to produce these degenerative conditions. As discussed in Chapter One, holistic medicine and nonspecificity breached the boundaries of mainstream biomedicine, yet increasingly they were gaining support from diverse branches of the medical community.

Selye’s radical theories benefited immensely from concurrent research in psychosomatic medicine, military psychology and fatigue. While World War II catalyzed Selye’s research by offering him new sources of funding, it also stimulated innovation in military psychological research and the professionalization of psychosomatic and psychoanalytic practitioners, which helped to legitimate this avant garde field of medicine. Selye’s radical theories gained credence from the proliferation of research in multiple aspects of stress-related diseases, as he gained professional validation as a leader in this new field of innovative research. Moreover, the maturation of psychosomatic theory and professionalism also offered Selye a powerful new linguistic device to represent his complex theory: “stress.”

71 Selye, The Story of the Adaptation Syndrome, 103.
IV. Military Support for Psychosomatic Stress Research

While Selye’s wartime research helped him refine his theory of the adrenocortical regulation of adaptive diseases, concurrent military-sponsored research regarding psychological responses to war helped to legitimate the psychosomatic foundation of stress. The CNRC and NRC both supported research examining the physiological responses to various adverse environmental factors, contributed to a more holistic understanding of the psycho-social influences on human health and disease. In contrast to the adrenocortical research conducted by the Cortin Committee and the SSBS, this research was psychologically-oriented, though it did occasionally mobilize endocrinological evidence to establish the somatic foundation of psychopathologies. As seen in the military funding of adrenocortical research, the CNRC and the NRC subcommittees funded independent scientific research in academic centers, drawing on the leadership of Harvard’s Fatigue Laboratory in expanding the scientific understanding of environmental precipitants of endurance, productivity and resistance to disease prior to the war. In addition, the US Army’s Neuropsychiatric Division spearheaded new in-field research and screening tactics to reduce the prevalence of neuropsychiatric casualties, recruiting leaders in psychoanalysis, psychobiology, and the emerging field of psychosomatic medicine.

As the ACMR and the CMR drew on the academic and industrial scientific resources of both the United States and Canada in the pursuit of wartime research goals, both committees benefited from the decade of research already compiled by the Fatigue Laboratory, and supported further work in the Fatigue Laboratory during the war. The ACMR helped to coordinate a collaboration between the Fatigue Laboratory and the Canadian Department of Health’s Industrial Hygiene Division in the investigation of factors to reduce fatigue, exhaustion,
overwork, etc.\textsuperscript{72} Part of this research involved a study of cold stress and protective clothing staged in the Prince Albert Peninsula in the Northwest Territory.\textsuperscript{73} During the war, the Fatigue Laboratory became almost entirely consumed with research conducted for the OSRD,\textsuperscript{74} as its principal source of funding shifted from the Rockefeller Foundation to the US federal government.\textsuperscript{75} Building on the basic research they had conducted over the course of the 1930s, the Fatigue Laboratory mobilized their knowledge of fatigue among laborers to study the physical capacity of soldiers and pilots. Under the Direction of William H. Forbes (during Professor of Industrial Physiology David Bruce Dill’s wartime service), and Acting Directors, Arlie Vernon Bock and Henry K. Oliver, both Professors of Hygiene, the Lab worked closely with the Quartermaster Corps, the Army Air Forces and the CMR, to develop strategies and equipment to help increase soldiers’ endurance in spite of adverse climatological conditions, such as intense heat, dryness, and humidity, as well as exhaustive physical activity, and

\begin{footnotesize}
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\item \textsuperscript{72} C.R. Meyers, Consultant Psychologist of Canadian Department of Health to Sanford V. Larkey, Chairman of National Research Council’s Subcommittee on Correlation of Information, April 3, 1941, Drawer 1, folder “Canada, 1941-1942,” ACSG.
\item \textsuperscript{73} R.E. Johnson to Canadian Army Staff, attn. Major Percy of Capt. Nieufeld, January 20, 1945, Box 1, folder 21, HFL.
\item \textsuperscript{74} It should be noted that even as they catered their work to serve military purposes, the Fatigue Lab continued to collaborate with industry, as evidenced by their ongoing work with General Electric in studies of temperature stress, product engineering, and other efficiency technology: heated gloves, anti-flak protective equipment and parachutes, heated flying clothing and casualty bags, heated shoes (instead of wool socks), heated blankets (for casualties), heated copper dummy used to determine optimum heat distribution and control electrically heated blankets. See, “A Brief Statement of the Wartime Relationships Between the Pioneer Products Division of the General Electric Company and the Fatigue Laboratory of the Harvard Graduate School of Business Administration,” Box 26, folder 17, HFL.
\item \textsuperscript{75} [untitled], Box 26, folder 17, HFL. On the history of the Fatigue Laboratories’ involvement in World War II medical research see G. Edgar Folk, “The Harvard Fatigue Laboratory: Contributions to World War II,” \textit{Advances in Physiology Education} 34 (2010): 119-127.
\end{itemize}
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insufficient dietary provisions. An essential component of this research was the development of assessment tools for determining the general condition of soldiers. They determined that four principal categories of factors, 1) physiological, 2) nutritional, 3) clothing, and 4) pharmacological, affected soldiers’ performance in heat.\(^{76}\) Just before the Japanese surrendered in August of 1945, the Fatigue Laboratory applied to the OSRD for a $22,000 renewal of the grant to study the effect of apparel and diet on fatigability—under which they had already received $116,481. The methods for measuring the physical condition and fatigability developed by the Fatigue Laboratory ended up being used by the US, British and Canadian Armies and Navies.\(^{77}\)

The Fatigue Laboratory also collaborated with both the USNRC’s Committee on Aviation Medicine and the CNRC’s Committee on Aviation Medical Research in reducing stressful conditions to which pilots were exposed, and developing means of treating those suffering from flight stress.\(^{78}\) Their research on aviation physiology—specifically focusing on the effects of respiratory deficiency at high altitudes, decompression illness, and extreme cold—proved invaluable to countering aviation fatigue caused by decreased oxygen absorption, which increased the likelihood of developing carbon monoxide poisoning.\(^{79}\)

\(^{76}\) “Summary of Work Done to Date Under Contract OEMcmr-328,” Box 26, folder 11, HFL.

\(^{77}\) Arlie Vernon Bock (Professor of Hygiene, Harvard) Application to OSRD Committee on Medical Research, “Physiological adaptations of man to cold including problems of diet and clothing,” Grant No. OEMcmr-54, August 5, 1945, Box 26, Folder 11, HFL.

\(^{78}\) “Proceedings of the Twenty-third meeting of the Executive of the Association Committee on Aviation Medical Research,” May 31, 1943, Box 2, ACMR.

Though their major source of funding shifted to the state during the war, the Fatigue Laboratory did continue to enjoy philanthropic support in their work. As of 1943, its research on aviation fatigue was subsidized in part by a $3,000 grant from the Josiah H. Macy, Jr., Foundation, through which they found “that mood and motivation have a large influence upon performance.” Inspired by the importance of psychological factors on productivity, the Fatigue Laboratory conducted further studies measuring the collateral influence of temperament, habits of sleeping and eating, and distractions, as well as the chemical influences of coffee, Benzedrine, alcohol, insulin, sugar, and carbon monoxide.80

The Fatigue Laboratory’s investigation of psychological determinants of endurance and productivity enlisted the help of two Boston-based biologists, Gregory Pincus and Hudson Hoagland, to study adrenocortical stimulation initiated by emotional states, with the hope of identifying a means by which to improve screening processes for fighter pilots.81 This work promised to lead to a pharmacological treatment for fatigue. In 1943-44, the NRC’s Committee on Research in Endocrinology awarded Pincus $3,000 (over $41,000 in 2015 dollars) for research on the detection of 17-ketosteroids (the end-product in the decomposition of the male sex hormones, androgens) in the urine of fatigued pilots.82 Pincus and Hoagland found that during states of heightened alertness and tension, such as are characteristic of aerial combat, the body produces an excess of ketosteroids, which could be detected through urinary analysis (and

80 “Work Done in the Fatigue Laboratory Largely on a Grant From the Macy Foundation,” enclosed with letter from W.H. Forbes to Dr. Frank Fremont-Smith, March 18, 1944, Box 1, folder 10, HFL.

81 “Informal Summary of Some Recent Contributions From the Clark Physiological Laboratories (1936-1942),” Box 114, folder 1580, WBC.

82 “Committee on Research in Endocrinology, Division of Medical Sciences, Program and Budget for the Year 1943-1944,” Box 80, folder, 1089, WBC.
are also present in other bodily fluids, such as sweat and saliva). Based on these findings, Pincus and Hoagland reported that “it appears that marked variations in the abilities of men to withstand fatiguing ordeals is related to their adrenal cortical functions,” indicating that “administration of suitable steroids might increase one’s ability to withstand the type of measurable stress” suffered by servicemen in combat. Pincus and Hoagland assessed several steroids for prophylactic potential, and found that soldiers given pregnenolone (which had been donated pro bono by the Schering Corporation) “reported feeling less fatigued and better able to cope with their jobs when they were taking it,” and that pilots given pregnenolone during flight tests had a fifty percent reduction in the level of ketosteroids in the urine. Yet, in follow-up studies of civilian stress among male Clark University students and industrial workers, they found administration of pregnenelone to be less effective in reducing fatigue, suggesting that it may be most effective “where motivation is high and where men are working under really trying conditions.”

Pincus and Hoagland’s research on ketosteroids dovetailed with that of McGill endocrinologist Eleanor Venning (sometimes in collaboration with R.D.H. Heard and J.S.L. Browne), whose SSBS-sponsored research used urinary analysis to show that during gestation women produce higher levels of cortical steroids. This was significant because it indicated that reproduction enhances protective endocrinological functions, but also because it confirmed that adrenocorticoids may be effective in detecting and treating stress. Inspired by Venning and Pincus and Hoagland’s research, for nearly a decade following the Second World War, military research focused on using the detection of ketosteroids in urine as a metric for assessing stress.

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levels in servicemen, in the hopes of developing a steroid-based pharmacological method for treating combat stress.  

It is likely that Pincus developed an interest in stress-research through a larger disciplinary quest to discover how hormones of the adrenal cortex influenced reproduction. Like Selye, Pincus began his career researching hormonal mechanisms of mammalian reproduction. Working as an untenured professor of zoology in the 1930s, Pincus had earned a reputation as an internationally renowned expert in reproductive endocrinology for his work on stimulating female fertility. In 1939, Pincus began to attract scholarly attention with the publication of his discovery of “fatherless” reproduction in rabbits by parthenogenesis. “Pincogenesis,” as it became known, was akin to modern in vitro fertilization, essentially involving the extraction of sperm and ova from a male and female rabbit, sensitizing the ovum with high temperatures, hormones and salts, manually fertilizing the ova with the sperm and implanting the fertilized egg in a female rabbit. In addition to his work with the Fatigue Laboratory, Pincus had also

84 Tully Long has argued that the military quest for a physiological intervention to reduce combat stress ultimately led to the recognition by 1953 that psychological factors could not be ignored in the etiology of stress, triggering a shift in research methods that incorporated behavioral conditioning, as well as biochemical intervention. See Tully Long, “The Machinery and the Morale: Physiological and Psychological Approaches to Military Stress Research in the Early Cold War,” in Stress, Shock and Adaptation in the Twentieth Century, 142-185.

received NRC support in the form of a $2,400 grant through the Committee on Research in Problems of Sex for research on the metabolism of the ovarian hormones in mammals. In the final year of the war Pincus and Hoagland would establish their own Institute for Experimental Biology which became a leader in both reproductive and stress research in the postwar period (discussed in Chapter Four).

Apart from the Fatigue Laboratory and the Aviation Committee’s research, the CMR also funded research examining the psychosomatic influences on digestive function, to address the high incidence of gastric ulcers among servicemen. Cornell psychiatrist, Harold Wolff was instrumental in conducting the research. From the outset of the war Wolff participated in military research as an Acting Physician-in-Chief of Neurology at New York Hospital’s Psychiatric Clinic. In June of 1941, Oskar Diethelm, the Chair of Cornell Medical College’s Psychiatry Department offered the Psychiatric Clinic as a resource for the CMR. Given the clinic’s experience in researching the psychosomatic manifestation of gastric ulcers, and recent reports of the British Armed Forces of a high rate of ulcers among servicemen, Diethelm suggested the Cornell Psychiatric clinic would be ideally suited for research evaluating whether ulcers suffered by naval servicemen were of organic or functional origin.

Wolff’s training in psychobiology provided him unique expertise in the psychosomatic dynamics of disease. From auspicious beginnings that involved studying with celebrated Harvard psychiatrist Stanley Cobb, and winning a coveted National Research Council

86 “Twenty-First Annual Report Committee for Research in Problems of Sex Division of Medical Sciences, National Research Council, for the year July 1, 1941, to June 30, 1942” [draft?], Box 78, folder 1060, WBC.

87 Oskar Diethelm to Comm. Ellsworth Moddly, June 25, 1941, Box 4, folder 4-2, Harold Wolff Papers, 1898-1963, Medical Center Archives of New York-Presbyterian/Weill Cornell, New York, NY. (hereafter HGW).
Fellowship in Medicine that enabled him to study under Ivan Petrovich Pavlov in Moscow, Otto Loewi in Gratz, Erich Schilf in Berlin, and Adolf Meyer at the Johns Hopkins’ Phipps Clinic, Wolff gained a firm grounding in the investigation of behavioral conditioning, and the measurement of endocrine functions governing physiological processes, such as sleep, sweat and skin resistance. Wolff first attracted scholarly attention (and substantial funding from philanthropies like the Rockefeller Foundation and the Josiah Macy, Jr., Foundation) for research in the neuro-physiological development of migraine and vascular headaches, as well as the conditioning influence of personality factors and life experiences in the sensory experience of pain. But by the onset of war in 1939, Wolff’s research had turned to focus on the relationship between emotions and gastric secretions.

During the war Wolff expanded on Walter Cannon’s research of the emotional stimulation of gastric functions with substantial support from philanthropic organizations, as well as the CMR. In collaboration with fellow Cornell psychiatrist Stewart Wolf, the two men examined a patient, Tom Little, who had a gastric fistula inserted in his intestinal tract that enabled them to directly measure changes in the secretion of digestive enzymes, as well as the integrity of intestinal tissues in response to various emotional triggers. They found that when

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88 Box 4, Folder 4-7, HGW.
89 Harold Wolff to Canby Robinson, April 20, 1930, Box 2, folder 2-11, HGW.
90 Box 3, folder 3-11, HGW.
91 Wolff and his colleague at Cornell, psychiatrist Bela Mittleman received over $18,000 from 1939-44 from the Macy Neurological Fund, as well as several smaller grants from the Friedsam Foundation and the Russell Sage Foundation for this research. See Box 3, folder 3-11, HGW.
92 In January of 1945, the CMR awarded Wolff $3,350 for a study of cardiovascular fluctuations associated with emotions, acute disease, and the convalescent state. Box 3, folder 3-11, HGW.
they presented cues that initiated emotional anxiety, Tom would develop intestinal inflammation that could ultimately lead to ulceration.\footnote{Stewart G. Wolf and Harold G. Wolff, \textit{Human Gastric Function: An Experimental Study of a Man and His Stomach} (New York: Oxford University Press, 1943).} This seemingly intractable evidence of the psychological influence on biological functions revolutionized psychosomatic medicine. Wolff and Wolf’s demonstration of the psychosomatic foundations of gastric function generated scholarly attention across traditional disciplinary divides and stood out as an icon of a burgeoning scientific field of psychosomatic medicine. Such physiological evidence of psychogenic disease offered psychiatrists a powerful means of validating controversial theories of mental illness as the positivist orientation of biomedical culture demanded empirical, reproducible results to document pathologies. By conforming to the somatic orientation of biomedical standards to demonstrate the psychosomatic nature of disease, psychiatrists like Wolff and Wolf helped to bridge the disciplinary boundaries that impeded a holistic examination of health.

\section*{V. Military Psychology and Combat Stress}

While Selye was not directly involved in the investigation of psychosomatic health, by the end of the war his theory of biological stress would benefit immensely from the scientific validation of psychogenic disease. By the early-1940s, a scientific field of psychosomatic medicine had emerged within the medical profession. Drawing together disparate currents of mind-body research from neurology, physiology and psychiatry, this heterodox field began to gain its own identity in the mid-1930s, marked by the Josiah Macy, Jr., Foundation’s publication of Helen Flanders Dunbar’s \textit{Emotions and Bodily Changes}, a compilation of current medical literature linking emotions and health.
Dunbar embodied the interdisciplinary nature of psychosomatic medicine. Before completing her medical degree at Yale University Medical School in 1930, Dunbar studied Medievalism and Christianity at Columbia, theology at Union Theological Seminary and psychoanalysis in Vienna under Felix Deutsch. Dunbar’s early interest in what she described as a false dichotomy between faith and science, presaged her subsequent fascination with the relationship between the mind and the body. In fact, it was through her position as the director of the New York Academy of Medicine’s Committee on Public Health and the Federated Council for the Churches of Christ in America, that she gained the financial support of the Josiah Macy, Jr., Foundation and was commissioned to write *Emotions and Bodily Healthy*, which was intended to be the companion to a second volume reviewing the religious literature on emotions and health.\(^{94}\)

Yet, it was Dunbar’s training in psychoanalysis that most profoundly shaped her medical philosophy. Hastened by his American lectures in 1909, the zeitgeist of Freudian psychoanalysis promoted the “dynamic” paradigm of psychiatry to dominate etiological and therapeutic models of mental health throughout the first half of the century.\(^{95}\) Focusing on each patient’s unique life history and personal problems, psychoanalysis employed talk therapy to uncover and release patients’ sublimated anxieties. In contrast to nineteenth-century psychiatry’s organicist tradition that linked mental illness with physical dysfunction, and emphasized surgical and other methods of physical interventions as the only means of effective therapy, dynamic psychiatry emphasized subconscious memory and repressed will as the origin of all neuroses.


Building on the psychoanalytical emphasis on individual personality, Dunbar’s 1943
*Psychosomatic Diagnosis* correlated personality types with disease—including, fractures, hypertensive cardiovascular disease, coronary occlusion, anginal syndrome rheumatic diseases, and diabetes—as it explicitly insisted that disease could not be studied independent of the patient.\(^96\) Dunbar’s fellow pioneer in psychosomatic medicine, and founding member of the American Psychosomatic Society, Franz Alexander disputed her theory, yet advanced a similar formulation of pathological profiling for disease. He proposed that conflict-specificity and organ-specificity rather than personality-specificity gave rise to particular psychosomatic complaints. For example, he correlated peptic ulcer with infantile oral fixation and adult aggressive tendencies. Alexander theorized that when under stress a person with this profile would suffer increased gastric secretions that could cause tissue damage. Alexander trained a generation of psychoanalysts as the head of the Chicago Institute for Psychoanalysis. Alexander and Dunbar’s formative influence on the growing field of psychosomatic medicine encouraged its psychoanalytical slant. As a result, by the beginning of the Second World War, the nascent field of psychosomatic medicine emerged as a major conduit of psychoanalytic principles, helping to integrate this once marginal field into mainstream psychiatry, and offering a somatic foundation to validate abstract mental and emotional problems. The maturation of psychosomatic medicine over the course of the 1930s created a systematically organized discipline and trained professionals that helped to rationalize the epidemic of war neuroses during the Second World War.\(^97\)


During the 1930s, the USNRC became interested in investigating psychiatric problems, creating the Committee on Problems of Neurotic Behavior in 1937 under the Inter-Divisional Committee on Borderland Problems of the Life Sciences. In 1938, the NRC’s Division of Psychology and Anthropology organized a conference on “Experimental Neuroses and Allied Problems,” which was attended by Josiah Macy, Jr., Foundation representatives Lawrence K. Frank and Frank Fremont-Smith. Frank and Fremont-Smith found the conference so fruitful that they offered $6,000 (approximately $100,000 in 2015 dollars) to fund a new journal of psychosomatic medicine. The creation of the journal *Psychosomatic Medicine* in January 1939, nine months before the invasion of Poland, “appeared to offer a view of the human mind firmly based in science,” and thus proved a strong foundation for this marginal, unorthodox field to eventually claim legitimacy.98 Yet, even still, for the first few years of its existence, the articles published in *Psychosomatic Medicine* were predominately authored by psychoanalysts who relied largely on individual patient case-studies, which lacked corroboration, and exhibited “little attempt to distinguish between fact and theory,” according to historian of the American Psychosomatic Society, Dorothy Levenson.99

Ironically, the loss of European subscription renewals during the course of the war led to a major advancement in the professionalization of psychosomatic medicine, the founding of a professional organization to unite researchers and support the publication of the journal. The creation of the American Society for Research in Psychosomatic Problems (ASRPP) was first proposed by Helen Flanders Dunbar in July of 1942, and after a surprisingly well-attended conference at New York’s Waldorf-Astoria Hotel that December, the fledgling organization

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99 Ibid., 49.
became a formal entity on May 11, 1943. The ASRPP culled together specialists in internal medicine, neurology, psychiatry and the medical sciences, providing a common agar for these distinct fields of research. From its first exploratory meeting in December of 1942, the ASRPP exhibited an interest in research to support the psychological health of soldiers, as evidenced by the meeting’s featured lecture on combat fatigue. Whereas, in the early years of the journal’s publication, most material was presented anecdotally, most articles were authored by psychoanalysts, and in general it exhibited “little attempt to distinguish between fact and theory,” the formation of the ASRPP signified a new concern to meet the standards of biomedical methodology that improved the credibility of the journal’s contents.\textsuperscript{100} For the duration of the war, \textit{Psychosomatic Medicine} published reports related to stress-induced disease and war neuroses, and by 1944 its readership had grown nearly three fold, to over 2,000 subscribers.\textsuperscript{101}

The war was a major catalyst for the professionalization of psychosomatic medicine. The very real loss of physical manpower due to psychological illness provided compelling evidence for the connection between physical and mental health, and the exigencies of the war effort offered psychosomatic researchers in different medical subfields a common ground for research, debate and activism. The wartime embrace of psychoanalysis for the treatment of war neuroses offered invaluable field experience to hundreds of psychiatric practitioners, provided numerous case studies documenting psychosomatic etiology, helped to develop effective therapeutic methods, and served as a major education conduit to sixteen million servicemen and the families and communities awaiting their return. Pioneers in military psychosomatic research, Lt. Col. 

\begin{footnotes}
\item [100] Levenson, \textit{Mind, Body and Medicine}, 46.
\item [101] Ibid., 65.
\end{footnotes}
William C. Menninger, and Roy R. Grinker were both active in the Advisory Board of *Psychosomatic Medicine* and the ASRPP.

As noted by Peter G. Bourne, a combat stress researcher at the Walter Reed Army Institute of Research during the Vietnam War, “combat psychiatry grew out of the need to care for individuals who under the stresses of battle suffered psychological disintegration.”

The tendency of combat to instigate psychopathologies was documented by medical experts at least as far back as the American Civil War. As discussed in the introduction, during the Civil War, Surgeon General of the Union Army, William Hammond noted the prevalence of cases of “nostalgia,” characterized by debilitating melancholia, severe homesickness and sometimes accompanied by physiological pathologies, such as palpitations, headaches, and nausea.

Also during the Civil War, the American physician Jacob Mendes Da Costa affirmed the somatic manifestations of combat-related neuroses, coining the term “irritable heart” (though, colloquially referred to as “Soldier’s Heart” or “Da Costa’s Syndrome) to describe a medical condition in which symptoms of cardiovascular distress, shortness of breath, chest pains, and palpitations, as well as sweating and fatigue are brought on by intense anxiety. The overwhelming numbers of neuropsychiatric casualties in the Russo-Japanese War led to the first use of military psychiatrists in the field, and in the First World War, American psychiatrist Thomas W. Salmon headed an official Neuropsychiatric Division overseeing the treatment of soldiers suffering from “shell shock” in the field, with the aim of expediting their rehabilitation and effectively returning them to duty. The British physician Lord Moran who served in the Royal Army Medical Corp during the First World War distinguished between the physical

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condition of “commotional shock,” and the psychological condition of “emotional shock,” in his influential book *The Anatomy of Courage*. Yet, this distinction was often overlooked in recognizing the larger significance of the medicalization of shell shock as evidence that “psychic stress and psychic stress alone could eventually turn the bravest man into a mentally disheveled remnant of his former self.”

Despite these advancements in the recognition and treatment of traumatic neuroses, the US military was ill equipped to treat psychopathologies of combat at the beginning of the Second World War. At the outset, there was a widespread sentiment that a decade of depression and a quarter-century of isolation had left Americans poorly prepared for war, and ill-suited to withstand German psychological warfare. In 1939, the William Alanson White Foundation formed a committee to mobilize civilian psychiatrists to assist the war effort, and the American Psychiatric Association (APA) created its own committee on Military Mobilization to support the Defense Department. In September 1940, the APA’s committee examined Canadian neuropsychiatric casualties at Christ Hospital for Veterans, and determined that many of the patients had predispositions to psychiatric illness that could have been detected in a more effective screening process, preventing the possibility of future breakdown in battle. As historian of World War II neuropsychiatry Rebecca Schwartz Greene has observed, “the Canadian military situation further convinced American psychiatrists that thorough screening was necessary” to implement a preventive approach to psychiatric health.


In October of 1940 the USNRC created its own subcommittee on neuropsychiatry to the Surgeon General of the US Army headed by Dr. Winfred Overholser of St. Elizabeth’s Hospital in Washington, D.C., and Harry Stack Sullivan, of the William Alanson White Psychiatric Institute.\(^{107}\) Sullivan and Overholser were keenly aware of the enduring problems associated with neuropsychiatric casualties and believed that they could be reduced through effective screening measures: since 1923 the United States had spent nearly $1 billion dollars on the treatment of the nearly 70,000 neuropsychiatric casualties from World War I, and as of 1940 mental patients occupied three out of five hospital beds in Veterans Administration hospitals.\(^{108}\) Sullivan and Overholser believed that such casualties could be largely reduced through effective screening procedures during the draft selection process, and together they designed a double-screening procedure aimed to detect and filter-out potential neuropsychiatric casualties. When he was appointed psychiatric advisor to the Selective Service in December of 1940, Sullivan implemented the double-screening procedure, training local draft board administrators to identify target behaviors, including mild maladaptive traits, such as emotional instability and reclusiveness, or chronic inebriety; compromised constitutional states, such as mental deficiency

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and neurosyphilis; symptoms of psychopathy, such as impulsive, delinquent or homosexual behavior; and personal or family histories of psychiatric or nervous disorder.\textsuperscript{109}

Unfortunately, even this targeted attention to psychiatric screening failed to effectively identify men with previous histories of mental imbalance. Sullivan resigned his post in November of 1941, and in response to a campaign spearheaded by the National Committee for Mental Hygiene to incorporate psychiatric procedures for documenting patient’s mental health histories in the screening process, Sullivan’s successor, Luther E. Woodward, a child psychiatrist with the New York City Department of Education, replaced it with a single comprehensive interview which documented each recruit’s life history.\textsuperscript{110} By the early-1940s, many psychiatrists had been introduced to Freudian psychoanalytical principles of repressed memory and the formative influence of early childhood experiences on adult personalities. Life histories were an integral part of the psychiatric profile, privileging environmental factors over fixed constitutional aberrations in the etiology and diagnosis of mental disturbances.

From 1942 to 1945, the Selective Service rejected approximately 1,875,000 men, twelve percent of the fifteen million who were examined, and eleven percent more than were rejected for service in World War I. Of the approximately sixteen million candidates approved for service, nearly 1,100,000 were treated for neuropsychiatric disorders, only 6-7 percent of which were due to psychosis (same as in WWI). Clearly, psychiatric screening was not sufficient to address the overwhelming number of neuropsychiatric casualties. US servicemen were in desperate need of psychiatric care. However, at the time of the attack on Pearl Harbor there were


only 35 psychiatrists in the Army, and less than 3,500 in the nation, 70-80% of whom worked in hospitals for mentally ill and therefore trained in the treatment of psychosis. The dearth of formally trained psychiatrists created an opportunity for psychoanalysts to contribute to the war effort—and to promote the scientific validity of their field in the process.

In August of 1942, Norman T. Kirk, Surgeon General of the US Army created a Neuropsychiatric Division within his office to advise him on psychiatric preparedness strategies. The Neuropsychiatric Division was initially directed by Dr. Roy D. Halloran, former superintendent of Metropolitan State Hospital in Boston. Halloran recruited mainstream psychiatrists drawn from the public hospital system, psychobiologists trained in the teachings of Adolf Meyer, and approximately 100 psychoanalysts educated in one of several new psychoanalytical institutes throughout the United States. “The psychoanalysts not only supplied key personnel, whose influence far outweighed their numbers,” as historian of the psychoanalytic movement Nathan Hale has observed, “they also developed theories, classification systems, and methods of treatment for the war neuroses,” which emphasized universal susceptibility fear and neuroses, as well as the fundamental influence of ego conflict in combat arising from the tension between opposing drives to fulfill one’s duty or maintain self-preservation. Under Halloran, the Neuropsychiatric Division appointed psychiatric consultants to general and field hospitals throughout both theaters of the war, and provided basic training in detecting neuropsychiatric illness for all medical staff and commanding officers. As of January 1943, the Neuropsychiatric Division created a psychiatric training school for the Armed Services at Lawson General


Hospital in Atlanta (later moved to Mason General Hospital in Brentwood, NY). The Army’s School of Military Psychiatry offered a four-week, 190-hour program of instruction, emphasizing psychoanalytical principles, like talk therapy, guided recall and morale-building to prepare psychiatric consultants for convalescent work in the field of combat. Students were drawn from diverse backgrounds in psychiatric training—organicism, psychobiology, psychoanalysis and Kraepelianism—and were provided clinical experience among the 250 to 300 neuropsychiatric patients routinely committed to the hospital. By the end of the war, more than 1,000 psychiatrists graduated from the training program.

As the military began to marshal psychiatric resources internally, the civilian community of professional psychiatrists continued to offer their assistance to the war effort, and strove to advance their own understanding of war-specific psychiatric concerns. The New York Academy of Medicine’s Thomas A. Salmon lecture series helped to advance military psychiatry by profiling the work of foreign psychiatrists with experience of treating neuropsychiatric casualties. In 1941, Dr. Robert Dick Gillespie, of the British Royal Air Force, and the following year, in 1942, Dr. Emilio Mira, former psychiatrist-in-chief for the Republican Army during the Spanish Civil War, each presented a series of lectures on the mental pathology of soldiers and civilians during wartime. Both Dr. Gillespie’s and Dr. Mira’s lectures were published as monographs, and became major conduits for communicating military psychiatric research to the larger professional community, and enhanced their capacity to offer support to military psychiatric


work. Civilian psychiatrists began formally contributing to the work of the Neuropsychiatric Division early in 1944 when Surgeon General Kirk asked the American Psychiatric Association to organize a civilian committee to act as consultants to the Secretary of War.117

The Neuropsychiatric Division

The neuropsychiatric consultants established mental hygiene units throughout both theaters of military operations, which treated soldiers suffering from combat-related afflictions. Their professional training made them sensitive to conditions that some interpreted as malingering. In January of 1944, the Washington Sunday Star printed a leaked press release drafted by General George Marshall, the Army Chief of Staff which erroneously reported that only one in five neuropsychiatric casualties were legitimate medical cases—the rest were alleged to be malingers. The article referenced General Marshall’s claims that neuropsychiatric rejections were dangerously jeopardizing Army manpower and that psychiatric disorders were not real sicknesses since they could not be physically documented, scientifically measured or objectively confirmed.118 The stigma of shell-shock still hung over neuropsychiatric casualties. Shell-shock patients were commonly considered to have suffered from constitutional weaknesses that


predisposed them to breakdown under the extreme pressures of war, and were considered to be irreparably weakened by their sickness. The involvement of psychiatrically trained medics in WWII, however, drew attention to the universal susceptibility of all servicemen to develop neurotic symptoms under the strain of combat, as well as the potential for future recovery if given access to effective treatment. Medical training in psychiatric principles enabled early recognition and treatment of symptoms of war neuroses. Neuropsychiatric interventions consisted of narcosynthetic treatment—combining sedation with talk therapy—and morale work.119 Because increased awareness of war neuroses was critical to early intervention, the Army filmed a series of group therapy lectures that educated combat units about potential threats to mental well-being and techniques to build health-protective group dynamics, and commissioned Frank Capra to create series of propaganda films, Why We Fight, to boost morale amongst servicemen and the general public.120 This health education campaign was instrumental in popularizing psychoanalytical principles—and troops retained this education long after their service.

Early in the war, military officials noticed a significantly higher rate of neurotic symptoms, such as fits of anxiety, extreme fatigue, irrational outbursts, and catatonia, among three principal groups: pilots, merchant mariners who survived torpedo attacks, and soldiers engaged in especially lengthy and bloody combat. Despite the rigorous examination process in selecting combat pilots, it seemed that the extreme pressures of aerial warfare eventually wore down even the most resilient and focused candidates. Given the frequency of cases of war neuroses among pilots, mental hygiene units began to refer to these particular cases as “flying

exhaustion,” or “pilot’s fatigue.” At a May 1943 symposium on military psychiatry organized by the American Psychiatric Association with the support of the Surgeon Generals of the Army and Navy, Lt. Col. John M. Murray of the Air Surgeon’s Office explained that the syndrome of “flying stress,” “arises chiefly as a result of the continuous and long-continued repression and suppression of the normal fear reactions present in all types of operational flying,” compounded by sleep loss and traumatic experiences, which eventually results in a break down signified by “hysterical and anxiety reactions, psychosomatic disorders, minor depressive swings, and mild hypochondriacal concerns,” and an aversion to flight.\textsuperscript{121} Victims of “flight stress” often suffered nightmares, phobias, hyper-sensitive startle reactions, aversions to loud noises, as well as physical symptoms of nausea, migraines, diarrhea, insomnia, anorexia, extreme muscular weakness, bed-wetting, and, perhaps the most common psychosomatic symptom of all, peptic ulceration.

A similar syndrome was observed in merchant seamen who had survived the sudden terror of German u-boat attacks. The problem was in fact so widespread, that in 1943 Surgeon General of the US Public Health Service (PHS) Thomas Parran convened a conference at the New York Academy of Medicine to discuss the development of ongoing therapeutic care for afflicted men. The proceedings of the conference ultimately led to the creation of a number of convalescent homes dedicated to the rehabilitation of afflicted seamen.\textsuperscript{122} Ground forces engaged in protracted and grisly battle, such as those undertaken in the amphibious New Georgia Campaign in the South Pacific in October 1943, and the Third Army’s 180-days of continuous engagement during the advance from eastern France into the Saar region of Germany, also


\textsuperscript{122} Deustch, , “Military Psychiatry: World War II, 1941-1943,” 440-41.
demonstrated a propensity to develop war neuroses, exhibiting symptoms including headaches, sensitivity to noise, amnesia, panic, muscular contractures or tremors, and palsies. The six-month siege of Guadalcanal beginning in August of 1943 produced a vast number of such cases, often referred to as “Guadalcanal nerves.”

The recognition of high rates of war neuroses in diverse fields of combat generated ad hoc nomenclature that reflected the subtle uniqueness observed among particular pools of patients. While it was not widely recognized during the war, in reality, marines suffering from “Guadalcanal nerves” experienced many of the same symptoms as pilots suffering from “flight exhaustion.” Furthermore, a patient suffering from gastric ulcers induced by the pressures of combat might be diagnosed with “gastric neurosis” by one doctor, or with “combat exhaustion” by another. As psychosomatic war neuroses were increasingly detected in isolated venues of the war, the lack of consistent diagnostic terminology proved to be a significant liability in documenting patients’ cases. In a report on psychosomatic medicine prepared for Surgeon General Kirk at the close of the war, Walter Bauer and Henry Brosin of the Neuropsychiatric Division remarked that “unsatisfactory nomenclature contributed to the ineffectiveness of the medical officer,” for example, if a patient suffered from an emotional or mental disability, “without apparent organic cause after painstaking examination, the medical officer in his role as a physiologist was keenly disappointed and more often than not at a loss for specific understanding and concrete treatment of the presenting complaint.”


124 Walter Bauer and Henry W. Brosin, “Psychosomatic Medicine in World War II,” unedited manuscript (December 5, 1945) Internal Medicine – Diseases – Psychosomatic
During the North Africa campaign, Roy Grinker, Chief of Neuropsychiatry at Michael Reese Hospital in Chicago and board member of the ASRPP, and his 32-year-old resident, John Spiegel, who was also in training at Franz Alexander’s Psychoanalytic Institute, developed a narcosynthetic method of treatment that combined the use of sodium pentathol to sedate patients and enable them to engage in individual and group talk therapy. Therapy sessions were aimed at resolving ego conflict and building group morale. Occupational therapy which made soldiers feel useful, and a speedy return to service—rather than infantilizing bed-rest or sick leave—were instrumental in restoring soldiers’ confidence in their own health and return to service. Through narcosynthesis, Grinker and Spiegel were able to return 72 percent of their nearly 1,200 patients to some form of duty, though very few were ever able to return to full combat.\footnote{Hale, \textit{The Rise and Crisis of Psychoanalysis in the United States}, 195.}

One particularly decisive factor in the success of this treatment was expeditiousness. Grinker and Spiegel found that the closer to the field of battle that a soldier was treated, the faster he could be expected to recover. In order to empower combat units to provide emergency care to neuropsychiatric casualties, Grinker and Spiegel published a therapeutic manual with the support of the Josiah Macy, Jr., Foundation. 45,000 copies of \textit{War Neuroses} were distributed to service personnel, instructing them on the identification of neuropsychiatric symptoms and the administration of narcosynthetic treatment. They explained that due to the diversity of soldier’s personalities and life histories, the symptoms of war neuroses could include, “startle reactions to sudden noises, amnesia, disturbed sleep, restlessness, fear, marked tremors, jerking limbs, incontinence of urine or feces, dejection, depression, confusion, occasional hysterical paralyses, recurrent nightmares, sudden fits of laughing or crying, muteness, feelings of weakness and

\footnote{Diseases, RG 112 Records of the Office of the Surgeon General (Army), 1775 – 1994, National Archives at College Park Maryland.}
dizziness, and functional gastric and heart disturbances.”¹²⁶ To some degree, a soldier’s neurotic symptoms may have been conditioned by previous behavior—for instance, if he had a history of gastro-intestinal problems or migraines, these conditions might be exacerbated by the stress of war. This connection between physical disorders and mental anxiety seemed to validate the psychosomatic theory of disease. It also endorsed a holistic and individualized style of treatment. Because soldiers could respond to “combat stress” with such a diverse variety of symptoms, it was necessary to cater treatment to each individual case.

With War Neuroses, Grinker and Spiegel also sought to destigmatize soldiers suffering from acute neurotic conditions. They insisted that there was an extremely low rate of malingering in the war, and that even if a soldier attempted to feign neuroses, treatment with pentothal would expose the farce. “The greatest problem associated with malingering,” they argued, “is the ready conclusion by many medical officers that mild neurotic symptoms and conversion phenomena are simulated.”¹²⁷ Education was necessary in order to spread awareness that war neuroses did not arise from a “lack or moral fiber,” but an understandable failure to adapt to a traumatic military environment. There was no difference between healthy soldiers and neuropsychiatric casualties except for the intensity and persistence of their anxiety. In fact, it may “be a more rational question to ask why the soldier does not succumb to anxiety, rather than why he does.”¹²⁸

Ralph Kaufman, one of the original instructors at the Army’s School of Military Psychiatry at Lawson General Hospital, later appointed as head psychiatric consultant during the


¹²⁷ Grinker and Spiegel, War Neuroses, 47.

¹²⁸ Ibid., 4, 115.
Tenth Army’s campaign against the Japanese at Okinawa and Guadalcanal embraced Grinker and Spiegel’s techniques, but found that sodium pentathol could actually “intensify amnesia and increase confusion, obstructing the recovery of forgotten memories,” and instead developed “a method of hypnosis that could be used close to the battlefield.” Kaufman found success with these methods, returning 83% of psychiatric casualties to duty.\textsuperscript{129} In the European theater, during the Italian Campaign, Frederick Hanson treated neuropsychiatric casualties with “simple exhortation and reassurance, rest, and sedation,” emphasizing the role of physical exhaustion and emotional stress in generating combat neuroses. Kaufman disapproved of Hanson’s therapeutic methods on the grounds that he was merely treating soldiers’ fatigue, and not the underlying psychological problems that produced their neurotic crises.\textsuperscript{130} These therapeutic discrepancies were accompanied by a dispute over the nosological classification of war neuroses. Karl Menninger, head of the Menninger Psychiatric Clinic in Topeka, Kansas and the brother of the second Director of the Neuropsychiatric Division, William Menninger, argued that the term “neuroses” inevitably stigmatized soldiers suffering from extreme fatigue. As an alternative, he favored the term “combat exhaustion.”\textsuperscript{131}

Many military and civilian psychiatrists feared that the proliferation of new diagnostic terminology during the war undermined the validity of these conditions. Edward A. Strecker, President of the American Psychiatric Association and consultant to the Secretary of War and the Surgeons General of the Army, Navy, and PHS worried that,

\textsuperscript{129} Hale, \textit{The Rise and Crisis of Psychoanalysis in the United States}, 196.

\textsuperscript{130} Ibid., 197-198.

\textsuperscript{131} Ibid., 198. When Col. Halloran died unexpectedly in November of 1943, he was succeeded by Lt. Col. William C. Menninger, see Deutsch, 429.
our psychiatric terminology is anachronistic, esoteric, difficult, irrational, and forbidding. It confuses our medical confreres, creates resistance, and isolates our understanding and help which should be available to medical colleagues. There is a crying need for a new terminology which is rational, not recondite, and which will be related to the familiar concepts of medicine and physiology. Our very terminology has isolated us and prevented a desirable and necessary permeation of psychiatry into medicine and medical education.\textsuperscript{132}

Clarity, consistency and accessibility were paramount to the validation and successful assimilation of these new psychosomatic theories in the larger medical field, and the public sphere. By the end of the war, the diverse range of terms used to refer to war neuroses during the Second World War—“combat exhaustion,” “pilot fatigue,” “flight stress,” “Guadalcanal nerves,” etc.—gradually gained a uniform medical identity as “combat stress,” offering the scientific community a consistent terminology with popular appeal. Grinker and Spiegel’s \textit{Men Under Stress}, a synthesis of their wartime research published in 1945 for a professional civilian audience, was instrumental in popularizing this linguistic shift.\textsuperscript{133}

The psychosomatic concept of stress also gained scientific credence through the conscientious efforts of Lt. Col. William Menninger. Trained by Franz Alexander in psychoanalysis and a strong proponent of psychosomatic theory, Menninger vociferously defended the “realness” of war neuroses against the brazen refutations of General Marshall, and other military officials. He insisted that most neuropsychiatric casualties were perfectly healthy, normal men before the war, many of whom were even cited for bravery in battle. However, the extreme pressures of combat eventually weakened their capacity to function normally. War made healthy men sick, through no fault or predisposition of their own. In order to defend the honor of neuropsychiatric casualties, Menninger sought to emphasize the scientific basis of war


neuroses. In 1944, he issued “Neuropsychiatry for the General Medical Officer,” using medical jargon to explain how subconscious conflict and repressed childhood experiences could be unleashed by the trauma of combat.\textsuperscript{134} On October 8, 1945, Lt. Col. Menninger delivered the annual Ludwig Kast Lecture at the New York Academy of Medicine on “The Modern Concept of War Neuroses,” explaining the enduring problem of war neuroses among the 315,000 returning veterans who had been discharged for neuropsychiatric illness.\textsuperscript{135} He insisted that “combat exhaustion” was a “normal response to abnormal situations in which the stress was far more severe than in civilian life,” and while most neuropsychiatric casualties could resume functional and productive work, their weakened conditions would require ongoing psychiatric care.

VI. Popularizing “Stress”

To a considerable extent, the success rate of neuropsychiatric treatment during the war did much to demonstrate the scientific validity of psychosomatic theory and treatment, with a recovery rate of nearly eighty percent among those who broke down in combat. Yet still, American servicemen suffered from a significantly higher rate of neuropsychiatric casualties than other nations. Nearly half of all medical discharges in the US Armed Forces (approximately 44,000 men) were for neuropsychiatric reasons, versus 17 percent among Russian troops, and 30 percent among the British.\textsuperscript{136} The sheer volume of American neuropsychiatric casualties helped to

\textsuperscript{134} Hale, \textit{The Rise and Crisis of Psychoanalysis in the United States}, 200.


\textsuperscript{136} Hale, \textit{The Rise and Crisis of Psychoanalysis in the United States}, 203-204; Greene, \textit{The Role of the Psychiatrist in World War II}, 531.
spread public awareness of and belief in the validity of “combat stress.” As veterans returned home, with stories of afflicted comrades or their own experiences of “combat stress,” the American public became intimately aware of the very realness of this disease. This mass cultural experience is depicted in the wildly popular Best Picture of 1946 (and recipient of six additional Academy Awards), *The Best Years of Our Lives*, which follows the story of four veterans struggling to assimilate to civilian life.

Persistent symptoms among veterans also created new public health concerns in providing psychiatric treatment for former servicemen. In 1948, the USNRC’s Committee on Veterans Problems found that among 1,475 enlisted men aged 18 to 25 who had been hospitalized for psychoneuroses in 1944, approximately 27 percent had no psychiatric illness, 33 percent had mild disorders and 25 percent had moderate or severe disorders and 11 percent suffered from personality or behavioral disorders. At least 40 percent exhibited symptoms including irritability, anxiety, gastrointestinal problems, and headaches—only 10 percent were entirely free of symptoms and most of the men reported that they felt their health was still worse than before they had entered the service. While over three-quarters of the men were employed full time, 14 percent were unable to hold full time jobs due to neuropsychiatric illness. A number of organizations, including the NCMH, Red Cross, the Veterans Administration and the War Manpower Commission supported the War Department and the PHS in educating the public about returning neuropsychiatric casualties to diminish the stigma of neuroses, and developing rehabilitation programs for psychiatric victims of war.

The experience of the neuropsychiatric consultants during the war taught that early intervention, psychoanalytic talk therapy, sedation, rest and exhortation were remarkably

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successful in returning neurotic patients to normal health. Consequently, while some of the postwar rehabilitation services developed clinical facilities to treat extreme cases of neuroses, most of them focused on providing outpatient services and education. The passage of the National Mental Health Act of 1946 heralded a new community-based initiative for mental health care and a mounting tide of deinstitutionalization, which increased public awareness of mental illness while providing new sources of funding for outpatient clinics (see Chapter Five).138 By 1947, nearly half of all psychiatrists in the United States worked in outpatient clinics or private practices (not state institutions).139

The community-orientation of mental health was facilitated by a massive expansion in the number of psychiatrists practicing in the United States, which rose from 1,346 in 1930 to 2,423 in 1940 to 5,856 in 1950.140 The vast majority of psychiatrists in the postwar US worked in private practice, however nearly twenty percent aided in the rehabilitation of neuropsychiatric casualties through work with the Veterans’ Administration (VA). By 1954, the VA employed ten percent of all US psychiatrists and enlisted another ten percent as consultants.141 Psychiatrists also began to favor private practice over institutional work as they became disillusioned with the overwhelming number of chronic psychotic patients in state hospitals, as well as the divestment of funding for these hospitals spurred by reports of ineffective and


139 Greene, The Role of the Psychiatrist in World War II, 528.

140 Ibid., 495, citing APA Membership, Carolyn Gifford, American Psychiatric Association Library.

141 Ibid., 530.
inhumane therapeutic practices. Albert Deutsch’s *The Shame of the States* helped to raise public awareness of the use of shock treatments, lobotomies, and potentially dangerous restraint methods in public and VA hospitals, as well as a widespread problem of inattention and indifference to patients’ needs. Mary Jane Howard’s novel *The Snake Pit*, which was released as a film in 1948, vividly depicted (and propagandized) the monstrous treatment of patients in state hospitals, heightening public concern and criticism of institutional psychiatric care.

As psychiatry moved outside of the institution, it became more conspicuous, and the public became more aware of psychiatric problems, concepts and treatments. Because postwar psychiatry was imbued with the psychoanalytical practices of wartime combat stress research, the popularization of psychiatry also helped to popularize the medical concept of stress. The war’s pathologization of psychological stress also helped to universalize and normalize it as a disease concept. Postwar North America assimilated a disease concept of stress that acknowledged environmental factors (rather than merely constitutional predisposition) as contingent influences on mental and physical health, and that perceived a dynamic continuum of health. These lessons of the war were of special relevance to civilians, for if healthy, young recruits suffered such high rates of neuropsychiatric problems, certainly the rest of the population might be less resilient to stress.

When the APA published their first *Diagnostic and Statistical Manual* in 1952—a watershed in the codification of new diagnostic and etiological categories that grew out of a classification scheme developed by the Army—*it emphasized environmental stress as a disease concept.*

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142 Grob, *Mental Illness and American Society.*

precipitating cause of neuroses, and defined stress as “the immediate emotional, economic, environmental, or cultural situation which is directly related to the reaction manifest in the patient.” The DSM-I created a classification for “gross stress reaction,” explaining that “under conditions of great or unusual stress,” such as extreme emotional or physical demands such as those suffered in war or natural catastrophe, “a normal personality may utilize established patterns of reaction to deal with overwhelming fear,” however, “when promptly and adequately treated, the condition may clear rapidly.”

Conclusion

World War II research on combat stress helped to universalize and destigmatize psychosomatic health and anxiety by associating mental stress with physiological symptoms and demonstrating its dynamic nature, these claims were endorsed by a scientific theory of disease advanced by a large group of medical professionals. The credibility that military research offered to psychosomatic medicine, military psychologists’ efforts to promote awareness of combat stress, the social education stimulated by hundreds of thousands of returning veterans accustomed to the reality of war neuroses, and the domestic media coverage of the war, encouraged the assimilation of the disease concept of stress in postwar North American society.

The popularization of the concept of stress offered Selye a linguistic devise that resonated in popular consciousness to describe the diverse harmful agents that induced degenerative disease. However, he did not experience an abrupt linguistic paradigm shift. Rather, he began to


use the term “stress” sporadically through the course of his publications from the late-1930s to the mid-1940s to variably describe harmful agents or a state induced by exposure to harmful agents. Because he was only gradually drawn to embrace this term to describe his research, he contributed to developing an ambiguous and unclear meaning of the nature of stress.

Yet, by the end of the war—likely due to the medical validation of the psychiatric theory of “combat stress”—Selye had come to fully embrace “stress” as the quintessential descriptor of the adaptive response to adverse stimuli. In the Spring of 1946 he published a grand synthesis of his theory of the GAS repeatedly describing “nocuous agents” as “stress.” The following year he also published a *Textbook of Endocrinology*, presenting an overview of the most current research in hormonal regulation of disease. First published in 1947, Selye’s *Textbook of Endocrinology* went through five printings by the end of 1948 (and a second edition in 1949) and quickly became the standard textbook for most medical schools in North America, educating a new generation of postwar medical professionals in the fundamental principles of Selye’s cutting-edge theory of stress. The first chapter of his textbook specifically outlined the basis of multicausal degenerative disease, claiming that, “the main, fatal syndromes of internal medicine (various cardio-vascular, renal, ‘rheumatic’ and old age diseases)… are probably by-products of faulty hormonal adaptive reactions to a variety of non-hormonal pathogenic agents,”

145 Organizational psychologist, Tim Newton has argued that since Selye did not outline a theory of stress until immediately after World War II, that the war itself must have been critical to the development of this theory (even despite Selye’s later insistence that his theory originated before the war). See Newton, ‘Managing’ Stress, 24. See also Theodore M. Brown, “‘Stress’ in US Wartime Psychiatry: World War II and the Immediate Aftermath,” in *Stress, Shock and Adaptation in the Twentieth Century*, 121-141.


147 Selye, *The Stress of My Life*, 89.
indicating a general maladaptation to stress. “The apparent cause of illness,” he continued, “is often an infection, an intoxication, nervous exhaustion or merely old age, but, actually, a breakdown of the hormonal adaptation-mechanism appears to be the most common ultimate cause of death in man.”¹⁴⁸

Selye’s own wartime research on conditioning factors that affected the adreno-pituitary regulation of diseases of adaptation helped to demonstrate the multicausal nature of these diseases, and in so doing, open scientific investigation of potential risk factors that contributed to these diseases. What would emerge was a therapeutic theory that placed responsibility for risk avoidance in individuals’ lifestyle decisions. This program of behavior modification carries its own psychosomatic implications—if you can control your susceptibility to disease through behavioral choices, then your mind ultimately governs your physical health. Selye did not seem to fully appreciate the confusion he would generate by using this psychological term to describe biological stress. However, by aligning himself with the burgeoning field of psychosomatic research, Selye gained a kindred group of heterodox medical researchers struggling for legitimacy, who had made great strides in improving their professional reputation over the course of the war (discussed in greater detail in Chapter Four).

Additionally, Selye’s inadvertent muddling of biological and psychological concepts of stress, perhaps ironically, created a scientific basis for more holistic investigations of health that examined the relationship between the mind and the body. By the early-1950s, Selye reflected that, “it was only gradually, through habit rather than logic, that the term [stress] slipped into common usage, as the concept itself became a popular subject for research,” revealing a

decidedly un-scientific process for the development of new medical terminology.\footnote{Selye, \textit{The Story of the Adaptation Syndrome}, 41.} \footnote{Selye, \textit{The Story of the Adaptation Syndrome}, 41.}

Characterizing the medicalization of stress as a process guided by changing customs rather than “logic” enabled an ambiguous definition to coalesce from the diverse fields of research that employed this term. Consequently, as “stress” emerged as a disease concept, it merged biological and psychological etiologies with a conspicuous lack of scientific precision, yet a great deal of functional value.
Chapter 3: Stress, Multicausal Disease and the Health of the Public

Introduction

The transformation of the political economy of medical research in the postwar period generated new funding incentives and investigative priorities. As the US federal government and the pharmaceutical industry took on newly powerful roles in supporting academic research, they both placed great importance on applied research that promised social benefits or marketing appeal.¹ Both state and corporate research funders found the emergent disease concept of psychoendocrine stress, to be an exceptionally appealing field of research and investment, as it promised to address the unique therapeutic needs of the postwar patient population. As “diseases of adaptation,” such as heart disease, cancer and arthritis were becoming increasingly prevalent due to the epidemiological transition that reduced mortality from infectious disease and extended life expectancy, biological stress provided an explanation for the most prevalent health complaints of North Americans. Selye offered an etiological interpretation that emphasized individual differences of lifestyle, while at the same time universalizing potential susceptibility. The concepts of stress, conditioning factors and adaptive disease helped to substantiate the emerging risk factor model of multicausal disease in the postwar period.

In the midst of this structural and diagnostic transition, Selye attracted recognition for his innovative research on the adrenal-pituitary regulation of chronic disease, and particularly, the conditioning influence of diet. He used his growing scientific authority to further develop lucrative funding relationships with state agencies and pharmaceutical companies. In 1945, he moved from McGill to the University of Montreal to direct his own Institute for Experimental

¹ The National Institutes of Health (NIH) also funded basic research on chronic diseases, though prioritized immediate public health risks. Because it was one of the few sources of funding for basic research in postwar North America, the NIH ultimately emerged as Selye’s largest source of funding.
Medicine and Surgery (IMCE)\(^2\), made possible, in part, by Frank W. Horner, Ltd.’s generous donation of a Victorian house to be converted into a state-of-the-art laboratory facility for the exclusive use of Selye’s institute. For the rest of the decade, Selye continued to rely on gratis chemical preparations from pharmaceutical firms, and the IMCE’s operational costs were funded by grants from numerous pharmaceutical firms, as well as US and Canadian federal government agencies—especially the newly reorganized US National Institutes of Health.

With Selye’s theory of adaptive disease now more soundly developed, he began to employ new terminology to describe how undue “stress,” exacerbated by poor diet, contributed to the development of ulcers, hypertension, and arthritis. Selye prescribed diets low in protein and salt, and high in carbohydrates to reduce the adverse cardiovascular manifestations of the GAS. However, diet-modification could only discourage the onset of disease or help to manage advanced stages of disease—it did not offer a cure. It was not until the commercialization of cortisone in 1948 and ACTH in 1949 that adrenocortical hormones were actually proven to effectively treat some chronic diseases. The pharmacological revolution generated by the therapeutic discovery of cortisone and ACTH finally validated Selye’s theory of stress.

I. The Institute for Experimental Medicine and Surgery

In the summer of 1945, the University of Montreal offered Selye an opportunity to found his own research institute, the Institute of Experimental Medicine and Surgery. The creation of the IMCE was made possible, in part, by the infusion of capital and infrastructural development offered through the Dominion Government’s intervention in the University of Montreal’s

\(^2\) As the University of Montreal is a French-speaking institution, Selye’s institute was officially named L’Institut de Médecine et de Chirurgie Expérimentales, and abbreviated as “IMCE.”
financial administration during the war. Moving to a newly constructed campus at the end of the war, the University did not have the resources to rebuild multiple departments and decided to invest in the development of at least one top-notch department: the IMCE.\(^3\) The IMCE was also directly funded by grants from a number of pharmaceutical firms, as well as philanthropies and the US federal government. The Canadian pharmaceutical firm, Frank W. Horner, Ltd., together with Gelatin Products also awarded Selye a three-year grant of $50,000 (approximately $593,000 in 2015 Canadian dollars) to support research at the IMCE.\(^4\) Selye also collected smaller grants from a number of US and Canadian pharmaceutical firms, including $1,200 (just over $12,000 in 2015 dollars) from Billhuber-Knoll Corporation, $1,200 from Schering Corp.-Montreal, and $4,500 from Des Bergers-Bismol Laboratories. In its first year of operations, the IMCE was also supported by a $2,000 grant from the Josiah Macy, Jr., Foundation and a $1,200 grant from the USNRC.\(^5\)

In addition, Selye brought with him a deed of property given to him by Frank W. Horner: The “Old Morgan Home,” a grand Victorian house on University Street adjacent to the University of Montreal campus became the headquarters for his new institute.\(^6\) According to the Montreal Gazette, “Dr. Selye said that the new building would be used mainly to promote further


\(^6\) “Memorandum of Agreement, Frank W. Horner Limited and the Royal Institution for the Advancement of learning,” November 1944, HSC; “Old Morgan Home to Be Used As Laboratory for Research,” *Montreal Daily Star*, September 20, 1944, folder I: Newspaper clippings, HSC.
research and graduate training along the lines of hypertension, rheumatic fever and hormonal products,” and hired thirty-five employees to staff the research and administrative needs of the IMCE. In order to smooth Selye’s transition from McGill to the University of Montreal, an arrangement was established in which the IMCE would share medical faculty from both universities, and was heralded as a testament to the enhanced prestige of Canadian science and academic research in Montreal.

Selye’s institute was an extremely orderly and efficient enterprise, reflecting his own professional and personal principles. The code of conduct included a mandate to never put off until later work that could be done at once, to never repeat procedures that another investigator had already performed, and to never perform work that someone of lesser training could capably carry out. Complimenting this protocol for efficiency and productivity was a credo of investigative curiosity and creativity. Selye set out “Maxims of the IMCE” which commanded:

1. If at all possible, do it now
2. If not possible now, “follow-up”
3. Never do yourself what a less qualified person could accomplish
4. Site visits
5. Flexibility of structure
6. Explain by example, not by argument
7. Keep a reserve list of agenda
8. Don’t touch what is going well
9. Give responsibility to the person who wants it
10. Smooth transfer of duties
11. Never overrule the decisions of a chief
12. Stop arguing as soon as your interlocutor has fully understood your point
13. Do one thing at a time, but many things concurrently
14. Never follow a “great idea” after the bottom has dropped out of it

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7 “Morgan Home is Donated to McGill as Annex to Faculty of Medicine,” *Montreal Gazette*, September 30, 1944, folder I: Newspaper clippings, HSC.

8 “A New Medical Center,” *Montreal Daily Star*, October 17, 1945, folder I: Newspaper clippings, HSC.

9 “Maxims of the IMCE,” folder: E: Institut de Médecine et de Chirurgie Expérimentales, HSC, emphasis added.
These basic tenets fostered an atmosphere that enabled the 35 researchers at the IMCE to coordinate their labor for maximum productivity. From its inception, the IMCE also exhibited a commitment to preserving the vastly expanding scholarly literature on new discoveries in endocrinology, carefully filing periodical reprints and monographs in the library that Selye had initially inherited during his fellowship at McGill from his mentor, Professor Beidl in Prague, and had since grown to over 200,000 works. By the end of the 1940s, the IMCE’s library was widely recognized as the world’s largest collection of scientific literature on endocrinology.  

As the head of his own laboratory, he developed funding relationships with numerous pharmaceutical companies and won contracts and fellowships from the US and Canadian federal governments and philanthropies. State and corporate contracts were crucial to Selye’s independence as a researcher and enabled him to cultivate a reputation as an expert authority on the hormonal regulation of stress. As he entered a new phase of his career, Selye also began a new phase of his research on the GAS, signified by the publication of a grand synthesis of his theory and supporting research in a special edition of *The Journal of Clinical Endocrinology*.  

Based on research funded by the Josiah Macy, Jr., Foundation and the Commonwealth Fund, versions of the 93-page, three-part opus appeared in at least six journals around the world in the Spring of 1946, though it was originally written in 1944 and presented before the first annual convention of the American Academy of Allergy.

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This article outlined the various phases of the GAS, the hormonal secretions and pathological changes associated with each phase, and the pathways by which these hormonal changes induced chronic diseases. Building on his description of the alarm reaction published in the *Cyclopedia of Medicine, Surgery and Specialties* in 1940, Selye further explained how the struggle to adapt to adverse environmental factors can contribute to the development of “diseases of adaptation,” such as hypertension, nephrosclerosis, rheumatic fever, periarteritis nodosa, gastro-intestinal ulcers, eclampsia and allergies, mediated by certain conditioning factors,13 stressing dietary risk factors such as high protein and salt consumption, fasting, and possibly nervous disturbances, such as surgical enervation. Selye now defined the GAS as “the sum of all non-specific, systemic reactions of the body which ensue upon long continued exposure to stress.”14 This entailed that over time, exposure to undue stress strained normal endocrinological mechanisms of adaptive defense, contributing to the onset of disease. As a result, “some of the

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13 Selye named the following potential conditioning factors: “cortical extracts increase resistance to traumatic shock, muscular exercise, colchicine, peptone shock, intraperitoneal injection of hypertonic glucose solution, KCl [potassium chloride], water intoxication, histamine, intestinal distention, menstrual toxin, microbial toxins and infections, partial hepatectomy, anoxia, heat, veronal, toxic tissue extracts, et al.” As well as in the “treatment of celiac disease, hemoconcentration due to ether anesthesia, acute confusion during typhoid fever or the puerperium, various acute infections, especially typhoid fever and diphtheria, psychoses, exhaustion due to fever therapy, burns, allergy, premature infants, ‘fetal shock’, tuberculosis, damage due to heat, cold or x-rays, etc.” See Selye, “The General Adaptation Syndrome and the Diseases of Adaptation,” *Journal of Clinical Endocrinology*: 164-65, 166.

most common fatal disease of man are due to a breakdown of the hormonal adaptation mechanism” caused by stress.¹⁵

Notably, throughout this article, Selye identifies a number of “stimulating” or “noxious agents” that instigate the GAS—including infections, cold, nervous strain, physical exercise and anoxia—and repeatedly insists that these agents generate “stress” (and “strain”), which essentially destabilize homeostasis and triggered the GAS. Because Selye’s grand synthesis of his research over the past decade appeared simultaneously in several journals throughout the world, it commanded attention from an extremely broad readership. In doing so, Selye announced to the world that he had embraced the term “stress” to describe his biological syndrome despite his initial fears that it would create unnecessary controversy. Selye also attracted the attention of the popular press, which promulgated the theory of stress to the masses. In December of 1946, *Life* profiled Selye’s work in a multi-page spread with detailed histological images, which conveyed to its readers that “the unrelenting stress of civilized life…overwork, fear and exposure,” placed excessive demands on regulatory adrenal hormones and led to “diseases of civilization.”¹⁶


Yet even as professional and public audiences became more receptive to his research, Selye compounded his critics’ ire and contributed to confusion about the nature of stress by failing to distinguish between stress as a cause or effect of disease. For the next decade his usage would waiver between claiming that “stress” caused the GAS, and that the GAS was itself a state of stress. This inconsistency fueled criticism that Selye’s theory was imprecise and unscientific for confusing pathways of causation, and for obscuring the actions of specific disease agents in

favor of an abstract catalyst.\textsuperscript{17} Selye would later reflect that “again and again, in the discussion periods that followed my lectures on the G-A-S, someone would get up and ask why I have to speak of ‘stress’ when I actually used formalin, cold or x-ray,” to which he would reply that adrenal stimulation was not exclusively stimulated by any one of these stimuli, but by the general condition of distress which they induced.\textsuperscript{18}

Though Selye was comfortable in the abstract nature of the term, many of his colleagues considered it “a purely hypothetical,” unreal entity that could therefore never be isolated, or objectively measured. To such allegations, Selye would point out that life itself is an abstraction, but is still a useful scientific concept.\textsuperscript{19} In retrospect, Selye would later admit that he consciously opted to “use an already accepted word in a newly defined sense,” much like Pavlov did in applying the word “conditioning” to describe a process of physiological sensitization. In doing so, Selye was able to appropriate cultural legitimacy based on the pre-existing connotations of stress, rather than “creating even more antagonism by a neologism.”\textsuperscript{20} Moreover, he would later confess that,

\begin{quote}
Frankly when I made this choice I did not speak English well enough to know the difference between ‘stress’ and ‘strain.’ In physics, ‘stress’ refers to an agent which acts upon a resistant body attempting to deform it, whereas ‘strain’ indicates the changes that are induced in the affected object. Consequently I should have called my syndrome the ‘strain syndrome.’ However, I was not aware of this subtle difference besides, at first I did not clearly distinguish between the causative agent and its effect upon the body.\textsuperscript{21}
\end{quote}

\textsuperscript{17} Selye, \textit{The Story of the Adaptation Syndrome}, 40.
\textsuperscript{18} Ibid., 40.
\textsuperscript{19} Ibid., 41.
\textsuperscript{20} Selye, \textit{The Stress of My Life}, 69-70.
\textsuperscript{21} Ibid., 70.
In his autobiography, *The Stress of My Life*, Selye complained of feeling constantly assaulted by critics in the first few decades of his work on the GAS, yet increasingly finding influential defenders of his research. He recalled one incident that occurred while he was still working at McGill, in which a young intern condemned his adherence to the concept of nonspecificity for “holding back progress… by centuries!” To which J.C. Meakins, the head of the McGill Medical School retorted that the young intern could rest safe knowing that “no one will ever say that about [his] work.”

While Selye remained primarily interested in elaborating the GAS, he found ways of making his still controversial and marginal theory relevant to a burgeoning study of chronic disease. The postwar period was marked by a substantial increase in life expectancy and an attendant epidemiological shift from mortality by infectious disease to a much higher prevalence of chronic disease. In the first year of the twentieth century, the average life expectancy for Americans at birth was 49.2. By the end of World War I, it had risen to 56.4, at the outset of World War II it had reached 63.6, and by 1950, the average American newborn was expected to live to the age of 68.1. The median age rose steadily from 22.9 in 1900 to 30.2 in 1950, while the total number of Americans over age 65 increased from 3.1 million (4.1 percent of the population) in 1900 to 12.3 million (8.1 percent of the population) in 1950, and rose by at least 4 million every decade thereafter.

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The rising standard of living facilitated both investment in science and Americans’ capacity to afford medical treatment, as well as state and federal investment in medical facilities that improved increased access to hospital care. Whereas, at the beginning of the twentieth-century, most Americans thought of hospitals as places of last resort, where one would reluctantly go to die, by mid-century they had by-and-large developed a faith in the efficacy of modern hospital care. In the year 1949, more than 16 million Americans were admitted to bed-care in US hospitals, and more than 86 percent of births were delivered in hospitals—compared to 37 percent only fourteen years earlier.\footnote{25} With increased access to hospital care, both the infant and maternal mortality rates decreased, the former from 100 to 31 per 1,000 live births between 1915 and 1949, and the latter from 57 to 9 per 10,000 from 1936 to 1949.\footnote{26}

Public health advancements that concentrated on environmental and hygienic interventions helped to reduce exposure to toxins. Water purification, sewer and reservoir construction, milk sterilization, and simple-hand-washing diminished the toxicity of common daily activities. New standards for food and drug purity protected consumers from potential poisons. And health literacy campaigns and visiting nursing programs helped to educate Americans about preventive strategies to protect their health. Americans were also living longer thanks to bacteriological advancements that enabled them to survive infectious diseases. At the


\footnote{26}{Williams, \textit{The United States Public Health Service, 1798-1950}, 800.}
beginning of the century, the three leading causes of death were pneumonia, influenza and tuberculosis. By 1951, Assistant Surgeon General, Ralph Chester Williams reported that pneumonia and influenza had decreased by 81 percent, and tuberculosis by 85 percent, while other communicable diseases that diminished life expectancy, such as typhoid fever, enteritis and diarrhea had decreased by over 95 percent, and common childhood diseases, like diphtheria, measles, scarlet fever and whooping cough had “almost been eliminated.” As a result, the vast majority of deaths (eighty percent) occurred among Americans over age 45 (compared to 46 percent in 1900).

As more and more Americans escaped mortality from infectious disease in their youth, they fell victim to chronic diseases in their old age. By the end of the 1940s, the leading causes of death had become heart disease, cancer and intracranial lesions (caused by stroke, cerebral hemorrhage, apoplexy, or other vascular disorders). In 1949, heart disease and cancer alone accounted for nearly fifty percent of all deaths, with the US death rate from heart disease at 351.5 per 100,000, and that of cancer at 137.6 per 100,000. In Canada, heart disease accounted for more than forty-five percent of all deaths. Heart diseases, including high blood pressure, arteriosclerosis, cardiac lesions, coronary thrombosis, and angina pectoris, emerged as the number one killer in North America, accounting for more death than the combined total of deaths caused by the next five major causes—cancer, accidents, nephritis, pneumonia and tuberculosis.


28 “Heart Disease Toll Heavy,” *The Montreal Daily Star*, October 3, 1948, folder I: Newspaper clippings, HSC.

29 George H. Waltz, Jr., “The Case of the Tired Heart,” *Maclean’s Magazine*, June 1, 1947, folder I: Newspaper clippings, HSC.
Older Americans also suffered from non-fatal, yet chronically disabling diseases, such as arthritis, rheumatism, cerebral palsy, multiple sclerosis and poliomyelitis, as well as mental diseases.\textsuperscript{30} The rise in chronic disease morbidity and mortality required an alternate method of therapeutic intervention that was more comprehensive and individualized. In 1949 there were an estimated 7.5 million Americans, and in 1950 one million Canadians suffering from arthritis.\textsuperscript{31}

Moreover, the aging patient population and changing disease demographics transformed patient needs, demanding that medical professionals, pharmaceutical manufacturers, academic researchers and politicians confront the new prevalence of chronic diseases. The public not only experienced this shift themselves, but became more acutely aware of the dynamics of changing disease prevalence through new pathways of health literacy, especially the work of science editors in prominent newspapers, such as Waldemar Kaempffert of the \textit{New York Times}; new popular science magazines, such as \textit{Scientific American} and \textit{Popular Science}; radio shows featuring medical experts and medical advertisements; and education campaigns spearheaded by voluntary associations, such as the National Foundation for Infantile Paralysis and the American Cancer Society.\textsuperscript{32}

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\textsuperscript{30} Williams, \textit{The United States Public Health Service, 1798-1950}, 774, 801. After 1949, the US implemented a new method for classifying cause of death, permitting physicians to report the condition they determined most responsible for death in cases where multiple conditions may have existed, which led to greater recognition of degenerative conditions that compromised health, especially in seniors.


\textsuperscript{32} Richard Shryock, \textit{American Medical Research Past and Present} (New York: Commonwealth Fund, 1947), 242-244.
\end{flushright}
II. Diet, Behavior and Risk

As Selye’s wartime research led him to recognize the connections between adrenocortical activity and the development of chronic, degenerative conditions, such as nephrosclerosis, hypertension and rheumatoid arthritis, in the postwar period he presented his research on the GAS as fundamentally important to the understanding of abnormal adaptive processes that contribute to the onset of these diseases. Selye’s continued research on dietary conditioning factors—fundamentally connected to his interest in diseases of adaptation—also placed him within a rapidly growing field of clinical investigation and popular interest: nutritional science.

From 1945-1947, Selye fine-honed his theory of the GAS as it relates to chronic disease, focusing on the conditioning influence of diet and physical stressors, as well as the powerful effect of prolonged exposure to diverse risks in the development of chronic, degenerative diseases, such as arthritis and hypertension. He made two critical observations in relation to these studies. The first was that stress itself can act as a conditioning factor, initially sensitizing tissues to become more resistant to harmful stimuli, but over time decreasing resistance to infection and disease. Just as an animal may become conditioned to withstand the damaging effects of excessive cold through repeated exposures, so too can it adapt to resist damage through repeated exposure to general stress. Selye’s second observation was that an organism’s response to stress depends not merely on the excessive presence of any particular hormone, but an imbalance of adaptive hormones—a phenomenon which Selye referred to as “inter-hormonal tension.” The key to reducing damage from stress, according to Selye, was to maintain an optimum balance of mineralo- and glucocorticoids. Thus, Selye expounded on Cannon’s theory of homeostasis by adding a more complex understanding of the actions of adrenocortical steroids in the intricate process of biochemical equilibrium.
In his first two years at the University of Montreal, Selye focused nearly exclusively on studying how the conditioning effects of diet influenced the course of the GAS. In a series of experiments primarily funded by the Commonwealth Fund and the PHS, as well as a number of smaller grants and laboratory materials provided by US and Canadian pharmaceutical firms, Selye examined the effects of salts, proteins, and sugars on experimental rats that had been sensitized to pituitary and mineralo-cortical hormones (such as, LAP and DOCA) through unilateral nephrectomies. He found that high-protein or high-sodium diets hastened the development of nephrosclerosis, while rats given a diet rich in glucose or acidifying salts developed a higher resistance to it. Selye concluded that the development of nephrosclerosis is directly proportional to the protein and salt content of the diet, but inversely correlated with carbohydrate content.33

Selye also found that diets rich in salt and protein increased the likelihood of developing not only nephrosclerosis, but also hypertension, periarteritis nodosa and myocarditis—all of which are major signifiers of cardiovascular disease. He discovered that rats sensitized by unilateral nephrectomy and high-sodium diets developed lesions similar to those caused by LAP and DOCA in the arteries, heart and brain vessels (periarteritis nodosa nodules) and kidneys (patches of nephrosclerosis) when exposed to stressors. Consequently, Selye deduced that the adaptive increase of corticotropic and corticoid hormone secretion when under stress, may result in an over-compensation that could ultimately cause diseases of adaptation.34


In its first year of operations, the IMCE received a $10,000 grant (approximately $130,000 in 2015 dollars) from the Sugar Research Foundation to research the effects of a high carbohydrate diet on diseases of adaptation. Building on Selye’s wartime research of nutritional conditioning factors, these studies found that while a high-salt, high-protein diet exacerbated heart disease and arthritis, a carbohydrate-rich diet seemed to protect against such diseases. Selye presented these findings before dozens of industry leaders at a convention organized by the American Chemical Society in Atlantic City on April 10, 1946. Not only did he extol the values of a high sugar diet in protecting against “rheumatic heart lesions, kidney ailments, hypertension and arthritis,” he also reportedly claimed that “the tension of present day life can be held down by diets high in carbohydrates.”


36 “A Nation’s Health is a Nation’s Wealth. Industry Aids Research,” Montreal Star, September 27, 1946, folder I: Newspaper clippings, HSC.

37 Berman, Hay and Selye, “Influence of High Carbohydrate Diets Upon the Development of Experimental Nephrosclerosis and Allied Cardiovascular Phenomena.”

38 “Disease Control Laid to Dieting. Scientists Reveal Findings on Many Ailments at Conclave,” The Butler, Pennsylvania Eagle, April 11, 1946, folder I: Newspaper clippings, HSC.
September of the same year, at a convention organized by the Sugar Research Foundation at the Mount Royal Hotel in Montreal, Selye even more explicitly asserted that “the main killers today are ‘diseases of civilization,’ such as hypertension, arthritis, and ulcers,” which he insisted could be cured “by means of diet.” He again implicated psychological factors as precipitating causes of such chronic diseases by making the bold claim that, “these diseases are the price we must pay for successful, hard-working people who are subject to mental distress.” Speaking on behalf of the trade association that funded his research, Selye used his scientific expertise to endorse the credibility of the sugar industry’s product, while at the same time, the publicity showcasing his high-profile association with the Sugar Research Foundation bolstered his authority as one of the foremost researchers of the endocrinological mechanisms of stress. Despite the Sugar Research Foundation’s auspice that it aimed to uncover “the truth” about the health effects of sugar, because it represented ninety-five percent of all North American cane and beet sugar producers, it clearly had a stake in emphasizing the health benefits of sugar. Invoking credibility as a seemingly objective academic scientist, Selye increased the marketability of sugar by, in many ways erroneously, offering scientific legitimacy to the nutritional value of sugar.

39 “Prospects of Active, Health Life Past 100-Year Mark Are Unfolded,” Montreal Gazette, September 27, 1946, folder I: Newspaper clippings, HSC; “Adult Life of 115 years Possible If We Learn More About Nutrition,” Montreal Herald, September 27, 1946, folder I: Newspaper clippings, HSC.

40 “Nutrition Declared Key to Longevity of Man. Importance of Diet Stressed at Dinner of Sugar Research Foundation Council,” Montreal Daily Star, September 27, 1946, folder I: Newspaper clippings, HSC.

41 “A Nation’s Health is a Nation’s Wealth. Industry Aids Research,” Montreal Star, September 27, 1946, folder I: Newspaper clippings, HSC.
In the five years following the close of the war, Selye found a niche for himself in the growing field of medicinal research in chronic disease. Since the mid-1930s, his work had focused on identifying the complex pathways of multicausal disease, struggling against a vestigial current of etiological specificity. However, in the postwar years, his controversial theory finally began to be assimilated into mainstream science as increasing numbers of medical experts became attracted to the investigation of multicausation and risk. Nutritional interventions, in particular, were among the favored behavioral interventions recommended by physicians and researchers in the early years of the Cold War. Mayo Clinic researcher Ancel Keys, who had conducted research on the physiological effects of high altitude with the Harvard Fatigue Laboratory, emerged as perhaps the most prominent medical authority on the relationship between diet and heart disease. During World War II, Keys had been instrumental in the Army’s design and adoption of K-rations to ensure that soldiers received adequate nutrition. And in the decades following the war he became a vociferous advocate for the low-fat, low-salt Mediterranean Diet based on his research comparing high rates of heart disease amongst affluent American businessmen and low-rates amongst postwar Europeans subsisting on near-starvation diets. In 1959, Keys and his wife Margaret published a cookbook of recipes designed to reduce risk for heart disease by diminishing fat, cholesterol and red meat consumption. With the American Heart Association and the New England Journal of Medicine endorsing Keys’ dietary recommendations in the mid-1950s, the low-cholesterol diet became a scientifically-vetted health craze.

42 “A Nation’s Health is a Nation’s Wealth. Industry Aids Research,” Montreal Star, September 27, 1946, folder I: Newspaper clippings, HSC.

43 Ancel and Margaret Keys, Eat Well and Stay Well (Garden City, NY: Doubleday, 1959).
Complimenting Key’s research on heart disease and nutrition, in 1948 the National Heart Institute began funding a longitudinal study of heart disease in Framingham, Massachusetts, which followed the “natural history” of disease in a normal population (rather than a clinical setting). By correlating their observations of characteristics in the participants prior to the onset of heart disease, the Framingham Heart Study demonstrated the statistical significance of comorbid conditions, like high blood pressure, high cholesterol levels, obesity and diabetes, as well as the risk associated with behaviors like smoking, consuming alcohol, or eating fatty foods, in the development of cardiovascular disease.44 The Framingham Heart Study advanced the understanding of attributable risk in the causation of disease, and introduced the concept of the “risk factor” into medical discourse.45

As diet-based interventions became increasingly popular, Selye gained recognition as a pioneer in this field of research. In 1946 he was among the original founders of the American Foundation for High Blood Pressure (that merged with the American Heart Association in 1949), which exemplified the postwar vogue of creating foundations dedicated to raising funds to study the causes and treatments for specific diseases, as well as the continued US-Canadian alliance in


medical research.\textsuperscript{46} By the end of 1947, Selye had gained new insight into the critical importance of balance in resistance to disease both in nutritional intake and chemo-physiology. An adequate balance between salts and proteins, on one hand, and sugars, on the other, was critical to the maintenance of health—as was a balanced secretion of stress hormones. Offering a more nuanced understanding of Walter Cannon’s theory of homeostasis, Selye proposed that chronic disease ultimately resulted from a failed effort to resist stress, which generated an imbalance of “inter-hormonal tension.” Disease could thus be avoided by carefully balancing hormones through a combination of dietary modifications and pharmaceutical medications. "Maclean’s Magazine," one of Canada’s most popular news journals, reported that in order to ward-off stress-related diseases, Selye’s research recommended a diet that “consists of little sodium and therefore little salt (long suspected of tending to increase the body’s blood pressure), low protein (eggs, meats, beans, etc.) consumption, and lots of carbohydrate foods (sugar, starch, etc.),” complimented by “hormone injections (such as testosterone) to build kidney tissue and control the pituitary, and ammonium chloride pills to reduce the sodium content of the patient’s system.”\textsuperscript{47}

The more funding that Selye accrued for the IMCE, the more independence he gained to conduct his research, and the more acclaim he garnered as an expert on stress-related illness. His laboratory became internationally renowned as a leading center for endocrinological research on degenerative and chronic disease, attracting illustrious visitors the world over. In 1947 and 1948, Dr. Bernardo Houssay of Buenos Aires, who won the 1947 Nobel Prize in Physiology for his

\textsuperscript{46} “Heart Disease Hope Offered. Researchers Hear Montreal Doctor,” \textit{Cleveland Star} March 15, 1946, folder I: Newspaper clippings, HSC; “Group Here Backs Heart Research,” \textit{Cleveland Press}, December 27, 1946, folder I: Newspaper clippings, HSC.

\textsuperscript{47} George H. Waltz, Jr., “The Case of the Tired Heart,” \textit{Maclean’s Magazine}, June 1, 1947, folder I: Newspaper clippings, HSC.
discovery of the role of pituitary hormones in regulated blood sugar, Dr. Maurício da Rocha e Silva of Sao Paulo, a renowned expert on allergy, and Dr. Reginald Smithwick of Boston University, who was respected as a preeminent authority on hypertension, all visited the IMCE.\(^{48}\)

Even as Selye gained a reputation as an expert on the adrenal regulation of cardiovascular, kidney and rheumatic diseases, he was increasingly celebrated in the press for uncovering the relationship between psychological and physical health, and Selye certainly encouraged this reputation, frequently indicting the ‘stresses and strains of modern life’ as precipitating factors in disease. On October 7, 1947, Selye opened the New York Academy of Medicine’s annual two-week conference, “Disorders of Metabolism and the Endocrine Glands,” by delivering the keynote Ludwig Kast Lecture on “The Diseases of Adaptation With Main Emphasis Upon Hypertension.”\(^{49}\) *Newsweek* reported that, “Dr. Selye brought his research up to date with a brilliant paper on the effects of worry and strain on the human heart and kidneys,” and described Selye as the director of a program investigating the “link between emotional tensions and disease.”\(^{50}\) *The Sun* reported that Selye’s talk explained “that in the present-day civilization man had created a situation which subjected him to greater strains than his body can withstand without damage,” and that it was “these pressures, worries, and emotional stresses,” that “result

\(^{48}\) “New U of M Labs Are Inaugurated,” *The Standard*, October 4, 1948, folder I: Newspaper clippings, HSC.

\(^{49}\) “Medical Academy Starts Fortnight. 10,000 Doctors to Hear Reports on Endocrine Disorders at Annual Gathering,” *New York Times*, October 7?, 1947, folder I: Newspaper clippings, HSC.

\(^{50}\) “Worry and the Heart,” *Newsweek*, October 20, 1947, folder I: Newspaper clippings, HSC.
in physiological changes which make the body more susceptible to diseases of the heart and kidney and possibly to other illnesses.”

The following April, at the American College of Physicians’ annual conference in San Francisco, Selye shared the key-note address with Cornell psychologist, Stewart Wolf (who had pioneered psychosomatic research on gastrointestinal ulcers with Harold Wolff in the early-1940s, as discussed in Chapter Two). Both Selye and Wolf spoke on aspects of the relationship between emotions and physical health from an evolutionary perspective, with Wolf presented as an expert on psychology, and Selye as an expert on physiology. Selye’s talk indicted emotional stress as a stimulus for increased blood pressure and heart rate, and emphasized the protective value of diets low in protein and salt, and high in carbohydrates to decrease the damage caused by emotional stress. Despite his lack of psychological training, and never having conducted his own clinical research assessing psychological stress, Selye’s authority to speak on such matters was assumed based on his growing professional reputation as a pioneer of stress research, and the increasingly inseparable association between biological and psychological stress.

By the end of the decade, Selye had come to appreciate that the unique “pathological situations” that organisms develop over time from their own cumulative adaptative experiences to environmental exposures, powerfully influence their capacity to resist or develop disease. Recalling Adloph Meyer, Harold Wolff, and the psychoanalytical emphasis on the pathological significance of unique life histories, Selye advanced the idea that each human being accumulates


a different etiological profile over the course of their lives due to their personal exposures to pathogens and other risks, endorsed the emerging etiological model that viewed certain chronic or degenerative diseases as the result of multiple and varied causal factors. Thus, individual differentiation in susceptibility to disease helped to explain why some people developed heart disease, arthritis or cancer, while others did not, and why certain factors that statistically correlated with the development of these diseases did not always, inevitably produce them. The concept of multicausal disease was a direct contradiction of Koch’s postulates and the doctrine of specific etiology. Because the theory of stress complimented the notion of risk, it also contributed to a vital expansion of biomedical theory that enabled it to reckon with the mid-century prevalence of chronic diseases.

At the same time, the appreciation for individual predisposition bore a strong parallel to the psychoanalytical and psychobiological emphasis on the importance of patients’ life histories in determining disease outcomes, and therefore increased the integration of psychological and biological theories of stress. By creating a powerful rhetorical and theoretical linkage between his own theory of biological stress and the psychological theory of stress, Selye was able to appropriate the medical valence that psychologists had cultivated through their wartime research. In his embrace of this new terminology, Selye invited further scrutiny for his already controversial theory. Yet, rarely were his experimental results challenged. In fact, his work was widely referenced by other endocrinologists and stress-researchers. It was not his methods that


54 In the first eight editions of the published proceedings of the Laurentian Hormone Conferences, Recent Progress in Hormone Research, Selye’s published work consistently ranked among the most widely referenced research.
were contested, for they rigorously complied with the standards of biomedical investigation; but his unified theory of general sickness, which directly contradicted biomedicine’s principle doctrine of specific etiology, continued to draw fire.

Because Selye’s research promised hope in combatting increasingly prevalent chronic diseases it began to attract public attention. The relevance of Selye’s findings reached beyond the professional scientific and business communities to a popular North American audience when they were featured in *New York Times* reporter, Waldemar Kaempffert’s column on recent innovations in scientific research, the same month that his work was profiled in *Life* (discussed on p. 168). As portrayed in the popular press, Selye’s research promised relief from not only chronic disease, but the myriad pressures of modern life.

Selye’s reputation in the public and scientific communities compounded his expert authority, increasing his capacity for attracting sizable grants and fellowships from the principal funders of postwar scientific research: pharmaceutical companies and the federal government. In the spring of 1947, Frank W. Horner issued the IMCE an additional grant for $15,000 ($178,000 in 2015 Canadian dollars) to study hypertension, and in the fall of the same year, the PHS awarded the IMCE a five-year grant of $27,540 (nearly $300,000 in 2015 dollars) for research on diseases of adaptation—the first grant ever issued to a Canadian University by a US federal agency, which Selye attributed to the fact that Americans were particularly interested in research linking disease with diet.55 Selye was right. Americans were becoming more interested

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55 “New U of M Labs Are Inaugurated.” Hyung Wook Park reports that the National Heart Institute’s Gerontology Study Section issued three grants of $27,540 each during this time period. See Hyung Wook Park, “Refiguring Old Age: Shaping Scientific Research on Senesence, 1900-1960,” (Ph.D. Diss., University of Minnesota, 2009). 341, citing “Medical Research Projects: Gerontology,” record Group 443, Records of the National Institutes of Health, Division of Research Grants, Records of the Gerontology Study Section, 1946-1950, Box 1,
in dietary interventions to manage chronic disease, due in part to the increase in heart disease, diabetes, hypertension and other diseases that were found to have nutritional risk factors, and in part to a newly active role of the federal government in funding research to benefit the public’s health.

III. The Politics of Postwar Funding for Medical Research

After World War II, the US federal government took on a leading role as the primary funder of scientific research in North America. During the war, the CMR alone had spent $15 million (about $206 million in 2015 dollars) on 450 contracts with universities, and 150 contracts with research institutes, hospitals and other private facilities, all drawing on the work of 5,500 scientists and technicians.\(^{56}\) The prodigious success of wartime research programs demonstrated the great utility of federal-private partnerships in research and implicitly encouraged further investment. International politics in the immediate postwar period, particularly the Cold War arms race, increased appreciation for the value of scientific research as a national resource, and a justification of continued federal support. Already, by the last year of the war, policy makers and public health officials were making plans to accommodate the changing medical needs of the postwar population. Proposals for postwar research goals came from the President, Congress, federal agencies and philanthropic interests. Thanks to the savvy political maneuvering of bureaucrats, politicians and philanthropists associated with newly developed disease associations, by 1950 the PHS and the reorganized NIH emerged as the largest funders of medical research in North America.

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The vast increase in state spending and bureaucratic development during World War II seemed to vindicate the ethos of Keynesian liberalism in the postwar era. The sheer fact that the decade-long struggle to reign in the Depression had finally proven successful through state expenditures (on an even grander scale than those of the New Deal) viewed as necessary for the war effort, was upheld as a testament to the importance of state intervention in economic planning and national development. While the majority of wartime agencies disbanded after 1945 (the USNRC’s Committee for Medical Research survived until 1947), they served as a model for the development of an expanded federal bureaucracy in the form of new specialized agencies and institutes in the postwar era.

The new federal support for scientific research signified the central importance of objective scientific analysis as the basis for sound policy. This principle developed over the course of the early-twentieth century as medical science proved its value in improving human health and quality of life, and was further endorsed by the great advancements facilitated through the OSRD’s planning and vindicated by the Allied victory. Not least of which, the development of methods for mass producing penicillin for the commercial market inspired greater faith in the bounty of biomedicine, as well as deference to scientific authority. Equipped with the power to easily treat bacterial diseases that previously often ended in death, North Americans in the postwar era came to view scientific research as a means of rationalizing the volatility of nature, and therefore, a fundamental national interest. As the Cold War escalated over the next two decades, the perception that scientific research was essential to national security offered further justification for federal subsidization.

While the state emerged as a primary funder of scientific research, private support proportionately decreased. However, both corporate and philanthropic interests continued to
support academic, nonprofit and for-profit research institutions. While the traditional large philanthropic organizations—the Rockefeller Foundation, the Josiah Macy Jr. Foundation, the Commonwealth Fund and the John and Mary R. Markle Foundation—remained lucrative funders of academic research, new and pre-existing disease organizations, such as the American Heart Association and the American Cancer Institute emerged as new sources of research grants as they came to prioritize research alongside public health literacy campaigns. Powerful lobbying organizations, disease associations also wielded their influence in the distribution of federal funding for research.

Even before the close of the war, policymakers began taking steps to provide for more expansive federal support for scientific research after the war. In November of 1944, President Roosevelt requested that Vannevar Bush, the head of the OSRD, outline recommendations for continued federal investment in medical research to continue the “war of science against disease” for the civilian population.57 Bush’s report, *Science: the Endless Frontier*, submitted in July of 1945, recommended the creation of a National Research Foundation to act as a,

> focal point within the Government for a concerted program of assisting scientific research conducted outside of the Government… [and] should furnish the funds needed to support basic research in colleges and universities, should coordinate when possible research programs on matters of utmost importance to the national welfare, should formulate a national policy for the Government toward science, should sponsor the interchange of scientific information among scientists and laboratories both in this country and abroad, and should ensure that the incentives to research in industry and the universities are maintained.58

Bush specified that the National Research Foundation must 1) have a stable source of funding to support long-range programs; 2) should be composed of members dedicated to the advancement


of science and of the Foundation, and familiar with the culture of scientific research and education; 3) solely administer extramural grants, and not have any internal laboratories; 4) be dedicated to basic research in public and private institutions of higher learning, but not become entangled in the internal administration of projects at these institutions; 5) be responsible to the President and Congress, but operate as an independent agency in its determination of research priorities.

The general principles of Bush’s proposal held wide appeal, but several of its minor stipulations aroused controversy, so that it was not until 1950 that the National Science Foundation came into existence under the National Science Foundation Act.59 In the meantime, Surgeon General Thomas Parran saw to it that the PHS—and the National Institutes of Health (NIH), the national medical research agency that functions under the PHS’s purview—emerged as the central coordinator, and largest funder of postwar research in North America. In his 1944 Annual Report, Parran outlined a six-point program for the improving public health throughout the country, consisting of: 1) sanitation reform; 2) expanded hospital services; 3) expanded public health services; 4) federal support for medical research; 5) professional medical services training; and 6) a national health care program. This broad program had the intent of stimulating research and providing sufficient services to effectively combat the scourges of mental illness.

59 For one, Bush’s emphasis on basic rather than applied research alienated support from disease associations and other specialized interests that believed federal funds should be directed towards research with clearly identified public use. Bush’s program was in many respects a counterproposal to a bill introduced three years earlier by West Virginia Senator Harley Kilgore. Though it failed to pass in the 1942 legislative session, Kilgore’s Science and Mobilization Act aimed to rationalize scientific research priorities by creating a federal agency authorized to determine research goals and hold patents on behalf of the public, and thereby diminish the control of elites private universities and an oligopoly of private firms. Accordingly, the scientific establishment and large corporate interests perceived Kilgore’s proposal as an overt threat, and lent their support to Bush’s proposal instead. Congress remained mired in this intractable conflict of interests, impeding the passage of either bill.
cancer, heart disease and arthritis. But, it also had the ulterior objective of enhancing the power and scope of the PHS by consolidating medical research and health service responsibilities under its purview. Since its creation in 1798 as the Marine-Hospital Service, the PHS had developed in an ad hoc fashion through the periodic enactment of disparate services and agencies. Parran’s omnibus bill offered the potential of unifying and streamlining these decentralized bodies, and thereby promoting more efficient national action. The broad nature of Parran’s proposal also invited criticism on each of its six points, but he was able to secure its passage by attaching it to a highly sympathetic bill to continue funding for a program for tuberculosis prevention begun during the war.  

Under the 1944 Public Health Service Act, the PHS became one of the very few federal agencies to be granted an unlimited and continuing Congressional authorization. Congress was likely persuaded to endorse increased federal funding for medical research, in part, by the PHS’s record during the war. In addition to the declining rates of tuberculosis, Parran had introduced a major venereal disease prevention campaign within the military and among civilians that had succeeded in reducing the annual incidence of syphilis to 200,000 cases, and the PHS division for Malaria Control in War Areas had drastically reduced malaria rates in tropical regions. These tangible gains stood testament to the powerful effect that federal support for public health initiatives could have on American health outcomes.

Perhaps the most influential, and yet least noticed provision of the Public Health Service Act empowered the Surgeon General to administer grants-in-aid to private research institutions

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60 Between 1941 and 1944, the PHS expanded the availability of chest x-rays that were used to detect nearly 200,000 cases of tuberculosis, most of which were in their early stages. See Bess Furman, *A Profile of the United States Public Health Service, 1798-1948* (Washington, D.C.: US Government Printing Office, 1973), 430.

to conduct medical research on behalf of the PHS. The Budget Bureau initially postponed funding this program until immediate war objectives had been met, but at war’s end, after NIH Director Rolla Eugene Dyer secured the transfer to the NIH of 250 of the OSRD’s outstanding research contracts totaling $800,000 (over $10.5 million in 2015 dollars), the PHS had even more reason to justify a Congressional appropriation for the grants program. The PHS administered 67 grants totaling $1.03 million (approximately $13 million in 2015 dollars) in the 1946 fiscal year, and the following year, added 129 more grants totaling $2.08 million (approximately $25 million in 2015 dollars).\(^{62}\) Over the course of the war, Congress appropriated $10 million for military research, but only $2 million for research on all other diseases not central to the war effort.\(^{63}\) The transfer of the OSRD contracts to the PHS signified the civilian inheritance of wartime research aid.

The PHS delegated responsibility for administering the research grants program to the NIH. Having undergone in the last two years of the war, major construction to expand intramural research and treatment facilities (designed with the aid of Norman Topping, who had overseen the design of Toronto’s Connaught Laboratories earlier in the war), the NIH was poised to, in the words of PHS historian Bess Furman, “serve as a symbol of the change in emphasis on medical research in public health from the communicable diseases, which were being controlled, to the chronic diseases of mankind.”\(^{64}\) To that end, in the late-1940s, the NIH oversaw the creation of several specialized institutes dedicated to funding and overseeing basic and applied research on chronic diseases, particularly, mental health, cancer and heart disease.


Philanthropies, especially new disease associations, played an important role in persuading Congress to appropriate funding for medical research. Indeed, the PHS owed a great deal to a powerful new lobby spearheaded by Mary Lasker, the wife of advertising magnate Albert Lasker that coined the notable brand names “Kotex” and “Kleenex,” and Florence Mahoney, who’s husband Daniel Mahoney owned a substantial interest in the Cox chain of newspapers (including among several others, the Atlanta Journal and the Miami Daily News).

With a new vision of large-scale philanthropy, the Laskers and the Mahoneys used savvy public relations and fund raising strategies to transform the American Cancer Society into a powerful interest block (and funder of research in its own right), increasing annual public donations to the ACS from $780,000 in 1938 (approximately $13.17 million in 2015 dollars) to $4 million in 1945 alone (nearly $53 million in 2015 dollars). However, the Lasker group realized that even such a dramatic increase in funds could not adequately support the great deal of research required to confront the cancer epidemic. Only the US federal government had sufficient funds to support such an undertaking.65

The Laskers sought to influence federal health policy by forming the Committee on the Nation’s Health to outline legislation and organize publicity campaigns, drawing illustrious members, such as health insurance pioneer Henry Kaiser, and the former First Lady, Eleanor Roosevelt.66 They also courted favor in Congress, in at least one instance, offering financial and media support for Chief of the Senate Subcommittee on Wartime Health and Education, Florida Democrat Claude Pepper’s reelection campaign for a Senate seat, in exchange for his agreement to sponsor a bill to create a new mental health division of the PHS. The Committee on the

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65 Strickland, Politics, Science, and Dread Disease, 36-37.

66 Ibid., 44-45.
Nation’s Health also appealed directly to President Truman to support increased funding for medical research of chronic and mental disease, and for a national health insurance program. On November 19, 1945, President Truman delivered a special message to Congress outlining his proposal for the development of national health program, calling for the creation of compulsory national health insurance, expanded public health services, hospital construction, and funding for medical education and research, all of which he declared to be essential measures to achieving health security as part of a new “Economic Bill of Rights.”

When President Truman appointed Leonard Scheele to succeed Thomas Parran as Surgeon General in April of 1948, Scheele quickly developed an alliance with the Lasker lobby. Scheele drafted legislation, and the Laskers provided funds, secured political allies, and enlisted the support of disease associations in Congressional hearings. The National Academy of Sciences (NAS) also pushed for the expansion of the NIH through the formation of a new consortium of health agencies within the recently expanded PHS that would be empowered to distribute grants and conduct their own scientific research that could inform national policy. Together, by June of 1948 they successfully achieved the passage of legislation creating four new centers under the renamed National Institutes of Health, and raising the NIH total appropriation for the 1951 fiscal year to $50 million (approximately $458 million in 2015 dollars).

In addition to the creation of the National Heart Institute (NHI), the National Institute


68 This legislation consisted of two acts passed in 1948—the National Heart Act, which created the NHI, and the National Dental Research Act, which created the National Institute for Dental Research—as well as the 1950 Omnibus Medical Research Act, which created the National Institute of Neurological Diseases and Blindness and authorized the Surgeon General of the PHS to create additional institutes, including the National Institute of Arthritis and Metabolic Diseases, also founded in 1950, as well as the National Institute of Allergy and Infectious
for Dental Research (NIDR), the National Institute of Neurological Diseases and Blindness (NINDB), the National Institute of Arthritis and Metabolic Diseases (NIAMD), the and the National Institute for Allergy and Infectious Diseases (NIAID), this legislation also strengthened the NIH’s extramural research program by enabling it to issue grants for research facility construction, and further solidified the power of philanthropic and political interests within the NIH by permitting laymen to serve on its advisory councils.

In 1941, the total federal budget for medical research was approximately $3 million (nearly $48.6 million in 2015 dollars), and total national expenditures for medical research were about $18 million (just over $290 million in 2015 dollars). The NIH’s budget alone was $700,000 for the 1941 fiscal year, less than one-third of which supported research grants, at a time when private foundations allocated $4.7 million for medical research. By the end of the war, the NIH budget rose to nearly $3 million in the 1946 fiscal year (approximately $36.62 million in 2015 dollars), of which $850,000 went towards funding grants, and in 1947, total Congressional appropriations for NIH totaled $8 million, a tenfold increase from 1941.69 In 1946, total federal expenditures for research were $28 million, while industry spent $55 million and philanthropies and other private sources spent $32 million on research. By 1951, federal expenditures for research totaled $76 million, industry spent $60 million and other private sources spent $45

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69 Strickland, Politics, Science, and Dread Disease, 27, 30.
million, totaling $181 million in national expenditures for research, of which 18 percent was distributed in grants and contracts.70

The restructuring of the NIH began with a vast expansion of the National Cancer Institute (NCI), which was originally created in 1937, its budget growing from $600,000 in 1946 (approximately $7.32 million in 2015 dollars) to $18 million by 1950 (nearly $178 million in 2015 dollars), and a whopping $92 million in 1960 (nearly $740 million in 2015 dollars).71 In 1950 alone, the NCI issued 30 grants totaling $6 million for the construction of research facilities in 28 institutions, as well as 354 grants totaling $3.33 million for research projects in the United States and six foreign countries.72 The same year, the NHI issued 388 grants totaling $4 million for the construction of research facilities, and research grants to 96 foreign and domestic institutions for studies relating to hypertension, arteriosclerosis, and heart failure, as well as various hereditary, environmental, dietary and renal influences on heart disease, the development of an artificial heart, and pharmaceutical treatment of heart disease.73 From 1950 to 1953, NHI funding for heart disease research increased from $3.82 million to $5.15 million, totaling $18 million over three years, while NIAMDD funding for arthritis and metabolic disease research increased from $685,395 to $1,345,000, totaling $3.4 million for the same time period.74


73 These studies also included research on the effects of ACTH, cortisone and other hormones in treating heart disease. See Williams, *The United States Public Health Service*, 814.

As a result of the growth of the NIH and the research grants program, by 1950, the PHS administered $13.6 million in grants, of which approximately $7.7 million funded research in heart disease, cancer, dentistry and mental health. In total, from 1946 to 1953, the PHS distributed over 7,000 grants totaling almost $100 million (about $100 billion in 2015 dollars). Consequently, in the postwar years, the US federal government surpassed the private sector as the principal funder of medical research in North America. Yet, the drastic increase in federal support obscures smaller, yet sizable increases amongst philanthropic and industrial interests. In 1941 total US expenditures for medical research were $45 million, with the government contributing $3 million (7 percent), industry contributing $25 million (55 percent), and the nonprofit sector contributing $17 million (38 percent). However, in 1947, when total medical research expenditures reached $88 million, the government contribution rose to $28 million (32 percent), while industrial investment rose to $35 million, it now represented 40 percent of the total, and nonprofit investment in medical research rose to $25 million, but fell to 28 percent of the total. This trend continued and by 1952, total US expenditures for medical research were $173 million, of which the federal government contributed $73 million (42 percent). Industry contributed $60 million (35 percent), and nonprofit agencies contributed $40 million (23 percent).

Despite its decreasing percentage of total US investments in medical research, philanthropic aid contributed $5.3 million for cancer research, $1.6 million for heart disease research, $1 million for arthritis and metabolic disease research and $4.3 million for neurological

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75 Williams, *The United States Public Health Service*, 818.

and mental disease research, representing a total of over $12 million in aid to medical research.\textsuperscript{77} The percentage contribution from the nonprofit and industrial sector fell, in part, due to their increased access to federal research grants and contracts. In 1952, nonprofits received over $18 million from HEW alone, and industry received $1.5 million for medical research from HEW, the Department of Defense, the Atomic Energy Commission, the Veterans Administration and Tennessee Valley Authority and the National Science Foundation.\textsuperscript{78} Nonprofits received the lion’s share of federal funds because this category encompassed educational institutions, hospitals, research organizations, professional and trade organizations and some public and governmental units.\textsuperscript{79} Philanthropies, particularly the newly created disease associations, also wielded considerable influence in the postwar research economy as they played an important role in advising the NIH in its distribution of research grants.

The PHS also supported medical research outside of the United States, issuing large grants to many Canadian institutions and researchers, among other countries. The legacy of the collaboration between the CNRC and USNRC during the war, created professional and bureaucratic alliances that endured in the postwar era. At the same time, US prosperity—and the export market and investment potential it generated—proved to be a crucial resource to Canada, as England, its previous favored trade partner, suffered a devastating postwar depression. Selye came to depend upon the PHS and the USNRC to fund his work in the postwar era, receiving $205,446 in grants from the USNRC Division of Medical Sciences between 1951 and 1956

\textsuperscript{77} Ladimer, “Trends and Expenditures for Medical Research, 1941-1952,” 117.

\textsuperscript{78} Ibid., 118, 120.

\textsuperscript{79} Ibid., 120.
alone—over $1.8 million in 2015 dollars. Selye strengthened his relationship with the US federal government by serving as an official advisor to the Surgeon General of the US Army on stress-related matters.

Immediately following the war, the ACMR continued to support Selye’s research, awarding him $4,000 for his "study of 'rheumatoid' changes produced by hormones" and issuing a $1,800 fellowship to Paul Dontigny to study with Selye. Over the course of the next two decades, Selye would receive much more substantial financial grants, as well as stipends for medical supplies from the dominion government, however he remained perpetually dissatisfied by the amount of support they were able to dispense. While the Dominion government contributed to medical research after the war, its support was significantly smaller than that of the US federal government.

As historian of medicine Alison Li has noted, the major “legacy of wartime committees was the creation of a permanent institutional structure for the funding and coordination of medical research in Canada.” On June 1, 1946, the CNRC created a new Division of Medical Research (DMR) to take over the responsibilities of the ACMR, and to oversee a new program of

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83 “Proceedings of the Seventeenth Meeting of the Associate Committee on Medical Research,” March 29, 1946, Box 6, CNRC.

84 Li, J.B. Collip and the Evolution of Medical Research in Canada, 158.
medical fellowships and grants-in-aid for peacetime research. It appointed Collip as the Director of the DMR and allocated a budget of $200,000 for the 1946-1947 fiscal year (just under $2.4 million in 2015 Canadian dollars). In its first year of operations, the DMR distributed a total of $171,000 in grants and fellowships (just over $2 million in 2015 Canadian dollars) of $1,200-$2,400 each. The DMR’s budget for 1948-49 was $352,576, including $269,983 in grants and $60,000 in fellowships. The following year, its budget increased to $538,525 (of which, $300,000 was distributed in grants and $75,000 in fellowships). That same year, the CNRC underwent two significant changes in administration—in March it appealed to the Canadian Arthritis and Rheumatism Society for advice in the distribution of CNRC grants and fellowships and it began overseeing the production and distribution of hormonal preparations.

The 1952-53 budget for the DMR was $616,926 (nearly $5.5 million in 2015 Canadian dollars), including $475,000 in grants, and $115,000 in fellowships. That year, the National Cancer Institute recommended that the DMR issue Selye a $12,000 grant for "studies on the relationship between hormones and tumorigenesis." The following year, the DMR’s budget increased slightly to $640,760, including $500,000 in grants and $115,000 in fellowships. In the 1953-54 fiscal year, the DMR granted Selye $18,500 and 7-8 grams of Growth Hormone for two

85 G.H. Ettinger, "A History of the Associate Committee on Medical Research," 42-44, Box 9, CNRC.

86 "Proceedings of the Seventh Meeting of the Advisory Committee on Medical Research," March 25, 1949, Box 11, CNRC.

87 "Proceedings of the Twelfth Meeting of the Advisory Committee on Medical Research," March 7, 1952, p. 3 and Appendix A, p. 5, Box 33, folder 30.24, CNRC.
Even as the DMR’s budget gradually increased, it was insufficient to meet the demands of modern “big” scientific research. By 1957, the CNRC’s total support for medical research in Canada was only $1.5 million (approximately $12.6 million in 2015 Canadian dollars), whereas in the United States, the NIH alone contributed $108 million in funding (just under $915 million in 2015 dollars), equivalent to about two percent of the US gross national product. While the DMR had contributed immensely to the development of medical research in the postwar period, its support had not kept pace with the scope and expense required by the research community it fostered. Though there were indeed more professional opportunities for Canadian scientists to work in Canada, they were by-and-large compelled to seek funding from outside of their own country. Selye was not alone in his heavy dependence on the United States to support his research. In doing so, he and his colleagues were also compelled to cater their research to meet the increased emphasis on applied rather than basic research of the postwar period. As Alison Li has noted, “the war had turned investigators’ attention away from fundamental research to a narrow range of practical problems,” at the same time that “the emergency situation also forced a close collaboration and coordination among academic researchers and industrial scientists.”

IV. The Postwar Transformation of the Pharmaceutical Industry

88 “Proceedings of the Fifteenth Meeting of the Advisory Committee on Medical Research,” March 9-10, 1953, p. 9, Appendix B, p. 2 and Appendix F, p. 9, Box 33, folder 30.24, CNRC.

89 Li, J.B. Collip and the Evolution of Medical Research in Canada, 164.

90 Ibid., 158.
The collaboration between the state and industry during World War II drastically transformed the pharmaceutical industry by vastly increasing the scale of pharmaceutical production, offering federal subsidies for the improvement of production facilities and fundamental research, and generating new markets for pharmaceutical drugs. But, in a less conspicuous way, it also radically altered the relationship between academic scientists and industry, by encouraging collaborative relationships that helped to overturn an academic tradition of discouraging industrial collaboration on the grounds that capitalist interests corrupted scientific pursuits. The financial desperation and changing shape of industry during the 1930s had begun to chip away at academics’ reticence to unite with chemical and pharmaceutical firms, leading prominent scientists to pioneer alliances with industry for long-term and specific research objectives. J.B. Collip and Frederick Banting were among these early pioneers who entered into long-term relationships with pharmaceutical firms, such as McKenna, Ayerst & Co., to manufacture insulin (and later Emmenin), since their university laboratories lacked the capacity to produce a sufficient supply of insulin. Industry collaboration made it possible for their revolutionary discovery to become available to a wider patient population.

While they were indeed at the forefront of a new trend of academic-industrial alliances, during the 1930s Banting and Collip were exceptional cases. The outbreak of war in 1939 generated new research and production that could only be met through the mobilization of all available scientific resources, while at the same time vastly reducing the stigma associated with for-profit research by creating a moral basis for academic-industrial collaborations. Moreover, wartime committees provided formal networking opportunities for academic and commercial scientists. As head of the Committee on Chemistry under the USNRC’s Division of Medical

91 Swann, Academic Scientists and the Pharmaceutical Industry.
Sciences, Dr. Alfred Newton Richards of the University of Pennsylvania used his long-time relationship with Merck & Co. to enlist the help of Merck’s Director of Research and Development, Dr. Randolph Major and several of his staff members on crucial war research projects that also involved academic committee members. Such wartime collaborations expanded the network of North American researchers and created relationships that endured in the postwar era.

The successes achieved through wartime research also exerted a lasting effect on pharmaceutical companies in the postwar era. For example, the NRC’s initiative to develop an efficient means of mass producing penicillin to treat soldiers in the field provided companies like Merck & Co. with new production facilities that continued to mass-produce lucrative compounds for postwar consumer-patients. And the fanfare surrounding the incredible therapeutic value of penicillin generated a faith and excitement for pharmaceutical innovations that created an eager expectation for additional pharmaceutical panaceas amongst consumer-patients confronting new disease challenges in the postwar era.

In the postwar era, concern with the increased prevalence of chronic diseases drove the pharmaceutical industry to invest its wealth (much of which was generated by antibiotic sales) in the development of new drugs that promised to help manage degenerative conditions. Although the pharmaceutical industry suffered a depression in the immediate postwar era, in the late 1940s and early 1950s, the development of prescription drugs, such as penicillin, cortisone, and

92 Despite its great success in the development of penicillin during World War II, immediately following the war, the pharmaceutical industry suffered a recession due in part to their over-dependence on this single product. A decline in the price of penicillin—from $2,955 per pound in 1945 to $282 in 1950—as well as competition created by the resurgence of the European drug market, caused many North American companies to scale-back production. See Peter Temin, Taking Your Medicine: Drug Regulation in the United States (Cambridge, M.A.: Harvard University Press, 1980), 66.
antihistamines, increased domestic prescription drug sales from less than $200 million in 1941 (approximately $3.2 billion in 2015 dollars) to $1.7 billion in 1957 (about $14 billion in 2015 dollars), according to a congressional investigation.\textsuperscript{93} Similarly, global pharmaceutical sales increased from $890 million in 1947 (approximately $9.5 billion in 2015 dollars) to $2.7 billion in 1959 (about $22 billion in 2015 dollars), while eight of the twelve largest pharmaceutical companies reported an annual decrease in profits. Pharmacists rather than pharmaceutical companies benefitted most from the growth of this new market in the immediate postwar period.\textsuperscript{94}

As they had before and during the war, corporate interests continued to support scientific research that promised marketable results. However, as the Cold War economy transformed the North American marketplace, they developed new promotional tactics and perceptions of marketability. Advertising, a central component of North American consumerism since the 1920s, gained a new prominence in the postwar economy, as consumption became an emblem of prosperity in a capitalist democracy, and purchasing power became increasingly interpreted as a means of asserting individual choice. The medical marketplace was dominated by the interests of three principal agents of the postwar economy: the state, the corporation and the consumer. To generate market demand for new drugs, pharmaceutical companies deployed “detail men” to doctors’ offices throughout the continent to educate and incentivize private practitioners to promote their new products. As pharmaceutical companies sought to promote products that


\textsuperscript{94} Tobell, \textit{Pills, Power and Policy}, 69, 60.
possessed the most consumer appeal, they prioritized development of products that provided quick and easy treatment for common ailments without the need for costly and time-consuming expert medical treatment, products that helped to manage chronic diseases or medical conditions that inhibited lifestyle or productivity, and products that indulged individual fantasies of personal improvement. With the enactment of amendments to the Food, Drug and Cosmetics Act in 1938 and 1951, the federal government essentially offered its endorsement to pharmaceuticals by designating products as generally safe, unsafe, or requiring the prescription of a medical expert.95

As will be discussed in Chapter Five, the 1951 passage of the Durham-Humphrey Amendments to the Food, Drug and Cosmetic Act created a distinction between over-the-counter and prescription drugs, and required that prescriptions drugs be dispensed only with the written authorization of a licensed medical professional. This encouraged pharmaceutical companies to direct drug advertising to doctors through medical journals and personal visits and correspondence with company “detail men.” The US federal government has never forbidden direct-to-consumer advertising, however, for most of the twentieth century, the pharmaceutical industry followed its Progressive Era custom of voluntarily complying with the AMA’s Code of Ethics which vehemently discouraged any activities for commercial profit.96 By the early-1950s,

95 Temin, Taking Your Medicine.


the AMA’s Code of Ethics had undergone significant revisions four times since its original adoption in 1847, yet it retained its prohibitions on medical marketing. While these stipulations were originally laid out in the 1847 Code in order to distinguish licensed medical professionals from quack doctors and peddlers of patent medicines, the anti-market orientation of allopathic medical practice proved to be an enduring standard of professional conduct. Over the first five decades of the twentieth-century, research-oriented pharmaceutical firms conformed to the AMA’s discouragement of direct-to-patient advertising as a means of signifying their production of ethical, not proprietary drugs. With the adoption of the “prescription” and “over-the-counter” designations for pharmaceuticals, compliance with the AMA’s Code of Ethics also became a technique of convincing doctors of a pharmaceutical firm’s integrity. Under the advice of trusted medical professionals, North Americans became accustomed to relying on prescribed

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97 Section of 7, “Advertising Methods to Be Avoided,” of the AMA’s Principles of Medical Ethics of 1903 states in part, “it is incompatible with honorable standing in the profession to resort to public advertisement or private cards inviting the attention of persons affected with particular diseases; to promise radical cures; to publish cases or operations in the daily prints, or to suffer such publication to be made; to invite laymen (other than relatives who may desire to be at hand) to be present at operations; to boast of cures and remedies; to adduce certificates of skill and success, or to employ any of the other methods of charlatans.” Section 8, Patents and Secret Nostrums,” further stipulates that “it is equally derogatory to professional character for physicians to hold patients for any surgical instruments or medicines; to accept rebates on prescriptions or surgical appliances; to assist unqualified persons to evade legal restrictions governing the practice of medicine; or to dispense, or promote the use of, secret medicines, for if such nostrums are of real efficacy, any concealment regarding them is inconsistent with beneficence and professional liberality, and if mystery alone give the public notoriety, such craft implies either disgraceful ignorance or fraudulent avarice. It is highly reprehensible for physicians to give certificates attesting the efficacy of secret medicines, or other substances used therapeutically.” See American Medical Association, Code of Ethics, 1903, accessed October 25, 2014, https://archive.org/details/principlesmedic0assogoog. On the evolution of the AMA’s Code of Ethics see The American Medical Ethics Revolution: How the AMA’s Code of Ethics Has Transformed Physicians’ Relationships to Patients, Professionals, and Society, edited by Robert Baker (Baltimore: Johns Hopkins University Press, 1999).
pharmaceutical treatments, and their increasing reliance on pharmaceutical drugs contributed to the immense growth, increased wealth, and political power of pharmaceutical companies.\footnote{On the federal regulation of pharmaceutical advertising see Jeremy A. Greene and David Herzberg, “Hidden in Plain Sight: Marketing Prescription Drugs to Consumers in the Twentieth Century,” American Journal of Public Health 100, no. 5 (May 2010): 793–803, doi: 10.2105/AJPH.2009.181255; Temin, Taking Your Medicine.}

According to a seminal study by renowned historian of medicine, Richard Shryock, by 1940 there were approximately 1,100 pharmaceutical firms in the United States, employing 22,000 workers and producing $365 million of goods annually (approximately $3.6 billion in 2015 dollars).\footnote{This calculation includes all pharmaceutical goods—both perscription and non-perscription medications. See Shryock, American Medical Research Past and Present, 161-162.} From 1939-1959, pharmaceutical sales increased from $300 million to $2.3 billion ($5.1 to $8.8 billion in 2015 dollars), as the number of detail men employed by North American pharmaceutical firms increased from 2,000 to 15,000 between the late-1920s to 1959.\footnote{Jeremy Greene, “Attention to ‘Details’: Etiquette and the Pharmaceutical Salesman in Postwar America” Social Studies of Science 34, no. 2 (April 2004): 272, citing Melvin E. Gibson, “Editorial,” American Journal of Pharmaceutical Education 23 (1959): 461-66, and Arthur F. Peterson, “The Professional Service Pharmacist,” Journal of American Pharmaceutical Association 12, no. 4 (April 1951): 212-13.}

By 1940, major pharmaceutical firms, like Parke, Davis & Co., Eli Lilly & Co., Abbot Laboratories and E.R. Squibb & Son all had training programs to prepare sales representatives, and by the end of the decade, they were all taught to adhere to the AMA’s Code of Ethics. As a result, in New Jersey alone, between 1936 and 1946, the number of prescriptions issued per year jumped from 7 million to more than 12 million.\footnote{Greene, “Attention to ‘Details’,” 274, citing Thomas H. Jones, Detailing the Physicians: Sales Promotion by Personal Contact With the Medical and Allied Professions (New York: Romaine Pierson Publishers, 1940) and “Prescriptions on the Increase,” Medical Marketing (1948): 7; “Selection of Detail Men” Medical Marketing (December 1944): 1-8.} Whereas in 1929 Americans spent only $190 million on prescription drugs (accounting for 32 percent of all medications), in 1949 they spent
$940 million (accounting for 57 percent of all medications), and in 1969, $5.395 billion (83 percent of all medications).¹⁰²

In the postwar period, the pharmaceutical industry played an important role in funding medical research, encouraging professional discourse and promoting popular health literacy (to urge the use of pharmaceuticals). The pharmaceutical industry provided critical funding for stress research, and also contributed to the formation of scientific networks and formal organizations that undergirded a specialized field of stress research. Pharmaceutical funding enabled the formation of the Laurentian Hormone Conference (discussed in greater detail in Chapter Four), which emerged in the mid-1940s as a clearinghouse for endocrinological research on stress. Selye consistently attended the annual meetings of the Laurentian Hormone Conference, where he was both lauded and criticized for his work. Selye presented his latest interpretation of his theory of diseases of adaptation before an illustrious group of fellow pioneers in endocrinological researchers at the 1948 Laurentian Hormone Conference.¹⁰³ He carefully outlined the foundation of his theory, the results of his recent nutritional research, and the theoretical implications for chronic disease. In the discussion following his presentation, a number of prominent endocrinologists, including George Sayers of Yale Medical School, Dwight Ingle of Kalamazoo’s Upjohn pharmaceutical company (who had participated in the compound E research with Kendall’s group at the Mayo Clinic), and Cho Hao Li of University of California-Berkeley, among others, seemed quite divided in their skepticism and exhortation of Selye’s methodology and theoretical claims. While some applauded Selye’s insightful


observations, several discussants debated the merits of Selye’s findings based on his use of DOCA. Li, who had recently developed a method for extracting pure ACTH from the pituitary glands of sheep and hogs (as will be discussed below), argued that it had yet to be proven that DOC existed naturally in the body, and therefore may not even be a hormone. He also insinuated that Selye might have been able to produce such pronounced pathological changes because he used toxically high dosages of DOCA. Swiss chemist, Karl Miescher of the Ciba pharmaceutical company defended Selye’s use of DOCA on the grounds that Tadeus Reichstein had conclusively proven that DOC was naturally produced by the adrenal gland. Finally, R.A. Cleghorn of Toronto’s Banting Institute, a former member of the SSBS, challenged Selye’s claim that conditioning factors posed universal risk, provoking him to explain why Eskimos were not particularly prone to hypertension, “if cold and high protein diets are bad things.” Despite his cheeky candor, Cleghorn had hit upon a fundamental weakness in Selye’s theory—it failed to account for differences in individual subjectivity to stress. Cleghorn’s criticism may very likely have influenced Selye’s developing theory of “pathological conditions,” though Selye never admitted so.

While Selye was openly criticized for his chosen dosage and use of synthetic steroids, it is also possible that continued resistance to Selye’s theory arose not necessarily from flawed methodology, but from the constraints of laboratory-based research, as opposed to clinical patient trials. Since Selye worked exclusively with experimental animal populations, he was unable to verify his theory that stress induced diseases of adaptation in humans. There had been attempts to test the efficacy of adrenocortical steroids in patients suffering from diseases of adrenal deficiency, such as Addison’s disease and Cushing’s disease, but such trials were found to result in inconclusive therapeutic benefits and had adverse side effects. For instance, since it
was first synthesized in 1937, researchers at Harvard and the Mayo Clinic had used DOCA in clinical trials to treat patients with Addison’s disease—a deficiency of adrenal production, characterized by enlarged adrenal glands, abdominal pain and nausea, skin darkening, decreased blood pressure, intense salt cravings, weight loss, fatigue, weakness and muscular or joint pain.104

In the mid-1940s, Harvard clinician, Dr. George Thorn demonstrated the effective use of DOCA in the treatment of Addison’s disease through a series of patient trials, administering the hormone orally, by subcutaneous injection and through the implantation of pellets underneath the skin.105 Though it was not realized at the time, DOCA’s effectiveness derived from its influence on mineral metabolism. Despite the success of these early trials, DOCA did have significant drawbacks. As a mineral-corticoid, it acted to suppress inflammation by regulating salt metabolism, causing side effects that included increased fluid retention, decreased potassium levels, paralysis, heartbeat irregularities, and in the most severe cases, death.106 In 1937, the Mayo Clinic recommended that ideal therapeutic conditions for victims of Addison’s disease should minimize potassium and maximize sodium chloride intake.107 But, by the late-1940s,

104 Though it was not recognized until much later in the twentieth-century, primary Addison’s disease is most-commonly caused by a deficiency of the glucocorticoid cortisol, which maintains blood pressure, reduces inflammation and regulates carbohydrate metabolism. Primary Addison’s disease can also be caused by insufficient production of the mineralocorticoid Aldoseterone, which also helps to maintain blood pressure by regulating salt and water absorption, and helping the kidneys to retain sodium and excrete potassium. Additionally, secondary Addison’s disease can be caused by a deficiency of ACTH in the pituitary or CRH in the hypothalamus, which ultimately stimulate the release of cortisol. See “Addison’s Disease,” The Mayo Clinic, accessed June 19, 2013 http://www.mayoclinic.com/health/addisons-disease/DS00361.

105 Kendall, Cortisone, 81.

106 Rooke, The Quest for Cortisone, 82-83.

107 Kendall, Cortisone, 81-82.
Edward Kendall’s research on compound E would offer a pharmaceutical treatment for Addison’s disease that far surpassed the effectiveness of dietary modifications.

V. The Discovery of Cortisone and ACTH

In the five years after the war, researchers at the Mayo Clinic and Merck & Co. led a major resurgence in the search for cortical steroids. After the rest of the Cortin Committee members abandoned the compound E development project, Jacob van de Kamp continued to act as a scientific liaison between Merck and the Mayo Clinic as they pursued their study of the development of steroids from bile acids. In 1944, Merck endocrinologist Lewis Sarrett developed a method of converting compound A into compound E and by the end of December, he had prepared the first few milligrams of compound E using this method—not from materials present in the adrenal cortex. Unfortunately for Merck, Sarrett’s technique produced too small a quantity to successfully develop compound E for commercial production. But by the end of 1945, Merck and Mayo succeeded in preparing nearly 100 grams of compound A and clinical trials were quickly begun on patients with Addison’s disease, only to yield disappointing results: compound A had little effect in treating Addison’s disease.

However, the exciting prospect of producing compound E was overshadowed by the immense cost and the yet undetermined usefulness of the compound. Merck was nevertheless steadfast in their commitment to the project. The group’s work took a turn for the better in the

108 Kendall, Cortisone, 110.

109 Sarrett developed an improved structure of compound A which involved bonding an oxygen atom to the carbon-11 steroid nucleus of DOCA to transform it into compound A, which could then be converted into compound E by changing a hydroxyl group at carbon 20 to a ketone. See, Kendall, Cortisone, 115-116.

110 Ingle, Edward C. Kendall, 270.
spring of 1947 when a new method for creating a strengthened structure promised to facilitate large-scale development of compound E for commercial use.\textsuperscript{111} However, even this improved process required nearly forty steps and yielded only a very small quantity. Over the next two years, Kendall and Sarrett refined the process and in September of 1948, “compound E was being manufactured by the gram instead of the milligram,” producing enough to test on human illness.\textsuperscript{112} But, in the meantime, Merck was developing legitimate suspicions as to the potential success of their project. By the beginning of 1948, Merck had invested over $13 million in the production of compound E and was growing anxious about the prospects of any further investment.\textsuperscript{113} Merck held a meeting on April 29, 1948 in NYC to discuss the future of compound E project, with Randolph Major making it explicitly clear that unless they could discover a use for compound E that would identify a potential consumer market, Merck would have to withdraw from any future work on compound E.\textsuperscript{114}

That fall, Kendall and his colleague Philip S. Hench, head of the rheumatology ward at the Mayo Clinic’s St. Mary’s Hospital, persuaded Merck to send him a small sample of Compound E for an experimental treatment of one particularly afflicted arthritis patient. Merck hesitantly sent five grams of compound E (worth $1,000 in 1948, and equivalent to $10,000 in 1948).

\textsuperscript{111} Sarrett developed a new technique of partial synthesis using bile acid, which enabled him to place an atom of oxygen at the carbon-17 atom, and Kendall improved on Sarrett’s method by introducing a double bond in ring A of compound E. See Kendall, \textit{Cortisone}, 117.

\textsuperscript{112} George W. Gray, “Cortisone and ACTH,” \textit{Scientific American} (March 1950): 30-36, folder I: Newspaper clippings, HSC

\textsuperscript{113} Rooke, \textit{The Quest for Cortisone}, 134.

\textsuperscript{114} Given the past use of adrenocorticoids (DOCA) in treating Addison’s disease, they first tried treating patients with Addison’s Disease with compound E, allotting Randal G. Sprague two grams of compound E for trials on his patients at the Mayo Clinic. See Kendall, \textit{Cortisone}, 119.
2015 dollars) to Kendall and Hench, and were shocked by their results.\textsuperscript{115} Hench’s patient, a young woman in her late-20s named Mrs. Gardner, was bed-ridden, unable to walk and barely able to move her arms, with absolutely no signs of improvement. After two days of treatment, which consisted of two daily injections of fifty-milligram doses, Mrs. Gardner was able to roll over in bed easily and demonstrated increased strength and appetite. After three days she was able to raise her hands over her head and make visits to several fellow patients. After five days she had lost almost all stiffness and joint tenderness, pain on motion was significantly reduced, her grossly-swollen knees had resumed a nearly normal appearance, and her appetite had returned so strongly that she was concerned about putting on weight.\textsuperscript{116} Nine days after beginning treatment, she was able to go shopping for three hours downtown, and claimed that “she had never felt better in her life.”\textsuperscript{117}

Kendall and Hench vetted these astounding results on five more patients in a controlled blind trial. Kendall reported that one of these patients, Mr. Moss,

responded in a manner even more dramatic than Mrs. Gardner. He had had the disease for over five years and it was of such severity that some of the muscles were atrophied and replaced with fibrous tissue, and the joints were badly swollen. He suffered much pain and was disabled. I saw Mr. Moss this morning. The pain is completely relieved, the joints are back to normal as far as swelling is concerned, and he has regained function in an amazing manner. Before treatment the fingers were so stiff that he could not clinch his fist. He cannot close his fingers completely today but the improvement is very striking. His improvement has been uninterrupted: his condition has been better each day than on the day preceding.\textsuperscript{118}

\textsuperscript{115}Rooke, \textit{The Quest for Cortisone}, 137-39.


\textsuperscript{117}Kendall, \textit{Cortisone}, 125-126.

\textsuperscript{118}E.C. Kendall to Dr. Randolph T. Major (Merck & Co., Inc.), October 12, 1948, Box 8, Folder "Merck & Co. 1948," ECK.
Once it had been determined that compound E could be effectively used to treat arthritis, Merck sought to expedite commercial production. They sent a staff chemist, Monty Miller to Rochester in November, and together, Miller and Kendall worked all day on Thanksgiving 1948 to develop large-scale method of converting intermediate compound into compound E. The conversion of bile acid to cortisone required more than thirty different reactions, distributed among three different task forces. By the end of 1949, the production process had been so thoroughly improved that the yield from the same amount of 1,269 pounds of starting material increased from 5 grams to 942 grams. Hench proposed that compound E be marketed under the name “cortisone,” modified from “corsone,” which implied a relationship with the heart, and thus gave a title to the ensuing frenzy of scientific interest in this miraculous drug.\footnote{Kendall, \textit{Cortisone}, 118, 147-48, 143.}

The supply of cortisone was so limited in the spring of 1949 that Merck would ship Kendall empty syringes and bottles containing traces of it, so he could prepare more of the steroid from the residue, hardly a sustainable or sufficient strategy to meet the research of therapeutic demands of the time.\footnote{Harry M. Marks, “Cortisone, 1949: A Year in the Political Life of a Drug,” \textit{Bulletin of the History of Medicine} 66, no. 3 (1992): 420.} The Mayo Clinic offered Kendall a new laboratory which enabled him to increase production while continuing research on steroids.\footnote{Kendall, \textit{Cortisone}, 148.} However, even with these expanded facilities, the combined resources of the Kendall and Merck labs were unable to generate a sufficient supply of cortisone.\footnote{Ibid., 144-45.} It required sixty-five pounds of bile to produce a half-pound of cortisone.\footnote{\textquoteleft\textquoteleft New Health Frontier: The Glands.
} Through the end of 1949, Merck was producing
approximately 200 grams of cortisone per month (derived from the bile acid of 800,000 cattle). Due to the scarce production output, a single injection of cortisone cost approximately $100 ($1,000 in 2015 dollars), and a three-week course of treatment cost approximately $18,000 ($180,000 in 2015 dollars).

Part of the problem lay in the exclusivity of production ensured by Kendall and Merck’s patent rights. As the inventor of compound E, Kendall earned patenting rights to cortisone, though he was not the only one with a legitimate legal claim to it. A total of four pharmaceutical companies—Merck, Ciba, the Schering Corporation, and Organon—as well as the Mayo Clinic each possessed a patent that gave them rights to some aspects of the production process for cortisone. Due to his firm, though perhaps romantic belief that “no physician engaged in the practice of medicine should profit from the exploitation of any drug, vaccine, or appliance used in the practice of medicine,” Kendall relinquished his patenting rights for compound E to the Mayo Clinic, leaving the Mayo Clinic and Merck with the only claims permitting the manufacture of cortisone per se. The Mayo Clinic delegated administration of the licensing of cortisone to the Research Company of New York, originally founded in 1912 to subsidize academic research with royalties from inventions, and actively involved in drug patenting by the late-1930s with their involvement with the Williams-Waterman Fund’s vitamin patents. Robert Williams, the Director of Grants for the Research Corporation of New York, which administered the patent for cortisone, reported that “of the thirty-odd steps required or the conversion of desoxycholic acid to cortisone there were several processes already patented by other firms who

124 Gray, “Cortisone and ACTH.”

125 Albert O. Maisel, “Hope for Millions,” McCall’s, September 1949, 151-160, folder I: Newspaper clippings, HSC.

126 Kendall, Cortisone, 100.
had been engaged in the steroid field for years”—Ciba, Organon and Schering.\textsuperscript{127} The Research Corporation created an agreement between each of the original four patent-holding pharmaceutical companies permitting any one of them to use patents held by the others, provided that any party profiting from the sale of cortisone pay a small royalty to be shared by all members of the group.

Yet, still fearing that insufficient production might limit its use and stigmatize cortisone as an elite or clinical drug, Merck and Mayo appealed to the National Academy of Sciences to coordinate production and distribution.\textsuperscript{128} Inspired by the great success of the NRC’s wartime committee to coordinate the mass production of penicillin, Merck appealed to their longtime associates, Alfred N. Richards, now president of the National Academy of Science (NAS), and Vannevar Bush, head of the Army and Navy’s Joint National Research Board, to assemble a committee to oversee the distribution of cortisone. This committee consisted of an impressive selection of elite scientists, including Chairman Chester Keefer, the former head of the NRC’s penicillin committee; Edward A. Doisy, who earned the Nobel Prize for his discovery of vitamin K; Hans T. Clarke, Cyril N.H. Long, Robert F. Loeb, Eli K. Marshall, and Joseph T. Wearn. Both Doisy and Long had served on the NRC’s committee on endocrinology during the war and were thus, no strangers to federal-academic-industry alliances. The committee attracted criticism for its elite composition and for the close relationship between several committee members and pharmaceutical firms, particularly between Richards and Merck. Representing the interests of the academic scientific establishment, the cortisone committee explicitly prioritized basic


\textsuperscript{128} Marks, “Cortisone, 1949,” 425.
research on the metabolic actions and physiological effects of the steroid, over any clinical applications. The committee felt little more could be learned about the benefits of cortisone in treating arthritis until its physiological actions were better understood. Perhaps predictably, this stance drew fire from a new guard of specialist scientists and recently formed disease foundations, who advocated clinical patient trials to determine the best applicability of the drug in order to expedite its therapeutic usefulness for patients suffering from arthritis and cancer. Prominent among these critics were none other than Philip Hench, as well as the Arthritis and Rheumatism Foundation, the American Heart Association, and the American Cancer Society.  

The committee perhaps underestimated the political weight of the disease foundations, which were largely dominated not by scientific representatives, but by lay trustees largely drawn from the business community. After Richards withdrew from the committee in early August, the NRC created a subcommittee of rheumatologists to advise the cortisone committee, but the damage had already been done. Represented by Mary Lasker of the American Cancer Society and Thomas Duckett Jones, president of the American Rheumatism Association and vice-president of the American Heart Association, in the summer and fall of 1949 the foundations collectively appealed to Surgeon General Leonard Scheele to petition the Congressional Appropriations Committee to allocate $1.1 million to the NIH for cortisone and ACTH research. Their bid was a success, and led to the creation of a new NIH committee headed by Lasker and Duckett to oversee NIH funding of cortisone research. While the NIH had the endorsement of the federal government, the disease foundations and the larger community of chronic disease specialists, the NRC committee lacked such powerful political and financial support. As a result,


\[130\] Ibid., 429, 432.
when their charter expired at the end of December 1949, Merck and the NRC declined to renew it and the committee faded into non-existence. In January 1950, after the NAS committee disbanded, Merck began marketing the steroid at $150 per gram (about $1,500 in 2015 dollars), which would adequately support a ten-day course of treatment.

Historian of Medicine Harry M. Marks argues that Merck’s failure to compel the NAS to “direct the evaluation and allocation of cortisone reinforced existing pressures for proprietary control over clinical drug research.” As a result, the disease foundations gained an “opportunity to demonstrate the political strength of their conviction that therapeutic 'breakthroughs' were the most important feature of medical research... (and) the weakness of a formerly authoritative scientific elite who failed to translate their intellectual vision for studying new drugs into a social consensus supporting their control of cortisone supplies.” Moreover, the backing of the disease associations helped to transform the NIH into a major conduit of federal-academic scientific collaborations in the postwar period.

The US example is not unique. Canada’s DMR also took responsibility for allocating cortisone for research purposes, through the creation of its own advisory committee. As a result, not only were the US and Canadian governments instrumental in organizing the original program to develop adrenocortical steroids during the war, but they also mediated access to these revolutionary new materials once they were finally available.

132 Gray, “Cortisone and ACTH.”
133 Marks, “Cortisone, 1949,” 421.
134 The ACMR created the Advisory Committee on ACTH and Cortisone around the same time as the NIH committee, just as the new drug ACTH was beginning to be marketed for therapeutic use. See Box 11: NRC, "Proceedings of the Eight Meeting of the Advisory Committee on Medical Research," November 28, 1949, Box 11, CNRC.
In 1943, George Sayers at Yale Medical School and Choh Hao Li at the University of California-Berkeley nearly simultaneously discovered methods of preparing anterior pituitary hormone extracts, Sayers using porcine, and Li using ovine pituitary glands, and announced their results in the same issue of *Journal of Biological Chemistry*.¹³⁵ Over the course of the next seven years, Li developed a relationship with the research subsidiary of the Chicago meatpacking firm, Armour & Co., who applied Li’s ACTH preparation technique in processing their excess hog pituitary glands to develop a method of producing ACTH on a large-scale. In 1946 Armour & Co. was able to supply a few grams of ACTH for laboratory research, but there was not yet a sufficient amount to conduct patient trials. In February of 1949, Armour & Co. provided Hench with enough ACTH to allot daily injections to two arthritic patients at the Mayo Clinic, which ultimately confirmed that “the anti-rheumatic effects of ACTH paralleled those of cortisone in practically every particular.”¹³⁶ Still by the end of 1949, Armour & Co. was producing only five pounds of ACTH per month, which was exclusively reserved for research in hospitals, clinics and laboratories. Yet, compared to cortisone, ACTH was significantly easier to produce in abundance, and was therefore slightly more affordable.

Armour provided Kendall with a “generous supply” of ACTH for laboratory and clinical experiments.¹³⁷ While the great success of cortisone in treating arthritis strongly recommended the therapeutic value of ACTH, there remained a lingering doubt among many members of the scientific community that it may have adverse effects on health. As Kendall would later explain,


¹³⁶ Gray, “Cortisone and ACTH.”

“the only reason for expecting that administration of ACTH might have another effect came from the hypothesis advanced by Dr. Hans Selye…that over-activity of the adrenal cortex is an etiologic factor in a large number of diseases,” and therefore, “the administration of ACTH would not relieve the symptoms of rheumatoid arthritis; rather, it would cause an exacerbation of the symptoms.” Selye’s research with DOCA and LAP certainly suggested this to be true, however, he had not yet fully come to realize the antagonistic balance of glucocorticoids and mineralocorticoids in regulating disease. As Kendall’s and numerous other researchers’ experiments would show, ACTH was in fact useful in the treatment of a great number of chronic diseases.

In October of 1949 John R. Mote, the medical director of Armour & Co. organized a two-day conference dedicated to discussing the recent breakthroughs in ACTH research. Scientists from across North America presented papers on their success in using ACTH to treat a myriad of real and imagined diseases, from arthritis, hypertension, asthma and pneumonia to alcoholism and homosexuality. The conference itself was unprecedented, for as one physicians remarked “no medical gathering in history ever heard reports of so many different diseases yielding to treatment with a single drug.” Walter Bauer of Harvard University Medical School captured the revolutionary sentiment that permeated the ACTH conference, remarking that “the astonishing ability of ACTH apparently to turn diseases off and on at will marks the opening of a new era in medicine.” And J.S.L. Browne of McGill emphasized the cathartic experience of being present at the conference, as attendees had the palpable “feeling we were witnessing the beginning of a

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revolution,”” which Browne was careful to point out, was in many ways “foreshadowed in certain research results that have been accumulating in Montreal over the last dozen years.”

The following month, Mote spoke at the mid-year meeting of the American Pharmaceutical Manufacturers’ Association, outlining the recent research in adrenocortical therapy. Alluding to Selye’s earlier experiments on adaptation energy as a variable in the onset of diseases of adaptation, Mote explained that “an animal or human being cannot withstand ‘acute stress’ indefinitely,” and eventually will lose its capacity for resistance as “adrenal exhaustion” causes decreases adrenal function. Mote went on to explain how Kendall and Hench’s experiments on collagen diseases—rheumatoid arthritis, rheumatic fever, lupus erythematosus disseminates, dermatomyositis, and scleroderma—researchers then turned to studying the effectiveness of ACTH and cortisone in treating chronic degenerative diseases, such as nephritis and nephrosis, as well as asthma, hay fever, eczema, and drug sensitivities. As this round of experiments showed remarkable effectiveness of ACTH and cortisone in abating the symptoms of these diseases, researchers then turned to studying their use in treating acute bacterial and virus infections, metabolic diseases and muscular dystrophies, as well as mental illness. All of this pointed to the conclusion, according to Mote, that “the adrenal gland plays perhaps the major role as to whether or not a person is sick or well, regardless of the illness or the cause thereof.” Mote assessed that “the discovery of the role of the adrenal gland in health

139 Gray, “Cortisone and ACTH.”

and disease has probably opened up the largest area of medicine... since the discovery of bacteria.”

In December of 1949, Li improved on his original salt-fraction method, by using the enzyme pepsin to break down ACTH molecules into submolecules consisting of at most eight amino acids. By decoding these simpler components of ACTH, Li offered a potential to synthesize the steroid more easily and produce it in large quantities. By January 1950, Armour began commercially marketing the drug for public use at the cost of $200 per gram (about $2,000 in 2015 dollars) or about $5,000 per ounce (about $50,000 in 2015 dollars). Production of ACTH required the pituitary glands of approximately 400,000 hogs to yield one pound, or two million hogs to yield five pounds of compound. While a twenty-day course of treatment for rheumatoid arthritis would require only one gram of ACTH, the pituitary glands of 500 hogs were required to produce this small amount. By mid-1950, Armour was producing enough ACTH to treat 10,000 people per year, and Wilson Labs had begun production of ACTH using sheep pituitaries, with an anticipated yield capable of treating 5,000 people annually. In June of 1950, Selye’s main pharmaceutical benefactor, Frank W. Horner, Ltd. announced that it


142 Gray, “Cortisone and ACTH.”


144 “New Health Frontier: The Glands”; “Montreal Doctor Claims New Clues to Disease.”

145 Gray, “Cortisone and ACTH.”

146 Morris Fishbein, “Guinea Pig for ACTH: A Struggle with Pain,” Collier’s, June 10, 1950, folder I: Newspaper clippings, HSC.
had developed a new process of producing ACTH involving large-scale extraction from bovine pituitary glands supplied by Canada Packers Ltd.\footnote{New Source of Supply for ACTH, Montreal Daily Star, June 14, 1950, folder I: Newspaper clippings, HSC.} Horner’s participation in the ACTH market contributed to enormous growth in the next five years, expanding distribution into the British West Indies, Central America, Cuba, India, Pakistan, and several South American countries.\footnote{New Era in Medicine: Laboratory Has Put New Magic in the Doctor’s Bag, Financial Post (Toronto), June 25, 1955, folder I: Newspaper clippings, HSC.}

VI. The Adrenocortical Revolution

As scientists identified more and more therapeutic uses for ACTH, and its commercial availability expanded, the North American public greeted these latest wonder drugs with eagerness that medical science had once again gratified their increasing expectation for pharmaceutical panacea. The medical community, in many ways, brokered the public’s indoctrination with ACTH and cortisone, both in personal interactions between doctor and patient, and by profiling their expertise in popular publications. In an article for Collier’s, Morris Fishbein, former editor of the Journal of the American Medical Association and founder of the Medical World News, reported the sensational story of one arthritis patient treated with cortisone:

On June 6, 1949, Jack Shanahan entered Wesley Memorial Hospital in Chicago, as a human guinea pig.” Shanahan was the director of the Chicago Sun-Times, had been in then newspaper circulation business for 43 years, and who had suffered from crippling arthritis for years, the past three of which he had grown accustomed to starting his day with 10 aspirin to dull the pain. He received experimental treatments of ACTH beginning June 20th, by the second morning he awoke with no pain.\footnote{Fishbein, “Guinea Pig for ACTH.”}
This news of such an amazing medical miracle must have had a powerful effect on lay readers, inspiring hope in medicinal cures for diseases they had come to interpret as a natural consequence of aging. And as the popular press often profiled the myriad of diseases which cortisone and ACTH were effective in treating, patients suffering from both life-threatening diseases, like tuberculosis and leukemia, as well as less severe diseases, such as eczema, psoriasis, myasthenia gravis, allergies, asthma, hay fever, drug sensitivity, and even chronic alcoholism and schizophrenia, were offered a simple cure—if only the could afford it.150

However, this hope was perhaps naively inspired, as medical science had yet to realize the potential risks of cortisone and ACTH treatment. As it turned it, both drugs bore quite dangerous side effects, including decreased resistance to infectious diseases, the potential development of Addison’s disease, and even death. Some experts sought to call public attention to these dangers, but their warnings were overshadowed by the excited praise extolled in the popular press. Writing for Collier’s, Fishbein highlighted the potential for ACTH to induce diabetes-like symptoms due to overactive adrenals, and collateral signs of virilism, including hair on the face, a deep voice and ruddy discoloration of the skin,” as well as obesity and high blood pressure (often seen with tumors of the pituitary).151 Perhaps, patients assessed these risks to pale in comparison to the benefits of ACTH, or perhaps Fishbein was merely in the minority in cautious medical experts. For whatever reason, despite increasing evidence of harm, the romance with ACTH and cortisone continued through the mid-1950s.

Sadly, Hench’s first cortisone patient, Mrs. Gardner, suffered a terribly adverse reaction to cortisone treatment, transforming from a bed-ridden arthritic, to a gregarious social butterfly,
to a near-psychotic within a month. In the first two weeks of treatment she gained increased physical capacity as well as increased reflex sensitization and mental quickness. She also developed a bloated “moon” face and stria (streaklike lesions) on her body, characteristic of Addison’s disease. Her mother became skeptical of the treatment her daughter was receiving at Mayo, and once Mrs. Gardner’s condition stabilized to the point where she was able to leave St. Mary’s, her mother refused to allow her to return when new symptoms set in. Her personal doctor in Indianapolis diagnosed her with lupus erythematosus, endorsing the mother’s suspicions that the Mayo Clinic’s experimental treatment had jeopardized her daughter’s health. He began to treat her with ACTH injections, which caused her adrenals to produce a DOCA-like substance, which not only failed to alleviate the inflammatory disease, but likely worsened it by causing her to retain salt and water. Mrs. Gardner ultimately died of acute pulmonary edema in December of 1954, and her mother refused to permit an autopsy.\textsuperscript{152}

Kendall, was particularly saddened by Mrs. Gardner’s death, and bitterly indicted the lack of precaution employed by medical experts and the media in their celebration of cortisone and ACTH. He later lamented that at the time, “statements were made before it was recognized that cortisone derivatives are a two-edged sword. When they are administered in large doses over long periods of time, symptoms of hypercortisonism appear. The effective use of cortisone was retarded by intemperate criticism that was highly emotional and unscientific.”\textsuperscript{153} He personally bore deep regret that his greatest scientific achievement was also the cause of so much harm due to the exaggerated fanfare aroused by ill-advised medical counsel and the media. In fact, when Kendall, Hench and Reichstein were awarded the 1950 Nobel Prize for their work in

\textsuperscript{152}Rooke, \textit{The Quest for Cortisone}, 156-57.

\textsuperscript{153}Kendall, \textit{Cortisone}, 150.
adrenocortical research, it did as much to commemorate the revolutionary potential of their work, as to confirm the public sentiment that cortisone and ACTH were in fact miracle cures. It was not until the mid-1950s that popular consciousness awoke to the real dangers of cortisone and ACTH side effects. Nicholas Ray’s 1956 film *Bigger Than Life* told a cautionary tale of an average man (played by James Mason) who quickly lost control of his life after he began taking cortisone pills to treat his polyarteritis nodosa (an inflammation of the arteries). Developing a dependency, he began abusing the pills and became emotionally volatile and violent, jeopardizing his job, his friendships, and nearly destroying his family. While this parable suggests that the downward spiral of cortisone treatment had become a common cultural referent, it is also a testament to the widespread popularity of the drug by the mid-1950s.154

Despite the dangerous side effects, cortisone and ACTH offered previously unimaginable relief for hundreds of thousands of patients. The increased prevalence of chronic inflammatory diseases created a vast market for such a “wonder drug,” and posed a significant threat to the public health that it demanded federal action to direct further research on the therapeutic applications of corticoids. The discovery of ACTH and cortisone also had the effect of validating the long-questioned theory of the GAS—which Selye now increasingly referred to as, the “stress” syndrome. The triumph of his stress theory was achieved, in part, through Selye’s own research with ACTH and cortisone, as well as the endorsement of his colleagues, but perhaps most importantly, through the enthusiastic response of the popular press.

154 *Bigger than Life* is purportedly based on a *New Yorker* article that portrayed a similar tragic decline caused by cortisone dependency. See Berton Roueche, “Ten Feet Tall” *The New Yorker*, September 10, 1955. See also, Adrian Danks, “’God Was Wrong’: Nicholas Ray’s *Bigger than Life*,” *Cinémathèque Annotations on Film* 50 (March 2009), accessed March 20, 2015 http://sensesofcinema.com/2009/cteq/bigger-than-life.
Since the early 1940s, Selye had occasionally written to Kendall, requesting various adrenocorticoid compounds for his experiments, and following Kendall’s discovery of cortisone in 1949, Kendall helped Selye to obtain a small supply of this precious new compound from Merck. Selye also solicited a sample of ACTH from Armour & Co., and with these two cutting-edge compounds, performed a series of experiments that elucidated his earlier observations on hormonal balance. He found that both ACTH and cortisone exerted a protective effect against anaphylaxis in rats treated with egg-white extracts (which contain proteins that are known for causing allergic reactions), while DOCA and LAP increased the severity of the reaction. Selye also examined the effects of ACTH, cortisone, DOCA and LAP on rats which had formaldehyde injected into their joints to induce arthritis (“formalin arthritis”), and found that while DOCA and LAP increased inflammation and severely aggravated joint swelling and stiffness, ACTH and cortisone reduced these symptoms. It seemed that ACTH and cortisone were natural antagonists to LAP and DOCA, and could therefore by used to counter the harmful affects of these mineralocorticoids. Thus, Selye found powerful confirmation of his theory that inter-hormonal tension was essential to successfully resisting injury from stress.

The discovery that pure adrenal and pituitary extracts were effective in treating chronic diseases was a powerful endorsement of Selye’s now nearly fifteen-year-old theory. No longer was the criticism that his results were tainted by relying on synthetic DOCA a viable critique of his work. Nor was the claim that his animal studies did not verify that the same physiological reactions took place in humans. The revelation of cortisone and ACTH’s therapeutic usefulness verified Selye’s theory that adrenocortical hormones did in fact regulate many diseases and also demonstrated that because the same physiological reactions were also found in man, “we were
able to transfer findings from lower animals to the human.” The premise of Selye’s theory was vindicated, and as the popular press excitedly seized on this momentous scientific discovery, Selye was frequently mentioned as the original discoverer of the adrenocortical regulation of chronic disease.

Foreshadowing a trend that would guide the rest of Selye’s career, the popularization of adrenocortical therapy propelled Selye into the limelight as a world-renowned expert on stress and hormones. Selye’s former colleague at McGill, close friend and fellow stress-researcher, J.S.L. Browne pointed out that Selye’s concept of stress was in fact “completely at variance with the older views of scientific medicine… with the idea of compartmentalized disease, which is the central dogma of modern medical practice,” and therefore it is necessary that “a great adjustment in our thinking has to be made.” Yet, evidently this transformation was well underway, as many scientists believed that like Hench and Kendall, Selye was a prime candidate for the Nobel Prize in Medicine and Physiology.”

Even a standard bearer of allopathic medicine like Dr. Morris Fishbein, editor of the Journal of the American Medical Association told a New York Times reporter that ‘Dr. Selye’s research has ushered in a revolutionary exciting new epoch in medical science.’ Prominent medical journals throughout the world heralded the professional legitimization of Selye’s theory, with the Journal of Clinical Endocrinology declaring that “the importance of Selye’s work is now well established,” the Swiss journal, Medical Hygiene boldly asserting that “much of the work being done by doctors throughout the world on hormones is

155 Gray, “Cortisone and ACTH.”

156 Ibid.

157 “Montreal Doctor Claims New Clues to Disease.”

based on the research originally done by Dr. Selye,”” and the Parisian *Press Medical* claiming that “’the theoretical basis of all recent discoveries with ACTH... can be found in its entirety in the discoveries of Selye and his school in Montreal.’”¹⁵⁹

This radical shift was evident both within and outside of academia as Selye’s research was increasingly profiled in the popular press. *McCall’s* magazine offered that “Selye’s early work was greeted with some skepticism,” in many ways because “specialists who had spent their lives studying single diseases could not readily accept the idea that their specialty was really just another manifestation of a general breakdown under stress—that high blood pressure and arthritis and kidney troubles might all be so intimately linked in origin.”¹⁶⁰ *Time* proffered despite the longtime resistance to his theory amongst the orthodox medical community, his legacy might yet be vindicated, for though Selye’s 1936 paper “attracted no more attention than Alexander Fleming’s first report of penicillin—and it may prove no less important to suffering mankind.” In fact, the authors insisted, Selye had laid the foundation for the recent breakthroughs in the therapeutic use of cortisone and ACTH, since “long before Hench and Kendall showed the near-miraculous power of ACTH and cortisone to reverse the course of rheumatoid arthritis, Dr. Selye had outlined the theory into which their facts fitted so neatly.”¹⁶¹

Several other reporters alleged that Selye was in fact “the first to suggest that injections of cortical hormones would help the human body in its natural fight against disease and sickness,” leading to “the production of ACTH and cortisone, and their amazing cures.” Yet, if anything, Selye’s earlier research with DOCA indicated the opposite—that administration of


¹⁶⁰ Maisel, “Hope for Millions.”

¹⁶¹ “Medicine: The Life of Stress,” *Time*, October 9, 1950, folder I: Newspaper clippings, HSC.
adrenocorticoids could induce disease rather than heal.\textsuperscript{162} It is likely that Selye’s recent realization of the antagonistic relationship between DOCA and cortisone had colored the press’s interpretation of his earlier work. Selye did advocate the use of ACTH and cortisone to treat stress disorders.\textsuperscript{163} He was outspoken in his hope that research would soon uncover a way to manipulate the body’s natural autopharmacological processes to treat and protect against disease.\textsuperscript{164} Thus, not only did Selye counter etiological specificity, but he also countered the allopathic tradition of treating disease after it had already developed. Rather, he advocated preventative therapy to support the body’s own natural healing processes. As a testament to how the discovery of ACTH and cortisone revolutionized biomedical etiology, in May of 1950, Selye announced to a meeting of the Canadian Medical Association that modern medicine was now able to “combat disease even when we cannot eliminate the cause.”\textsuperscript{165}

Many journalists credited Selye with opening an entire new field of research that promised to offer greater insight into the causes of “the mystery of those disease of unknown nature.”\textsuperscript{166} In the March 1949 edition of \textit{Scientific American}, P.C. Constantinides and Niall Carey, two researchers at the IMCE contributed an article explaining Selye’s research on

\begin{footnotesize}
\textsuperscript{162} “Montreal Doctor Claims New Clues to Disease.”

\textsuperscript{163} “Stress and Hormone Causes Many Diseases Canadian MD Finds,” \textit{The Telegram}, January 28, 1950, folder I: Newspaper clippings, HSC.


\textsuperscript{165} “Deterioration in Medical Service Foreseen in Compulsory Scheme,” \textit{Montreal Gazette}, May ?, 1950, folder I: Newspaper clippings, HSC.

\textsuperscript{166} Betty Davison, “Montreal Doctor’s Theory Said ‘Greatest Concept Since Pasteur,’” \textit{Montreal Gazette}, September 27, 1949, folder I: Newspaper clippings, HSC.
\end{footnotesize}
diseases of adaptation and contextualizing stress as a problem of modern life. Painting a rather
dire situation, they proclaimed,

One might question whether stress is peculiarly characteristic of our sheltered civilization, with all
its comforts and amenities. Yet these very protections—modern labor-saving devices, clothing,
heating—have rendered us all the more vulnerable and sensitive to the slightest stress. What was a
mild stress to our forebears now, frequently represents a minor crisis. Moreover, the frustrations
and repressions arising from emotional conflicts in the modern world, economic and political
insecurity, the drudgery associated with many modern occupations—all these represent stresses as
formidable as the most severe physical injury. We live under a constant strain; we are losing our
ability to relax; we seek fresh forms of physical or mental stimulation.167

Selye welcomed the media’s attention, playing into their interest to depict stress as an
indictment on tensions caused by modern life. He told the Ohio Times Gazette that “stress can
be defined as anything—a virus, running up a flight of stairs, mental tension, a wound—which
causes a change in the so-called normal function of all the body organisms.”168 He boldly
claimed that recent increases in cardiovascular diseases did not simply arise from the fact that
“people are living longer,” but because they were “living faster and spending our heritage of
adaptation energy more quickly.”169 Indicating the frenzied pace of modern life, Selye insinuated
that psychological and physiological stress are inextricably linked. Selye furthered pandered to
the public’s preoccupation with the psychological valence of stress by suggesting that cortisone
might be useful in treating “the stress of an irritating boss.”170

167 P.C. Constantinides and Niall Carey, “The Alarm Reaction,” Scientific American,
March 1949, 20-23, folder I: Newspaper clippings, HSC.

168 “New Concept of Medicine Outlined,” Times-Gazette (Ohio), April 7, 1950, folder I:
Newspaper clippings, HSC.

169 “Stress: The Real Killer,” The Star Weekly (Toronto), March 7, 1953, folder I:
Newspaper clippings, HSC.

170 “Stress and Hormone Causes Many Diseases Canadian MD Finds,” The Telegram,
January 28, 1950, folder I: Newspaper clippings, HSC.
Conclusion

Selye enthusiastically embraced his new celebrity status, and increasingly turned to the press as a medium to promote his research to popular audiences. In the decade following the therapeutic discovery of cortisone and ACTH, Selye emerged as the world’s leading authority on stress, but his public persona was not merely the result of his innovative research. With a special knack for self-promotion not commonly demonstrated by scientists, Selye used his corporate affiliations to enhance his professional prestige, and his scientific expertise to lend greater credibility to his pharmaceutical funders’ new products. At the same time, Selye’s pharmaceutical benefactors profited handsomely from the phenomenal demand created for these new wonder drugs, and in turn, he was rewarded with enhanced financial security for his ongoing research.

Selye’s marketing tactics helped to distinguish him from a growing field of stress researchers of diverse fields of expertise. This interdisciplinary stress science contributed to a revolution in disease etiology as it identified internal biochemical adaptive mechanisms, as well as psychodynamics and environmental pathways of stress. In this growing scientific field, Selye became a member of a transnational community of scientists undergoing a process of formal professionalization, as they formed new associations, published new scientific journals, and organized annual conferences. Yet, despite his iconic status as the “father of stress,” Selye’s influence over stress research waned as psychologists and psychiatrists took a more active role in the professionalization of stress science.
Chapter 4: The Professionalization of Stress Research

Introduction

The 1950s began propitiously for Selye, and for stress research in general. His theory of stress finally gained the validation of mainstream biomedical science through the confirmed therapeutic effects of the adrenocortical and pituitary hormones, cortisone and ACTH. While Selye did not directly participate in these revolutionary discoveries, he was widely hailed as a pioneer of the original endocrinological studies that undergirded Edward Kendall and Philip Hench’s work with cortisone and arthritis. After fifteen years of struggling to gain recognition for his unified theory of sickness, Selye was at last vindicated among his peers and the general public. While he continued to attract criticism for various aspects of his work, Selye earned an esteemed professional reputation as the preeminent icon of a growing field of respected stress researchers.

Along with his elevated status came new and ever larger funding opportunities, primarily through his two strongest sources of support: state agencies and private corporations. Selye maintained close relationships with the USNRC and the PHS, and continued to receive lucrative grants and supplies from pharmaceutical companies. However, while Selye’s colleagues served on federal committees that determined priorities in stress research, Selye missed the opportunity to participate in these decisions by eschewing public service. Similarly, while he participated in professional conferences dedicated to stress research, he most often did so at the invitation or approval of conference organizers, and did not participate in the administration of these professional organizations. Rather than assert leadership in the larger field of stress research, Selye reveled in his own chiefdom at the IMCE. While he was indeed well-respected by his colleagues in stress research, he failed to take a leadership role in the professional community,
and as a result lost control of the professional discourse on stress to a growing presence of psychiatrists who actively served on professional committees. Selye was a grantseeker, not a grantmaker in a field he pioneered. As his dominant sources of funding prioritized applied (rather than basic) medical research, Selye was forced to cater his research to appeal to the interests that informed the political economy of medical research.

I. "The Father of Stress"

The sudden onslaught of media exposure in the midst of the adrenocortical revolution showed Selye how to use public relations strategies to win popular support and private funding for his research. In May of 1950 Selye held a press conference to promote the publication of his *First Annual Report on Stress*, and then left on a lengthy lecture tour of Europe, South America and the United States which lasted until the late fall.¹ In its first printing, Selye’s *First Annual Report on Stress* sold out 10,000 copies.² The massive tome cost $14 (approximately $140 in 2015 dollars) and sold at a rate of twenty-five copies per day, outselling all other scientific monographs, except the Kinsey Reports on sexuality.³ While in the first decade after his discovery of the GAS there were only 700 journal references to his work, from 1946-51 there were approximately 5,500—and in 1953 alone there were 3,000.⁴ As historian Elizabeth Siegel Watkins has noted, 1950 marked the first mention of the term stress in *Index Medicus*, indicating

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² Fromer, “More Years of Youth.”

³ Harry Henderson, “Dr. Selye’s Medical Revolution,” *Magazine Digest*, May 1952, 43-48, (abridged from previous publication in *Maclean’s*), folder I: Newspaper clippings, HSC.

⁴ Henderson, “Dr. Selye’s Medical Revolution.”
its assimilation as a medical concept. And the first appearance of the term stress in the 1951 edition of the Reader’s Guide to Periodical Literature suggested its cultural assimilation followed very quickly thereafter.  

The popular press’s characterization of Selye as one of the most famous medical researchers in the world was perhaps a self-fulfilling prophecy, as it enabled Selye to gain immense leverage for his own research, and to help others. The Montreal Gazette reported that though he had no direct involvement in its development or distribution, given his professional reputation alone, with a simple phone call, Selye was able to obtain some of the precious supply of ACTH from a Chicago Lab for the experimental treatment of a Brazilian doctor’s wife who was stricken with leukemia. As evidence of his esteemed international reputation, in June of 1950 Selye gave the keynote lecture at the annual conference of London’s prestigious Heberden Society, and was given the honor of being the first Canadian awarded the Heberden Society Medal. Thereafter, he departed on a lecture tour of western Europe and South America, making appearances in Ireland, Holland, Paris, Frankfort, Vienna, Rome, Madrid, Switzerland, Portugal, Argentina and Rio de Janeiro, where he helped to organize a clinic in experimental medicine modeled after his own. In total he visited sixty-seven universities and medical societies, and along the way, received the medal of the Florentine Academy of Medicine, degrees from all five

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6 “Dr. Hans Selye’s ‘Stress Factor’ Is Seen Insight to Human Illness,” Montreal Gazette, May 26, 1950, folder I: Newspaper clippings, HSC.

7 “Will It Soon Be As Famous As Fleming?” Daily Express (London), June 2?, 1950, folder I: Newspaper clippings, HSC.
of the national universities of the Argentina, and was named an honorary member of National Academy of Spain.\footnote{8}

Such international acclaim led to Selye’s celebration as an emblem of Canadian national pride. Selye proudly emphasized that his new book, *Stress* was published in Canada as an illustration that “we can do such things as well here as anywhere else.”\footnote{9} The Canadian press enjoyed Selye’s celebrity perhaps as much as he did, proclaiming his discovery of stress as a “great step forward in the progress of Canadian medicine,”\footnote{10} and claimed that he alone successfully propelled “Canada to the front in medical research.”\footnote{11} At a time when Canadian politics were infused with concern for national independence and pride amidst an increasingly competitive international Cold War economy, Selye became a symbol of Canadian scientific excellence and cultural glory.

But Selye’s celebrity transcended national borders, as his new professional and public acclaim earned him honors and accolades throughout the world, including an appointment as an expert consultant to US Surgeon General.\footnote{12} By 1949, Selye had written over 450 scientific papers, published in North America, Latin America, Europe and Asia based on experiments with approximately 17,000 animals, and his *Textbook on Endocrinology* had become the standard text

\footnote{8}{“Widely-honored Scientist Leaves on New Mission in U.S.,” *Montreal Daily Star*, September 9, 1950, folder I: Newspaper clippings, HSC.}

\footnote{9}{“Dr. Hans Selye’s ‘Stress Factor’ Is Seen Insight to Human Illness,” *Montreal Gazette*, May 26, 1950, folder I: Newspaper clippings, HSC.}

\footnote{10}{“Tuberculosis Sources Many Besides Lungs,” *Montreal Daily Star*, September 26, 1950, folder I: Newspaper clippings, HSC.}

\footnote{11}{“Noted Medical Authority Speaks Here,” *Kingston Whig Standard* (Ontario), January 18, 1952, folder I: Newspaper clippings, HSC.}

\footnote{12}{Fromer, “More Years of Youth.”}
of most North American medical schools. His staff at the IMCE had grown to sixty-six, including thirteen research assistants from eleven different nations, as well as forty technicians and thirteen librarians.

Whereas he had once been ostracized by mainstream medicine, his stress theory was becoming increasingly mainstream and Selye was gaining increasing professional recognition. By 1954, *Reader’s Digest* reported that Selye’s work inspired the publication of nearly 5,000 research papers per year, and the research conducted at his institute was financed by forty-five funders, including individual donors, charitable and disease foundations, pharmaceutical firms, and the US and Canadian governments. His prestigious reputation also won him lucrative support from federal agencies, pharmaceutical corporations and disease foundations. His lab was reportedly “financed almost entirely by grants from the United States Public Health Department *[sic]*,” with the National Heart Institute providing the bulk of Selye’s financial backing. From 1950-1953, Selye also gained more than $15,000 from the Canadian Arthritis and Rheumatism Society (over $148,000 in 2015 Canadian dollars), and from 1954-1957 was awarded $90,000 (nearly $800,000 in 2015 dollars) from the New York-based Gustavus and Louise Pfeiffer

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13 Fromer, “More Years of Youth.”

14 J.D. Ratcliff, “Stress—The Cause of All Disease?” *The Reader’s Digest*, February 1955, 24-28; this article was also reprinted in foreign Reader’s Digests in French, Italian, Spanish, Cuba, Norway, Japanese, Danish, Finnish, German, Swedish, and Chinese, folder I: Newspaper clippings, HSC.


16 “New Health Frontier: The Glands.”

17 “Rats May Give Cure to Arthritic Diseases,” *Montreal Gazette*, June 5, 1953, folder I: Newspaper clippings, HSC.
Foundation and $10,000 (over $88,000 in 2015 dollars) from Warner-Chilcott Laboratories in New York.  

II. The Emergence of a Specialized Field of Stress Research

Amidst the cult of Selye-adoration, prominent voices from the professional medical community still challenged his theory. Even as the medical concept of stress became popularly assimilated, critics in the transatlantic professional medical community continued to assail Selye for 1) failing to consistently distinguish stress as a cause of disease or a disease itself, 2) obscuring specific relationships of disease causation in favor of his unified theory of disease, 3) inappropriately insisting on the primacy of the adrenal cortex in the causation of all diseases, and 4) lacking sufficient evidence to support his grand theory. The theory of stress was a perpetually contested medical concept, even as interest in stress research intensified in the postwar period. Yet, while Selye’s theory of stress continued to arouse controversy, the ongoing debates about the definition and relevance of stress reveal a process of disease conceptualization that drew on the expertise of a large community of researchers. In fact, the criticism of Selye’s research demonstrates other researchers’ active participation in the process of medicalizing stress. Gradually a growing literature and community of stress researchers offered legitimacy for this controversial concept. From its inception, the interdisciplinary nature of stress studies contributed to an extremely diverse body of research, drawing on biochemical evidence, psychological case studies, and clinical physiological observations. Indeed, the field was in many ways marked by its breadth rather than its specialization. Yet, even in its diversity, early postwar stress research was commonly signified by endocrinological evidence, particularly on the actions of adrenocorticoids.

$100,000 Gift to U of M for Research. Foundation Supports Famous Doctor’s Work,” Montreal Star, June 3, 1954, folder I: Newspaper clippings, HSC.
As such, Selye was a central figure in this nascent field, even as his theory of the GAS continued to draw criticism from many of his peers.

As discussed in Chapter Three, professional networks that had been forged through the wartime initiative for cortin research, as well as more interpersonal associations fostered through participation in the NRC research committee, undergirded the expansion of stress research in the postwar period. Some wartime collaborations resulted in lucrative funding relationships that survived the war. Postwar professionalization in stress research was supported by philanthropic associations, like the Josiah Macy Jr. Foundation, state agencies like the USNRC, and private corporations, such as Chicago’s Armour & Company meat packing firm, who subsidized academic research and undergirded professional networks by organizing conferences dedicated to recent research in actions of adrenocorticoid hormones.

In the late-1940s and early-1950s, a nascent community of stress researchers developed through a number of standard professional devices: they communicated through professional journals, such as *Endocrinology* and *Psychosomatic Medicine*, and met in professional organizations, such as Association for Research in Nervous and Mental Disease, and the American Psychosomatic Society. However, beginning in the late-1940s, the principal forum to vet stress-related research was the Laurentian Hormone Conference. A regular attendee of the conferences from the early years, pioneering endocrinologist Dwight J. Ingle later reflected that “the Laurentian Hormone Conference set new standards in a field previously dominated by physicians who were strangers to the laboratory by bringing together from all over the world
outstanding medical and nonmedical scientists from universities, state and private institutes, research hospitals, and industry.”

The Laurentian Hormone Conference first met in the late summer of 1943 at the Gibson Island Club in the Chesapeake Bay, supported with funding from some twenty pharmaceutical firms. The conference was such a success that its proceedings were published the following year as *The Chemistry and Physiology of Hormones*, and the conference continued to meet annually thereafter always around Labor Day and often at the Mont Tremblant Lodge in the Laurentian Mountains outside of Montreal. For the next twenty-four years, the LHC operated under the leadership of Chairman Gregory Pincus, director of Worcester Foundation for Experimental Biology, with the local arrangements coordinated by Dr. R.D.H. Heard of McGill University, and expenses paid for by pharmaceutical firms, which increased to 35 different contributing companies by the mid-1960s. The proximity to Montreal encouraged a tradition of organizing visits to laboratories in Montreal. In 1946, the conference began formally publishing its proceedings under the title, *Recent Progress in Hormone Research*, which enabled a larger professional audience to access the cloistered conference proceedings. While the LHC attracted the participation of many of the most renowned names in hormone research, it remained a highly

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20 After an incident at the first meeting of the LHC in which an African American member was denied admission due to the segregationist policies of the Gibson Island Club, the LHC intentionally sought to relocate outside of the southern USA in order to ensure that all members would be able to attend its meetings.

21 Initially, local arrangements were coordinated by Dr. R.D.H. Heard of McGill University, and later by Dr. A.D. Odell, of Canadian pharmaceutical firm Charles E. Frost & Co., among others.
selective group. Its size was intentionally limited to facilitate discussion, and meeting locations were chosen to impede drop-in visits from local scientists.\(^{22}\)

The Association for Research in Nervous and Mental Diseases (ARNMD) also adopted an elite profile in postwar stress research. In comparison to the LHC’s focus on endocrinological research, the ARNMD emphasized psychiatric and neurological aspects of stress. In December of 1949, the New York Academy of Medicine hosted a conference on “Life Stress and Bodily Disease” organized by the ARNMD. Selye served on the commission to organize the conference, along with ARNMD President Harold Wolff, Stewart Wolf, Roy Grinker, Franz Alexander, and a number of other notable medical experts of diverse specialization. The aim of the conference was to examine the extent to which psychiatry and psychosomatic medicine could account for cultural factors, though Selye’s contribution failed to engage larger social questions and remained closely focused on biochemical mechanisms of disease.

Selye began the conference with a paper he co-authored with his student Claude Fortier on “Adaptive Reactions to Stress,” outlining his new theory of the countervailing relationship between gluco- and mineralocorticoids.\(^{23}\) In the discussion period, he explained that “the general-adaptation-syndrome is the normal reaction of the body to stress. It is not a disease, indeed it develops in order to prevent disease and raise resistance. It is quite conceivable that stress sometimes causes disease, precisely because this reaction is insufficient, excessive or abnormal; perhaps derailments of this syndrome can result from an unbalanced production of the various corticoids.” He also explained that the polymorphic variations in GAS arose because


\(^{23}\) “Excess Hormones Cause Disease,” *New York Times*, December 3, 1949, folder I: Newspaper clippings, HSC.
target organs “appear to respond differently to corticoids produced under stress and depending upon the relative proportion of mineralo- and glucocorticoids, vascular damage or renal damage can predominate. Similarly, the effect of DCA upon the blood-pressure, the cardiovascular system and the kidney are inhibited by low-sodium diets, while its effect upon the adrenal cortex (production of atrophy) remains uninfluenced… depending upon the circumstances, hormones produced during stress may act upon one or the other organ system in a more or less selective manner.”

The initial response to his paper was largely positive, however subsequent discussions on the second day of the conference (which Selye did not attend) raised questions as to the plausibility of Selye’s theory. In particular, ARNMD Vice President, Columbia University Professor of Medicine, Dr. Robert F. Loeb, and President Harold G. Wolff questioned whether the adrenals actually function as a universal mediator of all stimuli. And Cornell psychologist Stewart Wolf alleged that while Selye had shown the involvement of the adrenal cortex in mediating stress reactions, he had yet to produce sufficient evidence to prove whether or not the adrenal cortex was solely responsible for producing diseases of adaptation, and whether hyperactivity or hypoactivity accounted for the derailment of the GAS.

Research was emerging in the late-1940s and early-1950s that challenged Selye’s theory of the primaricy of the adrenal cortex in adaptation and disease. Notably, senior research scientist at Upjohn Company (and as of 1953, professor of physiology at University of Chicago’s Ben May Institute) Dwight J. Ingle—who had formerly worked with Edward Kendall on the development of compound E—argued that rather than directly influencing cellular physiology,

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corticoids exerted a “permissive” nature that allowed for cells and tissues to respond to stressors. Ingle demonstrated that hormonal actions, such as the tendency for estrogen to inhibit hair growth or epinephrine to deplete the glycogen stored in muscles, were only possible when adrenocorticoids were present to allow these reactions to occur. Similarly, University of Chicago physiologist Rachmiel Levine demonstrated that steroids did not themselves directly weaken muscles, but led to the muscular weakening by blocking circulation.

On June 17, 1950, the British Medical Journal published a transcript of the first part of Selye’s Heberden Lecture, which synopsized the etiological dynamics of the GAS and pointed to its prophylactic therapeutic implications. While Selye had signaled his shift towards using the terms stress in his 1946 “Disease of Adaptation,” the Heberden oration revealed that he had come to a more specific use of the term stress to refer solely to a condition induced by exposure to stressors. Throughout his lecture Selye repeatedly referred to stress as the principal cause of a great number of chronic diseases, and made it clear that stress only operates through the GAS. The publication was met with acclaim as well as criticism, ranging from sober and constructive commentary to hysterical outrage and excessive platitudes, as revealed in the letters published in the British Medical Journal’s correspondence section in the following few weeks.

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26 The British Medical Journal published the second part of the Heberden lecture, which was based largely on lantern slides, in the June 10, 1950 issue. The first part of the Heberden lecture was published as Hans Selye, “Stress and the General Adaptation Syndrome,” British Medical Journal 4667 (June 17, 1950): 1383-1392.
While G.S.W. Evans proclaimed that “Professor Selye’s publications form a milestone in medical progress,” his praise was cast against shrewd criticism from several other British physicians. F.F. Roberts refuted the usefulness of a monistic pathology, pointing out that many

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of the diseases that Selye attributed to the GAS were also found to be caused by exposure to x-rays, and incredulously asked, ”are we to conclude that x rays act not directly but through the intermediation of the hypothalamus-hypophysis system?” He went on to question the logic of Selye’s theory, reflecting that according to Selye, stress is the “result of the action of one of its components (defence) upon the other (damage). But stress has been described as the action itself. Therefore stress is not only itself but the result of itself.” And moreover, because “all living organisms can respond to stress by the general adaptation syndrome, which… consists of damage and defence. Therefore stress, in addition to being itself and the result of itself, is also the cause of itself.”

F.N. Meiklejohn intensified the rancor of criticism, calling into question whether Selye’s research or his grand theory bore any significant relationship to the therapeutic uses of ACTH and cortisone. With detectable exasperation, Meiklejohn attributed the popularity of Selye’s stress research to the fact that it was “a comfortable new theory that helps us to think that we understand what we are doing in the practice of medicine, and allays some of our uncertainties and unquiet thoughts.” Yet, despite its alluring qualities, Meiklejohn bemoaned that Selye’s use of deductive reasoning, “overlooks one of the basic rules of science,” and dangerously threatened to submerge science “in a new Dark Age.”

In a less exasperated tone, H.N. Green complained that Selye’s Heberden lecture left him “in some mental confusion.” He doubted whether Selye’s theory applied to glucocorticoids as it did to mineralocorticoids, which called his entire theory into question since following the

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therapeutic discovery of ACTH and cortisone he had “built up further support for his concept largely on the basis of the therapeutic effect of these cortical hormones.” Moreover, Green disputed the methodological basis of Selye’s, denouncing the etiological value for human pathology of finding disease could be induced in rats with artificially high doses of DOCA and sodium. At last he predicted that “Selye's more recent ideas, even born as they are out of prodigious labours,” were unlikely to “survive, in their present form, for very long,” yet would very likely stimulate more productive research.30

The following summer, Selye earned a new round of criticism when Drs. M. Parkes and Fred Wrigley reported that they were unable to alleviate arthritis in rats by administering cortisone or ACTH, in contradiction of “the sole basis for Selye's startling theories.” Bernard Goldstein commented that Selye’s method of treating experimental animals with gluco- or mineralocorticoids was unfounded because “in the experimental animal we cannot deliberately influence the corticoid ratio by separately eliminating the actual source of one of these hormones, since both have the same source—the adrenal cortex.” In addition to his methodological critique, Goldstein indicted Selye for lacking sufficient evidence to support his hypothesis.31 In December of 1951, Edward Kendall contributed to the British Medical Journal’s coverage of the therapeutic applications of ACTH and cortisone. He noted the numerous therapeutic uses of cortisone in treating collagen diseases, but refuted the notion that this offered a unified theory of disease. Kendall suggested that while “the unexpected and far-reaching influence of cortisone on many diseases may be produced through its control of some causative agent which is common to


all of them,” as of yet, “the nature of this agent is unknown.” Consequently, there was not sufficient evidence to support a unified theory of disease, and therefore, “the hypothesis of the adaptation syndrome of Selye is not acceptable.”

Kendall’s admonition that Selye’s theory was predicated on insufficient clinical evidence was perhaps the most common and salient criticism against him. For Kendall and like-minded critics, Selye’s claim that adrenocortical hormones were the unifying element in all disease would require a lifetime’s worth of research to substantiate. To the extent that Kendall was highly critical of any exaggerated claims regarding the uses and implications of adrenocortcoids, he was also dubious of Selye’s claim that stress was a universal catalyst of various chronic diseases, instead contending that specific levels of different adrenocortical hormones triggered the onset of specific diseases. While the two men retained an amicable professional relationship—that was perhaps more enthusiastically pursued by Selye—Kendall made clear to Selye on a number of occasions that he doubted the merits of Selye’s theory on the grounds that he simply lacked clinical proof to make such broad claims.

Selye attempted to persuade Kendall of his theory, on several occasions sending him reprints of his articles (referencing experiments conducted with cortical steroids supplied by Kendall), as well as a copy of his First Annual Report on Stress. In a note thanking Selye for sending him Stress, Kendall made it quite plain that “at the present time [he did] not think the chemical work supports the idea that the clinical syndromes which you designate as disease of adaptation can be caused either by alteration of the chemical structure of any steroid in the adrenal gland or by a modification of the distribution of the constituents of the secretion from this gland, but I am convinced that further research will produce a definite answer to this

problem.” Kendall further outlined his objections to Selye’s theory with the simple distinction that his “conclusions and [his] interpretations of results on experimental animals and observations on clinical syndromes are not in agreement.” He explained that he could only be convinced of Selye’s claims if he were able to “accumulate results in the fields of physiology and pathology which will of themselves carry conviction or isolate the responsible hormones, abnormal products and other agents involved and study them individually and collectively and determine their influence in health and disease.” Kendall recognized that of course this was a formidable prospect that would take inordinate time and effort, yet insisted that this was the only appropriate course of action that might “bring to light an explanation which will be close to the truth.”

Selye responded to Kendall’s letter, acknowledging his criticism, yet pleading to persuade Kendall to accept his theory. Selye offered that he was "the first to admit that these hypotheses are far from being proven,” he yet insisted that despite its flaws, his theory was still useful. Quoting the foreword of his first report on Stress, he urged Kendall to admit that while “our facts must be correct, our theories need not be if they help us to discover important new facts,” for the theory of the GAS had led Selye to discover, “that desoxycorticosterone produces nephrosclerosing and periarteritis nodosa, that growth hormone, like desoxycorticosterone, sensitizes to various inflammatory phenomena, that ablation of the adrenals prevents thymico-lymphatic atrophy, lymphopenia and eosinopenia during the alarm reaction, and so forth.”

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33 E.C. Kendall to Hans Selye, August 28, 1950, Box 16, Folder S, ECK.


35 Hans Selye to E.C. Kendall, February 25, 1952, Box 11, Folder S, ECK.
Aside from their fundamental disagreement about the plausibility of Selye’s unified theory of disease, Kendall and Selye had contradictory views on the therapeutic use of adrenocortical steroids. While Selye leapt at the therapeutic possibilities of new adrenocortical treatments, Kendall cautioned that it was yet premature to speculate as to the medical promise of these drugs, and that recommending such interventions at this point was not only imprudent but potentially misleading and even hazardous. For example, in response to Selye’s letter on Christmas Day 1954 in which he forwarded a reprint of an article examining the antagonistic influence of aldosterone (a mineralocorticoid closely related to DOC) on cortisone, Kendall joined Selye in rejoicing that aldosterone had become available for clinical research and therapeutics, but cautioned him “for the sake of the young medical student and those others who look to you for leadership,” to resist assessing the worth of aldosterone “until the results of its use in clinical medicine are in hand.” Perhaps inspired by his own experience with the exaggerated reaction to the benefits of cortisone, he went on to warn that “if a premature statement is made it can lead to confusion and ultimately bring only regrets.”

Despite such admonitions—even from Kendall, whom he deeply revered—Selye pursued his stress research with an evangelistic fervor, convinced that it offered the greatest potential benefit to modern medical science and human health. He strove to take criticism constructively, and use it as inspiration to produce more precise and persuasive research. Yet, as a result, his experiments continued to take a reductionistic perspective of disease that saw stress as a highly mechanistic phenomenon that occurred within an organism due to biochemical changes, and as a result, he continued to promote a disease model of stress that failed to recognize broader social forces that surpassed individual control in the distribution of stress.

36 E.C. Kendall to Hans Selye, January 17, 1955, Box 11, Folder S, ECK.
While many of Selye’s peers, such as Kendall, encouraged reductionist experiments to improve his theory, some of his contemporaries warned of the dangers in such a limited perspective. Waldemeer Kaempffert, the *New York Times*’ science columnist, while giving due recognition to the revolutionary influence of Selye’s work, offered the worthy criticism that his theory of stress interpreted “all disease as the result of something that impinges on the body from outside and thus upsets the internal balance.” Not only did this formulation seem to inaccurately collapse all disease into a single category, but it did so by promoting a reductionist, unidirectional and mechanistic perception of the body. Kaempffert argued that Selye’s theory of stress failed to adequately acknowledge the extent to which an organism actually interacted with its environment and could in fact generate intrinsic pathological reactions.\(^{37}\) Indeed, as over time Selye himself would explicitly argue that “from the purely biological point of view, we are machines.”\(^{38}\) Consequently, Selye’s theory of stress offered a powerful optic for evaluating multiple causes of disease, but failed to account for a dynamic interface between organism and environment.

One might argue that Selye gave lip service to acknowledging the social pathways of stress when he indicted modern civilization for demanding impossible adaptations. Yet, his own research supported a view of disease that saw individual biochemistry as the critical variable in health. And as Selye embarked on a mission to proselytize his theory of stress following the adrenocorticoid revolution, it was this individualistic model that he promoted. Under pressure to compete for adequate financial support for his institute, he catered his research to appeal to the therapeutic concerns and economic interests of the three major pillars of the postwar medical


\(^{38}\) Selye, *The Stress of My Life*, 100.
market: the state, the pharmaceutical industry and the patient-consumer. Emphasizing conditioned risk and the cumulative manifestation of degenerative diseases of adaptation, Selye extolled concepts that were immensely valuable in understanding and combatting North America’s mid-century epidemiological concerns, and by doing so, insulated his research from impeachment in the eyes of biomedical research grantmakers and of the North American public. Ironically, this epidemiological valence would ultimately help Selye’s theory of stress to win legitimacy, despite his persistent focus on individual rather than population health.

III. State Funding for Stress Research

Selye rode the high tide of the adrenocortical revolution, taking advantage of state-directed access to ACTH, cortisone and human growth hormone (STH) to conduct basic research on the effects of these new miracle drugs on the course of the GAS. He continued to enjoy state funding through a number of grants with the NIH, the USNRC, and the CMR, as both the US and Canadian governments saw adrenocortical stress studies as a sound investment in public health. State support was crucial to the funding of stress research, and Selye was fortunate to receive federal grants from both the US and the Canadian governments. He also enjoyed an honored position as an expert consultant to the Surgeon General of the US Army.

Thanks in part to the availability of state funding, the field of stress research grew apace throughout the 1950s. Even amidst his growing professional and popular acclaim, Selye was but one of dozens of reputable stress researchers, and was far from the only one to benefit from the substantial support of state agencies. In fact, several of his esteemed colleagues were integrated

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39 In the 1952-53 fiscal year, the ACMR allocated Selye 15 gm cortisone, 15 gm ACTH, 10 gm hydrocortisone and $2,000 for the purchase of somatotropic hormone (the latter of which he never used). See "Proceedings of the Fourteenth Meeting of the Advisory Committee on Medical Research," October 6, 1952, p.6, Box 33, folder 30.24, CNRC.
into the bureaucracy that administered state funding, performing as “scientist statesmen,” who provided essential advice to determine which research projects merited funding and in doing so, shaping the cannon of stress research. Selye played a comparatively smaller role in the corporate liberal military-scientific-complex of the postwar era, as a grant recipient and only a nominal advisor. Selye did not participate in the most influential state agencies and committees of the postwar era, all of which were US institutions. However, since several of his Canadian colleagues, including J.S.L. Browne and R.D.H. Heard, accepted advisory positions on US federal research committees, it seems unlikely that Selye’s nationality removed him from these positions. Rather, as Selye often vocalized his resentment of professional activities that distracted from his own research, it is entirely likely that he was unmoved to take on policy-making responsibilities. (However, Selye did openly criticize national health research policy, as will be discussed in Chapter Six). As a result, Selye’s influence over the academic stress discourse decreased, as a cadre of largely psychiatrically-trained federal committee members gained discursive control.

The increasing psychiatric orientation of the field of stress research can be attributed, in part, to the US Army and USNRC’s formative influence on combat psychology research. The continued involvement of these agencies following WWII allowed for expert consultants, administrators and medical servicemen active in the Neuropsychiatric Division’s stress research during the war to perpetuate their research with little interruption. At the direction of the Surgeon General of the US Army, the USNRC Committee on Psychiatry’s formation of an Ad Hoc Committee on Stress (AHCS) in 1950 drew pioneers of combat stress research and the

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40 I borrow the term “scientist statesmen” from Dwight J. Ingle to describe scientists serving in an advisory or administrative capacity within federal agencies; akin to the industrial statesmen, or labor statesmen of the postwar era. See Ingle, “Gregory Goodwin Pincus, 1903-1967.”
development of adrenocortical pharmaceuticals together into a single agency guided by psychiatrically trained members (as discussed below). Prior to the formation of the AHCS, the PHS contributed to the psychiatric orientation of stress research with the formation of the National Institute of Mental Health (NIMH) in 1949, which offered sizable grants to psychiatrically-oriented stress research.

The National Institute of Mental Health

The NIMH was the institutional legacy of the Army’s Neuropsychiatric Division’s powerful influence on health priorities, and a testament to the widespread concern for the mental health of veterans and civilians during the postwar period. The abundance of men that had been rejected through improved screening measures for psychiatric deficiencies as taken as evidence that there was a pre-existing high rate of mental illness in the civilian population. And the fact that many of those who met mental health standards to be approved for service ended up developing neuropsychiatric disorders due to prolonged combat stress stood as evidence that even healthy individuals could become ill as a normal response to adverse environmental conditions.41

Additionally, the successful intervention strategies employed by neuropsychiatrists emphasized the importance of camaraderie, community and morale to mental health, and the harmful, infantilizing effects of extended hospital care.42 These lessons became even more relevant for domestic health policy with the return of nearly 700,000 veterans who were discharged due to psychiatric illness, over half of whom required ongoing care.43

41 Thomas A.C. Rennie and Luther E. Woodward, Mental Health in Modern Society (New York: Commonwealth Fund, 1948), viii, ix.


43 Rennie and Woodward, Mental Health in Modern Society, 143, 138.
Professional psychiatrists, especially those who had served during the war, emerged as a powerful voice in the immediate aftermath of the war, calling for mental health care reform. The National Committee for Mental Hygiene published a manual to help family and community members support soldiers’ readjustment to civilian life.\textsuperscript{44} The authors, Cornell Psychologist and former student of Adolf Meyer, Thomas Rennie and Luther Woodward, a social worker with the New York City Bureau of Child Guidance, later expanded the principles presented in the pamphlet in a monograph entitled \textit{Mental Health in Modern Society}, published by the Commonwealth Fund detailing the neuropsychiatric advancements made during the war, and the ongoing need for mental health care reform. They noted that tuberculosis and polio research and treatment received 20-40 times more public funding than mental health care, with approximately $600 spent per case of polio, versus $1.00 per case of mental illness.\textsuperscript{45} Rennie and Woodward emphasized the widespread effect of the war on the mental health of Americans, for not only neuropsychiatric casualties, but also returning servicemen who struggled to adjust to civilian life, for their families who struggled to cope with their loss during the war and understand their difficulty in transitioning to civilian life, for the hundreds of thousands of Americans who had lost a loved one in the war, and for civilians who had lived with the tension and scarcity of war for the past four years.

The mass psychiatric distress of the war provided a broad social education in the new realities of mental illness. To Rennie and Woodward, the mental health legacy of the war was a community-wide experience, rooted in social conditions. Therefore, community-wide and social

\textsuperscript{44} Thomas A.C. Rennie and Luther E. Woodward, \textit{When He Comes Back and If He Comes Back Nervous: With Guide to Community Resources} (New York: Rehabilitation Division, National Committee of Mental Hygiene, 1944).

\textsuperscript{45} Rennie and Woodward, \textit{Mental Health in Modern Society}, 402.
solutions would offer the most effective means of responding to mental health problems. They endorsed a transition to community-based mental health care, accompanied by broad education initiatives to empower local communities to support mental health therapy and to destigmatize psychiatric patients. Rennie and Woodward estimated that in addition to the 600,000 patients then in the nation’s mental hospitals, there were one million more in need of hospital care and 8 million more in need of outpatient therapy. Projecting that one tenth of the population would be unable to work or require hospitalization for mental illness at some point in their lives, they pointed out that the meager 155 psychiatric institutions and 758 accredited residencies then in existence were woefully insufficient to meet the mental health care needs of postwar Americans. Furthermore, they claimed that approximately 30 percent of visits to doctors’ office were due to psychiatric difficulties. “If prevention of mental ill health is to become a reality for the millions,” they proclaimed, “we must learn how to remove stresses in the environment as well as to strengthen the inner resources of individuals.”

In June of 1946, drawing on substantial bipartisan support and moved by a sense of duty to provide better care for returning veterans, Congress passed the National Mental Health Act. The NMHA realized the vision of PHS Chief of Medical Hygiene, Robert H. Felix to create a system of community-based psychiatric clinics, to reduce the numbers of mental patients in costly and seemingly ineffective state hospitals and invoke the moral principles learned in the war by enlisting the entire community in the therapy of neurotic conditions. In passing the NMHA, Congress authorized $7.5 million ($91.5 million in 2015 dollars) for the creation of a national psychiatric research center, the National Mental Health Institute within the NIH, and an advisory council to administer the new agency. While the NIMH failed to receive a

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46 Rennie and Woodward, Mental Health in Modern Society, 137-138, 154, 385.
Congressional appropriation in its first year, by 1960 its annual appropriation had reached $100 million ($804 million in 2015 dollars).

As the NIMH oversaw both mental health treatment and research, it fostered a community of mental health practitioners with a shared concern for the psycho-epidemiological demands of the postwar period. Membership in this community empowered stress researchers to influence both public policy and popular awareness of mental health issues.

IV. Scientist Statesmen

Two of the most influential of Selye’s fellow pioneers in stress research—Harold Wolff and Gregory Pincus—were both involved with the NIMH, and both wielded great influence over the development of stress research in the postwar period, through their own research, as well as their service on NRC and NIH committees. Perhaps most significant was their participation on the NRC’s AHCS, which in 1956 was converted to an official Subcommittee on Stress, organized under the Committee on Psychiatry. It is telling that the NRC’s stress committees took on a psychiatric bias, as they helped to determine the distribution of sizable grants and in doing so determine the general tenor of stress research in the postwar period. Consequently, the medical concept of stress became strongly aligned with the psychiatric discipline as it became increasingly assimilated into North American culture. Yet, despite the psychiatric orientation of the NRC Stress Committees, they were intended from the beginning to focus on physiological investigations, as prescribed by the initial organizing force, the US Army.

Gregory Pincus first developed contacts with the NRC and the OSRD through his wartime contracts with the Committee for Aviation Medicine studying the adrenocortical...

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regulation of flight stress. After the war, Pincus continued to organize the annual Laurentian Hormone Conferences, and to contribute to the growing fields of endocrinology and stress research through his own innovative work. Yet, despite his considerable professional service, he failed to attract much public attention. As his colleague, Dwight J. Ingle later noted, while “some scientists become great by making important contributions to knowledge—discovery in the laboratory,” Pincus’ greatness arose from his capacity for organization “and by making important applications of knowledge.”

While Pincus’ covert organizational savvy escaped public attention, it nevertheless exerted enormous influence in directing the development of the biomedical model of stress.

During the war, Hoagland and Pincus established the Worcester Foundation for Experimental Biology (WFEB), operating out of an old barn on the Clark University Campus. In addition to their studies on flight stress conducted for the Air Force, the WFEI also engaged in research on industrial workers, human aging and senility, and mental illness, publishing 150 papers in the ten years between 1934 and 1944. By 1944, Pincus and Hoagland had secured approximately $100,000 ($1.35 million in 2015 dollars) from philanthropic, corporate and state sources to support the independent operation of the WFEI, signified by its relocation to a converted estate in Shrewsbury, Massachusetts. While the WFEI maintained an affiliation with Clark University, it was also home to the Memorial Foundation for Neuroendocrine Research of Harvard, which brought it an additional $25,000 in annual funding, and it developed


49 “The Worcester Foundation for Experimental Biology,” April 14, 1944, Box 114, folder 1580, WBC.

50 “Biology Foundation Busy Harry P. Hovey Estate,” The Worcester Evening Gazette, August 1, 1944, Box 114, folder 1580, WBC.
strong ties to the Worcester State Hospital and served as the principal research center for the Massachusetts Department of Mental Health, for which it received $40,000 per year from the state for research. 51

The WFEB was dedicated to “conducting research in the medical sciences, particularly in the fields of biochemistry and physiology of hormones and in brain chemistry and physiology.” 52

But, in order to support its own research interests, the WFEB engaged in commercial work, as well. Thus, the WFEB was not only a major center of scientific innovation, it was also what Dwight Ingle described as a “bootstrap operation representing scientific free enterprise.” 53

Among the many accomplishments of the WFEB was the development of a method for processing large quantities of beef adrenal glands for the production of corticosteroids, which was undertaken partly due to the commercial benefits it promised to bring in to support other research. 54 As the WFEB embraced commercial steroid production to support its research

51 “The Worcester Foundation for Experimental Biology,” April 14, 1944, Box 114, folder 1580, WBC.

52 The WFEB began with an operating budget of $42,000 for the first five years, drawn from industry, philanthropic foundations and private donors, including the Rockefeller Foundation, the Macy Foundation, the National Academy of Sciences, the American Philosophical Society, the Guggenheim Foundation, and the Friedsam Foundation for Medical Research, as well as G.D. Searle Co., Parker Manufacturing, the American Optical Co., and funds from the federal government for aviation research. The operating budget was supplemented with additional grants that brought the annual budget closer to $60,000. See “The Worcester Foundation for Experimental Biology,” April 14, 1944, Box 114, folder 1580, WBC.


54 Ibid.
priorities, it brought in Erwin Schwenk, who maintained an independent contract with Schering Corp. that carried a $15,000 annual salary.\textsuperscript{55}

Despite its contribution to the adrenocortical revolution in the early-1950s, the WFEB was devoted to research on the biochemical and neurological mechanisms of psychiatric health. They were “concerned primarily with the mode of action of certain hormones from glands of internal secretion and with the role of brain catalysts (enzymes) involved in brain oxidations,” which Pincus and Hoagland believed likely to “be important factors in mental breakdowns.”\textsuperscript{56}

Given their interest in the neuroendocrinological regulation of mental health, in 1951, the WFEB entered into a joint agreement with the NIMH, to support a community mental health initiative by researching the physiology of psychoses and potential treatment with adrenocortical steroids. The project was initially funded with $80,000 (about $732,000 in 2015 dollars) from the NIMH and $85,148 (about $778,000 in 2015 dollars) from the WFEB, and was renewed in 1953 with an additional $50,000 from the NIMH (about $445,000 in 2015 dollars).\textsuperscript{57} Pincus also held a $41,110 grant from the PHS to study hormonal metabolism of cancers in vitro,\textsuperscript{58} and would later revolutionize reproductive science with his development of the birth control pill. However, Pincus’s greatest contribution to stress research in the 1950s arose from a study of the aberrant


\textsuperscript{56} “The Worcester Foundation for Experimental Biology,” April 14, 1944, Box 114, folder 1580, WBC.

\textsuperscript{57} “Joint Agreement Between the National Institute of Mental Health (NIMH) and the Worcester Foundation for Experimental Biology (WFEB),” June 18, 1951, Box 130, folder “USPH NIMH 1950-53,” GGP.

\textsuperscript{58} Research Grants Awarded by the Public Health Service 1950, PHS Publication no. 63”, p.30, Box 10, folder “U.S. Public Health Service, 1950-1951,” GGP.
adrenal function of schizophrenic patients. In a study funded by the NIMH, Pincus and Hoagland found that “schizophrenics tend to excrete large amounts of hitherto unidentified corticosteroids,” which could not be corrected by the administration of ACTH or cortisone.\textsuperscript{59} They deduced that such “abnormal steroidogenesis” suggested that schizophrenia was associated with a malfunctioning of the adrenal or pituitary glands.\textsuperscript{60}

The WFEB created an environment that fostered innovative stress research. Among the prominent stress researchers that came out of the WFEB was Pincus’ former laboratory assistant, Fred Elmadjian. Though formally trained in pharmacology and animal physiology, Elmadjian was self-taught in clinical aspects of human behavior, in part, through first-hand experience overseeing psychoactive drug trials with psychiatric patients at the Worcester State Hospital, where he served as Director of Biological Research and Director of Laboratories. Elmadjian would contribute immensely to the scientific understanding of the neuroendocrine foundations of adaptive responses to stress through his studies on not only psychiatric patients, but also soldiers, athletes, and primates (in preparation for early space travel). In 1952 he served as a civilian

\textsuperscript{59} Gregory Pincus to Dr. R. Felix, January 31, 1951, Box 130, folder “USPH NIMH 1950-53,” GGP. See also, “Proposal for the Adrenalectomy of Schizophrenic patients as a therapeutic procedure and as a means of specifically identifying the relations of adrenal steroids to psychotic behavior,” May 5, 1951, Box 9, folder “Hudson Hoagland, 1951,” GGP.

\textsuperscript{60} In addition to his stress research, Pincus also reignited his earlier interest in reproductive endocrinology in the postwar era. In particular, he began working on a means of using synthetic hormones to control fertility, still a controversial field of study in the 1950s. Consequently, he was hard-pressed to find philanthropic or state funding for his fertility control research, until 1956 when his friend, the notorious birth control guru, Margaret Sanger helped him to secure a sizable annual grant from Mrs. Stanley McCormack. McCormack would continue to support Pincus’s research on fertility control until she passed away in 1968, a year after Pincus’s own death. After the commercialization of the birth control pill in 1960, Pincus was also able to secure funding from the Josiah Macy, Jr. Foundation, G.D. Searle Co., and the Ford Foundation through the Population Council and the NIH. Once Pincus had secured sufficient funding for his fertility control research, his professional interest in stress waned. See Ingle, “Gregory Goodwin Pincus, 1903-1967.”
consultant, conducting endocrinological research in combat zones for the Operations Research Office’s study of combat stress in Korea. Measuring soldiers’ 17-ketosteroid levels before and after military engagements, the Korea stress studies revealed that long-term exposure to combat depressed adrenocortical activity and prevented the normal activation of adrenocortical resistance. Beginning in the 1960s, Elmadjian would also help to elevate stress research to mainstream status through his development of training programs as the National Institute of Mental Health’s Chief of Biological Sciences and Behavioral Sciences Training.

In addition to the research that the WFEB performed under NIMH contracts, Pincus also participated more directly in the NIH’s determination of research priorities, as a member of the NIH’s Mental Health Research Study Section, the Endocrinology Section, and the NRC’s Division of Medical Sciences’ AHCS, which was chaired by Cornell psychiatrist Harold Wolff. Much like Pincus, Harold Wolff initially developed ties to the NRC and the OSRD through his wartime research contracts with the CMR to develop diagnostic methods for screening for potential neuropsychiatric casualties, cardiovascular changes induced by emotional and pathogenic stimuli during convalescence, and post-traumatic headache.

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63 Ernest M. Allen (Chief of Division of Research Grants) to Gregory Pincus, October 1, 1951, Box 10, folder "USPH Study Sections 1951 NIMH & Endocrinology,” GGP.

At the close of the war, Wolff won several lucrative corporate and philanthropic grants that provided him a position of greater independence and esteem as the head of a new community-based psychiatric clinic at Cornell. In 1946 the Commonwealth Fund awarded him $28,500 to establish a pilot clinic in Cornell’s Department of Medicine, to provide psychiatric services to patients and training for psychiatrists and physicians. By the end of the 1940s, the Commonwealth Fund had begun issuing Wolff an annual grant of $133,200 to fund the psychiatric clinic. The Cornell Psychiatric Clinic would become an icon of the community mental health clinic in the postwar era.

Like Selye, Wolff gained greater independence and professional authority as the head of his own clinic. However, unlike Selye, he used his new position to enhance his professional service and strengthen his ties to the USNRC and the PHS. In April of 1946, Wolff was appointed to the National Advisory Mental Health Council, for which he provided expert advice to the US Surgeon General, the Director of the Mental Hygiene Division and his staff. The same month, Wolff participated in the CMR’s conference on postwar research, which brought together military and civilian medical experts “to discuss the desirability of and the means for continuing into the postwar period the organization of wartime activities of the National Research Council in its relation to the Federal medical services,” and to “establish a long-term follow-up clinical research program on Army material,” in the hopes that the progress made

65 [untitled], Box 3, folder 3-11, HGW.

66 Levenson, Mind, Body & Medicine, 99.

67 R. H. Felix, Director of Mental Hygiene for US Public Health Service to Harold Wolff, April 21, 1946, Box 4, folder4-6, Box 3, folder 3-9, HGW.
during the war would not be lost.\textsuperscript{68} At the urging of Col. William C. Menninger, ongoing study of neuropsychiatric problems was made a priority, as were ontological studies of the natural history of disease, and of chronic diseases such as cancer.

In early 1950, Wolff was offered a position as the Scientific Director of the NIMH, which he declined.\textsuperscript{69} He did, however, continue to work closely with several federal agencies in an advisory capacity, including the VA, the OSRD and the NRC. In June of 1948, Wolff was appointed Chairman of the NRC’s Committee of Neuropsychiatry,\textsuperscript{70} from 1946 to 1959, Wolff acted as the Senior Consultant in Neurology for the Bronx VA Hospital,\textsuperscript{71} and in late-November 1947, General Paul R. Hawley appointed Wolff to the Advisory Committee of the Neuropsychiatry Division of the Veterans Administration.\textsuperscript{72} Wolff used his advisory role on NRC and VA committees to support his own research. In 1948 and 1949, he received approximately $45,000 (about $445,000 in 2015 dollars) from the National Research Council’s Committee on Veterans Medical Problems for research in collaboration with Clara Torda on “The Nature, Specificity and Importance of Personality Features and of Life Situational Stresses in Epilepsy.”\textsuperscript{73} From 1947 to 1950, he was awarded over $30,000 (just under $300,000 in 2015 dollars) for his research on the nature, specificity, and importance of personality features and life situational stresses in epilepsy.

\textsuperscript{68} “National Research Council, Division of Medical Sciences, Conference on Postwar Research,” April 18, 1946, Washington, D.C., Box 4, folder 4-6, HGW.

\textsuperscript{69} R.H. Felix, NIMH Director, to Harold Wolff, March 16, 1950, Box 3, folder 3-1, HGW.

\textsuperscript{70} Lewis H. Weed to Harold G. Wolff, June 28, 1948, Box 4, folder 4-7, HGW.

\textsuperscript{71} Lt. Col. H.C. Hardegree to Harold Wolff, February 7, 1946, and A.L. Kleinman to Harold Wolff, February 26, 1959, Box 3, folder 3-9, HGW.

\textsuperscript{72} Paul R. Hawley, Chief Medical Director Veterans Administration to Harold Wolff, November 17, 1947, Box 2, folder 2-1, HGW.

\textsuperscript{73} The Nature, Specificity and Importance of Personality Features and of Life Situational Stresses in Epilepsy,” Project No. 37, 1948, Box 4, folder 4-7, HGW.
dollars) by the VA for research on personality, stress and epilepsy. In February of 1951, Wolff applied for a $40,000 grant from the PHS for research on epilepsy and stress, noting that steroids such as ACTH had been found to reduce convulsive seizures in predisposed humans.

Wolff also performed research and training funded by several different NIH divisions. In 1952, Wolff applied for a $7,560 grant from the NIH for research on the “Relation of Life Stress to Cardiovascular Adaptive Mechanisms and to Essential Hypertension”, in 1955 he received a $26,245 grant (nearly $230,000 in 2015 dollars) from the National Institute of Neurological Diseases and Blindness for graduate medical training, from 1955 to 1960 he received over $82,000 (about $694,000 in 2015 dollars) from the NIH for research on the effects of electrolyte balance and norepinephrine on vascular headaches, and in 1957 and 1958 respectively, the NIH granted Wolff $13,851 (about $114,000 in 2015 dollars) for research on life experiences and illness amongst individuals in homogenous groups, and $51,222 (nearly $419,000 in 2015 dollars) for research on life experience and diabetes. In November of 1958, Wolff was

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74 E.H. Cushing to Harold Wolff, June 17, 1947; Alfred H. Lawton to Harold Wolff, May 21, 1949; Lawton to Wolff, May 22, 1950, Box 3, folder 3-9, HGW.

75 Application for Grant-in-Aid, “Nature of Metabolic Enzymatic Processes Involved in the Initiation of Convulsive Seizures”, February 19, 1951, Box 4, HGW.

76 J.M. Ellis, Project Review Officer for the National Institutes of Health to Harold Wolff, March 1, 1952, Box 4, folder 4-6, HGW.

77 Edward P. Offut, Chief of Extramural Programs, National Institutes of Health to Harold Wolff, March 21, 1955, Box 4, folder 4-6, HGW.


79 NIH Grant No. M-1531, “A Study of the Illnesses Occurring in Members of Homogeneous Population Groups and Their Relationship to Individual Life Experiences,”
awarded a $41,370 contract (about $340,000 in 2015 dollars) with the US Army for a “Study of Stress, Metabolism, Immune Mechanisms and Susceptibility to Illness.”

In 1955, Wolff served as a consultant for the OSRD Technical Advisory Panel on Biological and Chemical Warfare. He also continued to serve on a number of NRC committees, including the Committee on Army Research and Graduate School, and the Executive Committee of the Division of Medical Sciences. Indeed, his service on NRC committees became so demanding that as of 1953 he was compelled to decline participation in all but two committees: the Subcommittee on Stress and the Committee on Medicine and Surgery. He served on both committees until 1958, when they were both disbanded in the course of a restructuring of the NRC’s committee structure.

Wolff had developed a close friendship with the Director of the Central Intelligence Agency Allen Welsh Dulles after treating Dulles’ son for lingering neuropsychiatric problems following a traumatic injury in World War II. In 1954, Dulles reached out to Wolff to direct a

October 11, 1956, and NIH Grant No. A-2615, “Life Experience and Adaptive Reactions in Young Diabetics,” February 26, 1958, Box 4, folder 4-6, HGW.

Lt. Col. William W. Cox to Harold Wolff, November 3, 1958, Box 3, folder 3-9, HGW.

“Department of Defense Notification of Personnel Action re: Harold G. Wolff,” December 29, 1955, Box 4, folder 4-6, HGW.

M.C. Winternitz to Harold G. Wolff, June 15, 1951, Box 4, folder 4-7, HGW.

M.C. Winternitz to Harold G. Wolff, July 5 1951, Box 4, folder 4-7, HGW.

R. Ketih Cannan to Harold G. Wolff, July 14, 1953, HGW; Harold G. Wolff to R. Keith Cannan, July 25, 1955, Box 4, folder 4-7, HGW.

R. Keith Cannan to Harold G. Wolff, Sep. 10, 1958 (two letters), Box 4, folder 4-7, HGW.

Mrs. C.T. Dulles to Harold Wolf, Aug., 1957, Box 3, folder 3-2, HGW.
secret CIA project under the auspices of the MKUltra program, to investigate the mind control tactics practiced by the Soviet and the Chinese. With a $70,000 grant from the CIA (nearly $620,000 in 2015 dollars), Wolff drew together the Society for the Investigation of Human Ecology, to conduct experiments on the effects of social dislocation among expatriated Chinese, followed by similar studies of Hungarian immigrants and Puerto Rican migrants, respectively.87

In the late-1950s, the Society for the Investigation of Human Ecology began a study of former prisoners of war held captive by North Korean forces with the intent of determining the extent to which so-called “brainwashing” tactics could compromise a soldier’s loyalty.88 Despite the sensitive nature of its research, the results of the Society for the Investigation of Human Ecology’s research were vetted through scholarly peer review, with reports of its findings presented at conferences and published in scholarly journals.89 Fitting with Wolff’s general research interests, his work with the Society for the Investigation of Human Ecology focused on aspects of the psycho-social environment as they related to human health and adaptive capacity to resist disease. The substantial support that Wolff received from the CIA for his work with the Society for Human Ecology enabled him to pursue his stress research. During the same time period, Wolff continued his own stress research, focusing on psycho-social determinants of

87 Under Wolff’s leadership, the Society for the Investigation of Human Ecology consisted of consisting of Adolf A. Berle (Columbia University School of Law), Lawrence E. Hinkle (Cornell University School of Medicine), Joseph C. Hinsey (Dir. NY Hospital, Cornell Med Center), Carl R. Rogers (University of Wisconsin Department of Psychiatry), John C. Whitehorn (Dir. Johns Hopkins Department of Psychiatry). See NIH Grant No. M-1531, “A Study of the Illnesses Occurring in Members of Homogeneous Population Groups and Their Relationship to Individual Life Experiences,” October 11, 1956, Box 4, folder 4-6, HGW.

88 Society for the Investigation of Human Ecology, Inc., Annual Report (1957), Box 6, folder 6-15, HGW.

health and individual thresholds for psychiatric strain, headache, constipation and epidermal sensitivity to pain.  

**Stress and Disease**

In 1950, Wolff published *Stress and Disease*, a seminal collection of papers on the physiology of stress outlining his psychobiological theory of stress and disease causation, as well as critical research supporting it. Wolff described stress as a dynamic and perpetual state resulting from an individual’s relationship with its environment over time. He explained that whereas in physics “stress” arises from internal resistance to a load or external source of pressure generating strain on an object, in biology “stress becomes the interaction between external environment and organism, with the past experience of the organism as a major factor,” the load “becomes the stimulus or the external environmental agent,” and may be sustained, repeated or acute.  

Moreover, in Wolff’s description of biological stress, “the setting in which disease germinates assumes primary importance,” and becomes a principal factor in the definition of “adaptive and protective patterns used in meeting day-to-day dangers and threats of danger.” Stress arises from “microorganism, climate, chemical and physical forces,” as well as interpersonal “disruptions, hindrances and threats,” that demanded bodily adaptations. While initially these responses may be “appropriate in kind,” they may still be “faulty in amount,” and more importantly, over time they may condition behavioral adaptations that become harmful when

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92 Wolff, *Stress and Disease*, vi.
unnecessarily initiated. Essentially, stress becomes harmful because man “reacts not only to the actual existence of danger, but to threats and symbols of danger experienced in his past.”

In contrast to Selye, Wolff offered a comprehensive bio-psycho-social assessment of harmful environmental factors, including cultural factors, gender and familial relationships, hazardous industrial labor, military risks, and infectious disease, and focused on specific stress-related disorders, such as gastrointestinal and peptic ulcers, headache, constipation, hypertension, acne, diabetes, cancer, and neurological disorders. Wolff heavily emphasized the subjective individual evaluation of stress, well over a decade before psychiatric stress research began to focus on life events and coping strategies (discussed in Chapter Six). He described how a “situation takes on noxious significance only in terms of its meaning to the individual based on his innate characteristics, his past experience and future goals.”

Wolff’s theory of stress presented an etiological model that highlighted the importance of the conditioning effect of the host’s perception and past experiences, rather than merely a universal threat of a pathogenic stimulus. This implicitly incorporated a cognitive component in disease causation. Wolff’s interpretation of stress was highly subjective and individualistic, acknowledging the influence of personal heredity, conditioned behaviors, and life experiences, yet it was also rooted in an awareness of social processes, such as an individual’s responses to cultural pressures. He advocated an ecosocial, multi-directional approach to understanding disease in man, claiming that psychological stresses gain symbolic importance based on cultural experiences, which differ from man to man. He also emphasized social change and misanthropy.

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94 Ibid., 3.

95 Ibid., 5-6.
as precipitating factors in disease causation, where a lack of feelings of purpose, organization, roots, and belonging or an increased sense of difficulty and loneliness contribute to poor psychological health and increase vulnerability to disease. He insisted that “man’s ability to adapt, that is to remain free of disease, depends not only on his own inherent capacities and past experience, but also on his motivation and the support and refreshment that his environment can afford him.”

Whereas Wolff focused on the external environment—physical, social, cultural, etc.—as the primary agent inducing stress-reactions, Selye focused on an organisms’ internal environment, as it is regulated by endocrinological mechanisms. In *Stress and Disease*, Wolff cites Selye’s research on the capacity of very different stimuli to invoke the similar reactions within an organism, which emphasizes the fundamental difference in their perspectives: Selye sought to establish a mechanistic biological syndrome, while Wolff sought to identify a dynamic force regulating the relationship between the body, mind, and environment. Wolff specifically disputed Selye’s insistence on a specific paradigm of stress. Taking issue with the fact that “the widespread acceptance in medicine of the term ‘stress’ has led to the assumption that stress is something specific from which one might anticipate a specific bodily response,” Wolff countered that “stress is about as specific as any experience and, through the integrative activity of the brain, may yield almost any kind of response.”

While Selye certainly acknowledged a great diversity of stressful stimuli and stressful responses, he nevertheless insisted upon a formulaic adaptive syndrome experienced by all

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humans, and regulated by the endocrine system. Wolff challenged the centrality of the pituitary-adrenal axis on the grounds that “adrenocortical hormones do not produce all so-called stress reactions [but] only a relatively stereotyped pattern of metabolic changes.” Moreover, Wolff criticized the theory of adrenocortical primacy on the grounds that it failed to explain how adrenocorticoids might produce contradictory effects in different situations, such as the retention or elimination of salt or water, or the stimulation or cessation of gastrointestinal secretion. It was the central nervous system, Wolff insisted, that determined the physiological pathways of a stress response. He placed far more importance on the regulatory role of the nervous system, than that of the endocrine system, with the brain acting as the center of sensing and assessing stressful environmental threats, to which it adapts and develops patterned physiological responses. From this formulation, Wolff determined that “a conspicuous portion of man's illnesses is a function of his goals, his methods of attaining them, and the conflicts they engender,” so that prolonged stress accompanied by feelings of lack of control “may drain a man of hope and of his health,” but when accompanied by a sense of fortitude for survival, “he is capable of enduring incredible burdens and taking cruel punishment.”

Whereas Selye maintained a reductionist perspective of biological health, Wolff saw “the individual as a living system entirely dependent upon maintaining a satisfactory relationship with his total environment,” including “his ability to maintain a satisfactory body temperature; a satisfactory intake of food, fluids and air; a satisfactory elimination of waste products, and a satisfactory amount of rest and activity,” as well as “to maintain a satisfactory relationship with other human beings in his environment.” Failure to regulate these forces effectively may result in negative feelings, such as “anxiety, fear, anger, loneliness, sadness, and dejection,” often

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accompanied by “other unpleasant sensations of hunger, thirst, fatigue, sleeplessness, excessive warmth, or coldness, and all sorts of pain,” all of which “originate within the human body as a result of disturbance of body processes.”

V. The USNRC Ad Hoc Committee on Stress

In 1950 Wolff solidified his status as a pioneer in the field of stress research with the publication *Stress and Disease*. In November of the same year, he was nominated as Chairman of the NRC’s newly formed Ad Hoc Committee on Stress (AHCS). Joining him were a distinguished group of stress researchers in the United States and Canada—J.S.L. Browne of McGill, Rene Dubos of the Rockefeller Institute, Ralph Gerard of the University of Chicago, David M. Levy of Columbia University, Stewart Wolf of Cornell Medical School, John C. Whitehorn and Curt Richter of Johns Hopkins, and George Thorn of Boston’s Peter Bent Brigham Hospital. The AHCS was born of the Army’s considerable interest (and capacity to invest) in research to improve soldiers’ capacity for service, and because Drs. Selye and Wolff “had made the concept popular.” Yet, while Wolff was elected chairman, Selye did not take part in the committee’s operations. That Browne, a former colleague at the McGill Biochemistry Department who had worked with Selye on shock research for the SSBS, was appointed to the committee and Selye was not raises questions about Selye’s desire to take part in the determination of federal


100 "National Research Council, Division of Medical Sciences, 'Ad Hoc Committee on Stress'”, Box 19, folder "USPH Study Sections 1951 NIMH & Endocrinology," GGP.


102 Ad Hoc Committee on Stress, “First Meeting Agenda,” March 13, 1951, folder “MED: Com on Stress, 1951-1953, Ad Hoc: Meetings,” DMS.
stress research priorities, or his peer’s desire to include him in such endeavors. Given Selye’s
disdain for competitive funding in the medical sciences, it is entirely likely that he viewed such
forms of professional service as a distraction from his work as a bench scientist. Yet, it is also
possible that lingering suspicion of the merits of his ambitious theory may have influenced the
committee organizers.

The AHCS was specifically dedicated to study three areas of research outlined by the
Army: 1. the development of a simple test to measure stress in soldiers and help determine an
appropriate metric of combat tolerance, 2. a prophylactic or therapeutic method to be used in the
field for alleviating acute stress derived from trauma or shock, 3. methods to help increase
tolerance of stress arising from combat duty.\[103\] The committee oversaw experiments to test the
effectiveness of ACTH, cortisone and other steroids in protecting and treating soldiers against
stress.\[104\] The Army’s initial proposal for the development of the AHCS specifically “proposed
to omit the psychological and psychiatric aspects of the problem from the initial discussions,” in
favor of a focus on physiological manifestations of stress, especially in reaction to “traumatic
wounds, burns, surgery, battle fatigue, etc.”\[105\] However, under Wolff’s chairmanship, and
largely populated by fellow psychiatrists, the committee increasingly came to focus on questions
of psychology. Moreover, despite their mandate to adopt a biological model of stress in the
pursuit of a physiological intervention to treat it, from the outset of their service committee

\[103\] Lt. Col. H.E. Ratcliffe to Dr. M.C. Winternitz, November 29, 1951, folder “MED: Com on Stress, Ad Hoc: General, 1950-1953,” DMS.


\[105\] Col. John R. Wood, Chairman of the Medical Research and Development Board to Dr. M. C. Winternitz, Chairman of the Division of Medical Sciences of the National Research Council, November 20, 1950, folder “MED: Com on Stress, 1951-1953, Ad Hoc: General,” DMS.
members expressed that they believed “there is no likelihood of a simple physiological or psychological test for degree of exhaustion or liability for crack-up being devisable at present.” Nor, did they believe it would be possible to develop a pharmaceutical drug to treat exhaustion. The psychological orientation of the AHCS became official in 1956 when it was converted to a formal Subcommittee on Stress organized within the CMR’s Division of Psychiatry.

The AHCS’s psychological bias is indicative of a larger trend in military stress research, which historian of military stress research Tully Long has argued is evident in the 1953 Walter Reed Medical Center’s Symposium on the Role of Stress in Military Operations, and the later psychoendocrine research of John W. Mason. The effort to develop a physiological metric for evaluating stress levels quickly led researchers to recognize the importance of individual differentiation in appraisal and behavioral conditioning, and made it plain that stress could not be bifurcated neatly into physiological and psychological dimensions. Long goes onto explain that the Symposium on Stress raised awareness that “these issues of motivation and morale, while ostensibly the domain of psychology, had real consequences for the successful functioning of the soldier in the heat of battle,” and “in an effort to solve the very practical problem of keeping boots on the ground in combat situations… neither the mental nor physiological aspects could be left out of the equation.”

In his call to form the AHCS, Wolff defined stress as “an environmental change, assault, or threat which calls forth unusual protective or adaptive measures in order to maintain homeostasis.” As such, the AHCS concerned itself with a diverse range of issues including:

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106 “ Thoughts on the Stress Subcommittee,” DMS.
changes in an individual’s environment, interpersonal troubles, feelings of unrewarded effort or monotony, sleep loss, lack of oxygen, malnutrition or starvation, isolation, incarceration, extreme changes in temperature, catastrophe, stifled growth or development, rapidly changing culture, the breakdown of hierarchy or authority, trauma and burns, sudden physical impairment, infection, intoxication, dehydration, blood loss or mineral depletion.108

But the AHCS did prioritize the original three objectives laid out by the Army. By March of 1952, the AHCS had determined that it was impossible to develop a uniform test for detecting degrees of stress or determining individual breaking points, and had identified ACTH and cortisone as potentially useful agents in treating acute stress and increasing tolerance for stress, and was engaged in ongoing research to develop these methods.109 By the time it was disbanded in 1958, the committee spent approximately $2,000,000 (nearly $18 million in 2015 dollars) on adrenal physiology and psychosomatic mechanisms. Committee members described their efforts over the years as a “poorly coordinated and rather haphazard group of projects,” and their operations as being “largely muddled by elite debating on the meaning of stress and the virtues of interdisciplinary cooperation.”110

In 1950, prior to the formal creation of the AHCS, Selye was awarded a $14,904 (about $147,000 in 2015 dollars) grant to study changes in the thymicolymphatic system caused by the


110 “Thoughts on the Stress Subcommittee,” DMS.
growth of cancerous tumors.¹¹¹ In February of 1953, Selye applied to the AHCS to renew a grant to research stress-assessment tests¹¹², and in June of the same year he applied for renewal of a grant investigating the effects of STH resistance to infections, intoxication and wound healing.¹¹³ Overall, Selye received at least $205,446 in NRC support from 1951 to the beginning of 1956 (equivalent to about $1.83 million in 2015 dollars)—the largest amount that the AHCS awarded to any researcher under contract as of 1956.¹¹⁴ By that time, its members felt Selye’s work had become so heavily concentrated on basic research to develop new methods for assessing organic effects of steroids that it was distracting from actual research on stress. Nevertheless, they approved his new grant proposal for a two-year study to develop a “standard stress-index,” and study systemic factors in response to focal infection and the influence of stress on infection,”¹¹⁵ and renewed his existing contract to study resistance to stress and wound healing.¹¹⁶

While Selye, Wolff and Pincus all derived a great deal of financial support for their research from PHS and NRC grants, unlike his peers Selye did not serve as a scientist statesman.

¹¹¹ "Research Grants Awarded by the Public Health Service 1950, PHS Publication no. 63", Box 10, folder "U.S. Public Health Service, 1950-1951", GGP.

¹¹² Minutes of the Eighth Meeting of the Ad Hoc Committee on Stress, February 24, 1953, folder “MED: Com on Stress, 1951-1953, Ad Hoc: Meetings,” DMS.

¹¹³ Minutes of the Ninth Meeting of the Ad Hoc Committee on Stress, June 22, 1953, folder “MED: Com on Stress, 1951-1953, Ad Hoc: Meetings,” DMS.


¹¹⁵ “Current Status of Stress Projects,” DMS.

¹¹⁶ Col. R.P. Mason to R. Keith Cannan, February 15, 1956, and “Seventh Meeting of the Subcommittee on Stress of the Committee on Psychiatry of the National Research Council, Tentative Agenda,” March 26, 1956, Box 21, folder “National Research Council, 1956,” GGP.
Rather, the viability of his work—like all researchers not enmeshed in the power structure of grantmaking—was subject to whether they chose to award or decline his grant applications. As Expert Consultant to the Surgeon General of the US Army, Selye received considerable support from the Army Medical Service (at the recommendation of the National Research Council’s Division of Medical Sciences), totaling at least $144,186 (approximately $1.28 million in 2015 dollars) from June of 1951 to July of 1956. While Selye received substantial funding from the Army, his involvement in military stress research seems to have been superficial. While other prominent stress researchers, such as Harold Wolff, Gregory Pincus and Richard Lazarus, a young psychiatrist at Johns Hopkins, not only received military contracts, but served on stress research committees and participated in military symposia, Selye did not undertake such forms of professional service. While the Walter Reed Symposium on Stress attracted more than 100 attendees, with Pincus and Lazarus, as well as George Thorn, Hudson Hoagland and

117 In 1951, the Ad Hoc Committee on Stress rejected Selye’s original proposal for a study on the “Effect of Somatotrophic Hormone (STH) upon Wound Healing and Convalescence from Traumatic Injuries,” but suggested they would be willing to accept a modified proposal examining the effects of STH on wound healing without Selye’s proposed examination of nutritional factors. See “Minutes of the Second Meeting of the Ad Hoc Committee on Stress,” May 22, 1951, folder “MED: Com on Stress, Ad Hoc: Meetings, 1951-1953,” DMS.

Noting that Selye had done considerable research in the past two years, in 1953, the Ad Hoc Committee on Stress approved Selye’s proposal more vaguely titled “Research on Tests Likely to Help in the Assessment of Stress in Man.” See “Minutes of the Eighth Meeting of the Ad Hoc Committee on Stress,” February 24, 1953, folder “MED: Com on Stress, Ad Hoc: Meetings, 1951-1953,” DMS. A few months later they renewed Selye’s contract for the study of the effects of STH on wound healing. See “Minutes of the Ninth Meeting of the Ad Hoc Committee on Stress,” June 22, 1953, folder “MED: Com on Stress, Ad Hoc: Meetings, 1951-1953,” DMS.

Fred Elmadjian participating as conference panelists, there is no record of Selye even attending the conference.\footnote{119}

In addition to funding from the US federal government, Selye benefitted from smaller yet still important grants from the Canadian Dominion Government. From 1952-1953, on the recommendation of the National Cancer Institute, the CNRC awarded Selye a $12,000 grant (about $108,000 in 2015 dollars) for “studies on the relationship between hormones and tumorigeneisis.”\footnote{120} The following year, Selye was awarded two grants by the CNRC—one for “studies concerning the mechanism of the general adaptation syndrome,” and the second for research on “the interactions of corticoids and growth hormone.”\footnote{121} In the course of his work under this latter grant, Selye accidently invented a new method for evaluating adrenocortical arousal by caustic stressors. While attempting to administer an injection to a laboratory rat he was distracted when some visiting scientists entered his laboratory, and accidentally injected a bubble of air underneath the rats skin.\footnote{122} This bubble—which Selye named the “granuloma pouch,” and informally referred to as an inflammatory pouch—just so happened to provide an ideal contained organic environment. Initially, he used the granuloma pouch technique to evaluate the inflammatory response initiated by croton oil, in rats pretreated with cortisone,

\footnote{119} Symposium on the Role of Stress in Military Operations.

\footnote{120} That year the CNRC issued a total of $475,000 in grants. “Proceedings of the Twelfth Meeting of the Advisory Council on Medical Research,” March 7, 1952, folder 30.24, Box 33, CNRC.

\footnote{121} Selye was awarded $18,500 for both studies, out of a total of $500,000 in grants distributed by the CNRC that year. “Proceedings of the Fifteenth Meeting of the Associate Committee on Medical Research,” March 9-10, 1953, Ottawa, p. 9., Appendix B, p. 3, and Appendix F, p. 9, folder 30.24, Box 33, CNRC.

\footnote{122} Selye, The Stress of My Life, 220.
ACTH, COL, DOC or STH. Anti-inflammatory hormones, such as COL inhibited the formation of an inflammatory barricade that protects the surrounding skin from the corrosive properties of the irritant, whereas pro-inflammatory hormones, such as STH or DOC increased the formation of an inflammatory barricade and the production of protective fluids to combat the corrosive irritant.


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These experiments were critical to proving that not all diseases improve when treated with anti-inflammatory hormones since the lack of an inflammatory barricade may cause further destruction if enabled to spread throughout the body. The granuloma pouch technique proved useful in a variety of other experimental situations, as well, such as evaluating the toxicity of substances and the carcinogenic properties of tobacco tars. Selye was so enthusiastic about the potential uses of the granuloma pouch technique that he let this research distract him from the responsibilities prescribed by his grants. Selye also sought to renew AHCS grant applications to continue work on the granuloma pouch technique, but they were rejected on the grounds that they were too heavily focused on basic research. Despite the seemingly apparent conflict of interest, Selye also proposed work on the granuloma pouch technique in grant applications to the CNRC. In his interim report for 1953-54 to the CNRC outlining his progress on a grant issued for “studies concerning the mechanism of the General Adaptation Syndrome,” Selye conceded that he had yet to finish the contracted work, but explained the discovery of the granuloma pouch technique, and proposed that the CNRC patent the procedure.

By the time the AHCS disbanded in 1958, Selye had transitioned into a new phase of his career, in which he sought greater independence by promoting his research directly to the public and disregarding professional censors (as will be discussed in Chapter Five). It is possible that the discontinuation of the AHCS allowed Selye’s even greater scientific authority in the public


125 “Current Status of Stress Projects,” DMS.

126 “Proceedings of the Fifteenth Meeting of the Advisory Committee on Medical Research,” March 9-10, 1953, Ottawa, Appendix F. p. 9, folder 30.24, Box 33, CNRC.
mind. At the very least, it is an interesting coincidence that Selye began a new campaign to promote stress literacy at the same time that the committee was disbanding. There is evidence to suggest that by the late-1950s some of Selye’s fellow stress pioneers had come to believe “stress” had outgrown its usefulness as an etiological concept. Reflecting on the discontinuation of the Committee on Stress, John Spiegel wrote to Keith Cannan Director of the NRC’s Division of Medical Sciences that “in spite of having written a book which featured the word ‘stress,’ I have always thought the concept was mainly a heuristic one and that it eventually would give way to more precise methods of describing the organism-environment interchange.” Regretting that this had not yet come to pass, Spiegel pronounced that “we have used up whatever fruitful and stimulating ideas which were brought out by employing the stress concept,” and he predicted that, “it will be remembered mainly as a stepping stone to broader purchase on the relations between physiology, psychology and sociology.”127 While stress would continue to be a magnetic topic for medical research, Spiegel was at least prescient in his hope that it would become more concerned with psycho-social dynamics—a critical transition which Selye failed to embrace.

**Conclusion**

Selye’s research interests diverged from those of the AHCS as he became more defensive of the need for basic endocrinological research and the AHCS became more interested in the physiological manifestations of psychological stress. While Selye wrote of his conscientious effort to respond productively to criticism of his research, Wolff and Kendall’s criticism of the syndromic model of stress and adrenocortical primacy in disease causation seems to have, if

anything, mustered Selye to defend his theory even more adamantly. Yet, because Selye failed to productively respond to his colleagues’ criticism, he ultimately lost power in the growing field of stress research to the mounting influence of psychologists and psychiatrists.

By the mid-1960s, the psychiatric dominance in stress research was apparent even in the largest health organization in the world. In 1964, the World Health Organization’s Expert Committee on Mental Health issued a technical report on *Psychosomatic Disorders*, “stressing that man in health and disease, functions as a psychosomatic unit” and that “the conceptual separation of mind and body in medicine is not only unreal but also unfruitful.” In doing so, the Expert Committee advanced the view that an individual is a “complex dynamic system in an unstable state of equilibrium, acting and adapting to changes in the environment and to changes within the system, and therefore medical experts must “have an outlook that is broad enough to comprehend all the major factors involved in illness—social, cultural and psychological, as well as organic and hereditary.”

In a section devoted to discussing the role of stress and strain in illness, *Psychosomatic Disorders* acknowledged the psychological basis of stress, and the adverse effects that it can have on human health. Echoing Wolff’s description of stress, *Psychosomatic Disorders* emphasized individual differences in the perception of stressful situations based on past experiences and personal development, as well as the precipitating role of interpersonal relationships and traumatic events. While *Psychosomatic Disorders* very nearly equated anxiety with stress, it did not even mention the concept of biological stress or the possibility that

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physiological disease might affect psychological health.\textsuperscript{129} The psychological bias embraced by the WHO Expert Committee on Mental Health is not unusual given the increasing dominance of psychiatrists in stress research in the 1950s and 1960s, as well as the concurrent medicalization of anxiety. In fact, while Selye’s research remained focused on elucidating the hormonal regulations of chronic diseases, he too espoused the psychiatric interpretation of stress, as he struggled to promote popular awareness of his theory.

\textsuperscript{129} Psychosomatic Disorders, 8.
Chapter 5: Stress in the Postwar Medical Marketplace

Introduction

As state, corporate and consumer interests converged in their mutual desire to combat the increased prevalence of chronic disease, Selye marketed his stress research to emphasize its importance for combating chronic diseases of adaptation, and incorporated the new medical model of dynamic anxiety as a major risk factor for stress-related diseases. He also recommended therapies that corresponded with postwar economic interests, encouraging patient-consumers to individualize care through self-selected dietary and behavioral modifications, and when necessary, to seek doctor-prescribed treatment with anxiolytic and hormonal pharmaceutical drugs.

At a time when his colleagues operated within the scientific professional community to guide federal stress research, Selye sought influence by appealing directly to the North American public. While state and corporate funders continued to dominate the medical research economy in the 1950s and 1960s, the central importance of consumerism to the postwar economy elevated the power of patient-consumer interests in the validation of research pursuits. Prime among these were concerns with managing chronic disease, and treatment for the increasingly prevalent diagnosis of anxiety. The growing power of pharmaceutical companies in the postwar medical marketplace reinforced patient-consumers’ desire for pharmacological therapy, and pharmaceutical companies seized upon the psychosomatic valence of stress to market both anxiolytic drugs and adrenocortical hormone preparations.

Selye actively encouraged the North American public to perceive stress as a determinant of health. He used public relations and marketing strategies as mediators of popular health literacy in order to encourage the assimilation of his theory of stress, appealing to the public’s
health concerns and preferences for simple pharmaceutical therapies and self-controlled behavioral interventions. In doing so, he promoted a disease model that conformed to the individualistic consumer-orientation of the postwar economy. And by endorsing behavioral interventions that supported the belief that physical health could be controlled by mental will, he implicitly endorsed the psychosomatic basis of stress.

I. Direct-to-Consumer Health Literacy

While Selye benefitted substantially from state funding for his research, he prioritized his own independent laboratory work over direct involvement in federal research administration. In contrast to fellow pioneers in stress researchers, like Pincus and Wolff, Selye viewed professional service and advisory appointments as distractions from his research. Yet, by evading such powerful administrative positions, Selye’s influence over the direction of academic stress research outside of the IMCE diminished. Moreover, his reluctance to perform as a scientist statesman left him dependent on others to approve his requests for funding, and as a result, he had to cater his research to appeal to funders’ interests. Selye’s experience with the AHCS is a poignant symbol of his mounting frustration with grantsmanship. He resented the instability of yearly contracts, the capriciousness of grant referees, and the emphasis on applied rather than basic research. This frustration likely led him to develop a strategy to bypass scientific critics and appeal directly to the public to endorse his theory.

In the mid-1950s he began to promote his research in popular news media and trade literature. Selye seized on his newly won acclaim to expand his authority beyond the scientific community. He lectured widely throughout North America, Europe and South America—apparently, not considering such extensive travel a distraction from his research—and gave
countless interviews to the popular press, always concertedly promoting his theory of the GAS as he sought to “sell” stress to the public. In 1950 he founded his own publishing company, Acta, Inc. Medical Publishing to handle the production of his Annual Reports on Stress, his Textbook of Endocrinology and a compilation of several of his lectures on stress entitled, The Story of the Adaptation Syndrome. He also appeared in several educational films produced by pharmaceutical companies, academic publishers and universities.

Selye developed a great affinity for self-promotion, using the mainstream media to directly appeal to the North American public as a means of encouraging the assimilation of the biomedical theory of stress, but also to actively cultivate his own reputation as the world’s foremost authority on stress. Selye became synonymous with stress, as stress became a core medical concept to explain the modern prevalence of chronic and mental disease. As he strove to popularize stress, Selye enlisted the support of patient-consumers to validate his theory. This helped to attract further support from state, pharmaceutical and philanthropic patrons, all of whom shared an interest in alleviating the chronic diseases plaguing North American patient-consumers. Despite his dependence on state largesse, Selye rebuked the prioritization of applied research, and was partly inspired to appeal to popular audiences as a means of transgressing grantmakers’ subordination of basic research. Even as the established scientific and medical

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1 “Better Understanding Required Between Scientists, Politicians” Montreal Gazette January 29, 1963, folder I: Newspaper clippings, HSC.

2 Elizabeth Siegel Watkins has argued from the 1950s to the 1980s, both professional and popular discourse contributed to the acceptance of the medical legitimacy of stress. Critical to the multidirectional circulation of information about stress were popular reports on stress that exploiting pre-existing cultural values and medical knowledge that drew on the concepts of neurasthenia, nervousness, nervous breakdown and depression. However, “stress” ultimately gained recognition in the medical and popular imagination as it became “incorporated into the diagnosis of anxiety,” and “implicated as a risk factor for chronic disease.” See Watkins, “Stress and the American Vernacular,” 49-70.
communities were increasingly embracing his theory of stress, Selye ultimately achieved validation for his work in the medical marketplace, by acclimating to the consumer orientation of the postwar period.

II. *The Stress of Life*

Perhaps the greatest turning point in Selye’s career was his publication in 1956 of *The Stress of Life*, a synthesis of his theory of stress written for a popular audience and published by McGraw Hill. *The Stress of Life* was extremely popular in North America and beyond, was translated into over a dozen languages, and quickly rose on trade best-seller lists throughout the western world, signaling the popular assimilation of the concept and terminology of biologic stress. Before the end of 1958, *The Stress of Life* sold out five editions.3

With the publication of *The Stress of Life*, Selye was able to transcend the judgment of the scientific community and appeal directly to public opinion to validate his theory of stress. In *The Stress of Life*, Selye simplified complicated scientific processes through the use of two primary strategies—pictorial representations in the form of clearly labeled diagrams, and analogies. He offered clinical evidence to support his theory, responding to the most salient points of criticism against his work. But, he also unabashedly presented an expository narrative of his own discovery of stress, emphasizing the personal “psychologic [sic] processes which led to its discovery.”4 In doing so, Selye invoked authority based on his allegedly impartial scientific expertise, while also implicitly asserting the natural basis of stress by unfolding what appeared to be an inexorable process of discovery.

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4 Selye, *The Stress of Life*, 5.
Selye recounted his earliest observation of the syndrome of general sickness when he was a medical student in Prague, and his later observations of the triad of symptoms and triphasic nature of the adaptive response to diverse nocuous stimuli in his work on female sex hormones at the McGill Biochemistry Laboratory. He placed his own work in a tradition of ground-breaking endocrinological research, including Claude Bernard’s theory of the _milieu intérieur_ and Walter B. Cannon’s theory of homeostasis, as well as in a historical cannon of clinical endocrinology, from Starliss and Bayling’s discovery of hormones and Banting and Best’s discovery of insulin. Lacking any pretentions of modesty (a trait which he explicitly deplored), Selye even went so far as to liken himself to Louis Pasteur for revolutionizing the entire field of medicine. Selye also strove to demonstrate how his research employed traditional biomedical investigative methods, emphasizing that he employed the falsifiable clinical methods outlined in Robert Koch’s postulates to produce the evidence supporting his theory. Selye claimed that his experiments with DOCA were guided by Koch’s postulates, ironically using this icon of specific etiology to defend his theory of general sickness.\(^5\)

In order to demonstrate the scientific basis of his theory, Selye marshaled an ethos of positivism by presenting facts allegedly derived from empirical observations of nature, and a reductionist optic by explaining complex processes as a product of their simplest, most fundamental components. Selye laid bare his positivist orientation in plainly stating (and declaring the scientific worth of) his clinical observations, as well as in recounting his own experience of discovery. He prized the measurability of spatial and temporal dimensions of the physiological basis of stress as fundamental to proving its legitimacy.\(^6\) His reductionist position

\(^5\) Selye, _The Stress of Life_, 137-138.

\(^6\) Ibid., 33.
is similarly evident in its tendency to simplify the complex relationships between different biological systems by analyzing their behavior at the cellular level using accepted methods of bioassay. Selye insisted that, “to understand a complex thing you must take it apart systematically.” He relied on positivism and reductionism to present the theory of stress as a natural law—a claim that far exceeds his actual evidence, and a contradiction of his repeated claim that theory need not be correct in order to produce factual evidence.

The publication of *The Stress of Life* represents the popular introduction of a new paradigm of medical etiology that framed the understanding of health in the latter half of the twentieth-century. Selye’s theory of stress centered around an understanding of disease as the cumulative result of many stressors that wear down the body’s capacity to protect itself. By demonstrating that over time all human beings develop an increased susceptibility to disease due to physiological changes and depleted adaptation energy, the concept of biologic stress generated a dynamic rather than discrete interpretation of pathology, much like the dynamic model of mental health popularized in the postwar era. Selye’s model of biological stress implicitly created a theoretical continuum of health and disease, universalizing the potential for disease and rendering even healthy individuals latent victims of stress. Despite his provocative claim that he did not think that “anyone has ever died of old age yet,” Selye insisted that stress is essential to life and could even offer therapeutic benefits, such as in the stress of shock therapy, bloodletting or athletic exercise. Trying to avoid stress, he cautioned, was both futile and unhealthy, therefore, one should strive to find a healthy balance of stress. Selye was clearly aware of the

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7 Selye, *The Stress of Life*, 49.

8 Ibid., 276, 3.

9 Selye, *The Stress of Life*, 299. He later elaborated on this concept of countervailing stresses with his theory of eustress (good stress) and distress (bad stress), as discussed in Chapter
significance of his research on disease of adaptation with regard to age-related illness, as he noted that since the turn-of-the-century bacteriological science had improved life expectancy from 48 to 69.8 years in 1956 only to leave the beneficiaries of increased life expectancy to face the unanticipated consequence of dying from “wear-and-tear diseases… caused by stress.” He remarked that this phenomenon yielded the paradoxical lesson that “the more man learns about the ways to combat external causes of death (germs, cold, hunger), the more likely is he to die from his own voluntary, suicidal actions.”


Understanding “degenerative” disease as a product of maladaptation proved to be a powerful rubric with which to confront the health problems of the aging North American population. Consequently, Selye’s theory of biologic stress helped to reconcile biomedicine with the increased prevalence of chronic diseases at mid-century (as discussed in Chapter Three). This new medical paradigm emphasized the multicausal nature of disease and the important influence of idiopathic exposure to risk. Selye’s theory of stress was first and foremost predicated on a recognition that as it strove to acclimate to environmental changes, the body...
mounted a general biochemical response to a diverse number of harmful agents. As such, it emphasized the relationship between an organism and its environment, while at the same time offering the potential to unify different disciplinary perspectives and distinct observations of disease. Because Selye placed great importance on the role of selective conditioning on individual health, his theory of stress served to uphold an individualistic interpretation of disease as the result of idiopathic experiences. Because individuals exhibited vastly different thresholds for stressors and expressed such a diverse array of symptoms arising from their physiological responses to stress, they also required highly individualized therapies that responded to their unique histories of risk—their hereditary background, their previous exposure to disease agents, their life-style choices, etc.

Perhaps inadvertently, this view of idiosyncratic risk parallels the psychological emphasis on patient life histories espoused by Adolf Meyer and students of psychobiology throughout the first half of the twentieth-century, as well as Harold Wolff’s emphasis on individual conditioning. In this respect, as well as the dynamic interpretation of health it promoted, the theory of stress articulated in *The Stress of Life* bridges the boundary between biological and psychiatric disciplines. By calling upon individuals to use mental will to make appropriate decisions about managing their own stress levels, Selye implicitly endorsed the perception that stress was fundamentally a psychosomatic condition. Moreover, Selye’s repeated insistence on the conditioning influence of psychological factors served to substantiate the popular linkage between stress and psychological distress. While on one hand he stated very plainly that “stress is not nervous tension,” on the other, he not only attributed physiological disease to psychological factors, but even claimed that “mental tensions, frustrations, the sense of insecurity, and aimlessness are among the most important stressors,” with “migraine headache,
gastric and duodenal ulcer, coronary thrombosis, arthritis, hypertension, insanity, suicide, or just hopeless unhappiness actually caused by the failure to find a satisfactory guide for conduct.”

Yet, while the description of stress put forth in The Stress of Life signaled the assimilation of a new perspective for evaluating disease, it did not represent a Kuhnian paradigm shift. Not only did Selye conscientiously conform to orthodox methodology, but he built his theory on the merits of research that came before him. In numerous instances he described stress in ways that resembled earlier medical theories, from Hippocratic ponos, to neurasthenia’s emphasis on finite “nervous force,” and more recently, on the scaffolding of Bernard and Cannon’s theories of balance. While Bernard argued that the body maintains a steady internal state, and Cannon argued that the body is constantly engaged in a “fight or flight” struggle to maintain these ideal conditions, Selye went even further, arguing that the body is perpetually engaged in a struggle of resistance against injury as it strives to balance a triad forces induced by exposure to stressors: 1) the stressor’s effect on body, 2) internal tissue defense, and 3) internal tissue surrender. This involved an inherently antagonistic relationship between the body’s drive for self-preservation and aggressors, both external and internal. This theme of tension and balance recurred in many different expressions in Selye’s theory of stress—between organism and environment, pro- and anti-phlogistic hormones, nervous and endocrine regulation, et al. Selye deduced that “disease is not just suffering, but a fight to maintain the homeostatic balance of our tissues, despite

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12 Ibid., 47.
13 Ibid., 92, 55-56.
damage,” involving an element of stress, “in the sense in which the engineer speaks of stress and strain in connection with the interaction of force and resistance.”  

Interestingly, throughout *The Stress of Life*, Selye repeatedly defends his choice of the term “stress” as a medically appropriate and culturally relevant word. He claims that when he first discovered the GAS in the mid-1930s, he “often used the term biologic stress, in referring to what caused this syndrome,” yet when he first published his findings in the July 1936 edition of *Nature* the “violent” opposition to his use of this word in a physiological sense, “because in everyday English it generally implied nervous strain.” In order to avoid distracting from “the real issues,” he chose the “less obnoxious” phrase, “noxious agents.” He noted that at this time, “one of the greatest objections against [his] use of the term stress was that it might lead to confusion with other possible meanings of the word,” but insisted that this fear was unfounded as no such confusion had yet arisen. Yet, at the same time, Selye admitted that he initially contributed to etiological confusion by choosing “stress” to describe a condition that was more appropriately analogous to the physics concept of “strain.” Moreover, Selye’s description of how he came to select the term stress seems disingenuous as it suggests that he was solely responsible for the introduction of this term. On the contrary, while Selye surely was the first to use the term stress to describe the GAS specifically, Walter Cannon, Fatigue Laboratory scientists, Pincus, Wolff and dozens of other researchers had used the term in grant applications and scientific publications since the late-1930s. Furthermore, the fact that Selye began using this term at the end of the Second World War strongly suggests that his decision was influenced by

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15 Ibid., 30.

16 Ibid., 39.
the legitimization of the term in association with “combat stress,” and therefore fundamentally rooted in the psychological sense of the word.17

Selye’s claim that stress became accepted “gradually” through habitual use seems a likely explanation. However, it presumes that popular acceptance was an indication of a coherent common understanding of the relationship between psychological and biological stress. Yet, as Selye actively sought recognition as the “father of stress,” he obscured collateral professional and popular forces that helped to popularize the concept of stress, and claimed intellectual ownership of the concept of stress. In the mid-1960s he began a friendly correspondence with the maverick media theorist, Marshall McLuhan, which revealed his belief that “stress” needed to be sold to the public in order to gain widespread acceptance, and that the popular media was an ideal means of communication. Over a decade before McLuhan urged that Selye recognize the importance of language as a principal medium “which informs our nervous system,” Selye clearly understood this principle quite well, since he chose a term imbued with cultural meaning to convey his complex scientific theory to as broad an audience as possible.18

On one level, The Stress of Life represents a prescient strategy to promote health literacy beyond the strictures of the biomedical research community. Yet in other respects, it can be seen as an overt attempt to manipulate a scientific debate to center on Selye’s own terms. The extent to which the new terrain of the medical marketplace influenced this strategy is evident in the ways in which Selye altered his disease model to appeal to the concerns of North American patient-consumers afflicted with anxiety and chronic, degenerative diseases. He highlighted the


primary role of emotional stress in the development of diseases of adaptation, evidencing a recognition of the cultural valence attached to medicalized anxiety, and he recommended various self-help strategies that enabled consumers to shop for therapies that best suited their unique battery of symptoms. Emphasizing that each individual must find their own balance of productive and destructive stressors—a concept which he would develop into a formal theory of distress and eustress over the course of the next decade—Selye presented stress as a highly individualistic and idiopathic condition, that required personal intervention in health management.

Selye believed that the foremost benefit of stress research was that it offered the possibility to improve health by mimicking the body’s own physiological protections against injury, either through the administration of pharmaceutical drugs or through various methods of behavior modification. From these empirical, clinical observations, Selye constructed a code of behavior “to guide our actions in conformity with natural laws.” Advancing what he called the “philosophy of gratitude,” Selye insisted that egotism is a natural impulse associated with the drive for self-preservation. Therefore, he suggested that it is in accordance with natural law, and in the best interests of the individual and of society, to “induce another person to share with me my natural wish for my own well-being.” And in order to inspire this gratitude, Selye called upon each person “to express himself as fully as possible, according to his own lights.”

19 Selye, The Stress of Life, 253, 256-57.

20 Ibid., 4.


22 Selye, The Stress of Life, 299.
insisted that pursuing your own talents to the best of your ability is the best way to earn the
gratitude of your fellowman and at the same time avoid incurring undue stress.

Selye encapsulated his theory in the credo: “fight always for the highest attainable aim;
but never put up resistance in vain.”[23] He instructed each individual to learn his or her own
thresholds for stress and to carefully budget his or her adaptation energy, just as one would pace
themselves in drinking alcoholic beverages.[24] When confronted with seemingly intractable
stressors, Selye encouraged adopting tactics of diversion or deviation to disrupt the “grooves”
that perpetuated a stress response (which he likened to the psychoanalytical theory of sublimated
memory).[25] Diversionary tactics may involve taking a walk to distract oneself, reading a book,
taking a nap or smoking a cigarette. Even unhealthy behaviors could be therapeutic if they
succeeded in derailing a unrelenting stress response.

Selye must have realized that in prescribing these behavioral changes to avoid stress-
induced disease, he was tapping into a new market for self-help propaganda. He admitted as
much in acknowledging the recent increase in “books and articles of late, which tell you 'how
to...': how to achieve peace of mind, how to enjoy life, how to become a millionaire or
centenarian, and how to be a success in general.”[26] Yet, at the same time that he offered this
“precise program of conduct,” he also insisted on the impossibility of prescribing a one-size-fits-
all remedy for stress-reduction. Rather, forcing oneself to conform to a program of behavior,
Selye claimed, might itself be a stressful experience if it were to limit ones capacity for self-

24 Ibid., 261.
25 Ibid., 267.
26 Ibid., 294.
expression. He encouraged idealism rather than pragmatism on the grounds that, "'realistic people' who pursue 'practical aims' are rarely as realistic and practical, in the long run of life, as the dreamers who pursue only their dreams."27

The Popular and Professional Response to The Stress of Life

While Selye earned international fame in professional circles following the adrenocorticoid revolution, with the great success of The Stress of Life and the media blitz that accompanied its release, he secured his status as the pre-eminent authority of stress in the eyes of the public. For laying out a new theory of medicine and establishing new research methods to measure it, Selye was heralded as the “map-maker,” and “the charter” for other stress researchers.28 By 1956 he was a member of 62 scientific societies, sat on the editorial board of sixteen scientific publications in the United States, Canada, Germany, Switzerland, Sweden, The Netherlands, and Spain.29 Selye’s international renown brought great esteem to the University of Montreal, the City of Montreal and to Canada, as a whole.30 Selye employed various promotional techniques to vastly expand his audience to include the global scientific community and the public sphere.

To accompany the release of The Stress of Life, Selye also released a short film, “Stress and the Adaptation Syndrome,” produced by the Canadian National Film Board, Research and

27 Selye, The Stress of Life, 294.


30 “U. of M. Marks Anniversary for Dr. Selye,” Montreal Gazette, March 7, 1956, folder: I: “Newspaper clippings,” HSC.
Scientific Films, Inc., and Pfizer Laboratories.31 “Stress and the Adaptation Syndrome” brought Selye’s research to a scholarly audience far beyond North America, with Pfizer even producing a Japanese pamphlet to accompany the film, after it became extremely popular among Japanese audiences.32

Both professional and popular reviews of The Stress of Life were by-and-large very positive. Many reviewers expressed the sentiment that the medical community and the general public had already embraced the foundations of Selye’s theory—1) that hormones are fundamental to the regulation of health; 2) that one’s health is ultimately a product of the function of the organism as a whole;33 3) that disease may arise from an internal struggle against harmful environmental stimuli;34 4) that dietary modifications can reduce blood pressure and the risk of heart disease;35 and 5) that there is a profound relationship between physical and psychological health.36 While some reviewers celebrated Selye’s “unusual mixture of

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philosopher, humanitarian and scientist,” others focused on the worth of his endocrinological research and theory of stress. Many reviewers echoed eminent British surgeon, Sir Heneage Ogilvie’s pronouncement in the introduction to the first edition of *The Stress of Life*, that Selye’s work on stress offers “perhaps the greatest contribution to scientific medicine in the present century.” And alongside this new medical paradigm came personal empowerment and responsibility to develop an enhanced awareness of individual “strains and stress of living and how to protect ourselves against them”—especially in light of the increased lifespan, and the potential for developing chronic diseases and psychiatric illness later in life.

However, *The Stress of Life* was not received without criticism. The *London Times* emphasized that despite the abundance of literature on Selye’s theory, readers must bear in mind that it was still “an unproven concept” and its merits were yet debated by medical experts, for as Selye “plunged deeper and deeper in his attempts to rationalize it, it has become so complex that even many of his earlier adherents are becoming rather skeptical of its validity.” *Nature* offered that “indeed, it is difficult to avoid feeling that his concepts are so wide that they include

37 Review of *The Stress of Life, Lector Medicus* 2, no. 2, folder: I: “Newspaper clippings,” HSC.


too much.” So, even though readers may agree with his call for a “‘new type of medicine.’” Selye’s theory was too ambiguous to produce such a radical change by itself.  

The popular press was much more forgiving of Selye, than his academic peers. Popular journalists seldom acknowledged that anyone contested Selye’s theory, and the few who did found the implications of his theory to be so alluring that they outweighed the professional criticism. Offered the potential that stress research might be a new way of confronting “all diseases and indeed all human activities,” some found it simply too “hard to resist a man with the vision and zest to foresee a time when we may all live to be a hundred,” and by managing our stress, realize that “happiness and peace of mind can produce health and long life.”

Selye promoted The Stress of Life with zeal, beginning with a high-profile press conference in Montreal on November 21, 1956, in which he claimed that modern man was exposed to no more stress than prehistoric man, who derived anxiety from his search for food, shelter and safety. Modern man, by contrast, was confronted with entirely different kinds of environmental and emotional stressors, and Selye’s book offered useful advice for adapting to these modern stressors. In proposing such a claim, Selye presented himself as an emissary of public health literacy, helping North Americans to make educated lifestyle decisions to improve their own health.

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Selye’s publisher, McGraw Hill also undertook a publicity campaign, printing widely circulated advertisements prominently featured in medical journals and popular magazines and newspapers. Several publicity circulars presented *The Stress of Life* as a guide to reduce stress-related disease risks, claiming that it “tells how to handle ourselves during the stress of everyday life, how a knowledge of bodily changes during stress can help us to tune down when we are wrought up, to overcome insomnia, and many other practical applications,” and elsewhere, that the book, “shows clearly how you can use this information [about the physiological basis of stress] to improve your own health and state of mind—conserving adaptive energy, reducing nervous tension, and enjoying the benefits of stress!” In this way, Selye was offering valuable advice to “thousands of American men and women who want to live healthier, happier lives,” and enjoy the bounty of the American way of life. In order to persuade readers of his credibility, McGraw Hill strove to bolster Selye’s medical authority by describing him as “the Einstein of Medical Science,” and quoting the *Journal of the American Medical Association*’s praise that Selye’s concept of stress may “prove to be one of the significant medical advances in understanding the nature of disease of this century.”

*The Stress of Life* was a true sensation in the popular news media. Regional newspapers big and small, and popular magazines in Canada and the United States reaching national audiences, featured Selye’s theory, process of discovery, and philosophy for living with stress. *Newsweek* proclaimed that Selye’s theory that stress is a normal, physical response of the body to

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45 McGraw Hill advertisement for *The Stress of Life* “Your Health is Important... Read *The Stress of Life,*” folder: I: “Newspaper clippings,” HSC.


“the wear and tear of life,” had been verified by the treatment of rheumatoid arthritis with ACTH and cortisone, and therefore, was now generally accepted by modern medicine.\textsuperscript{48} \textit{Time} celebrated Selye’s advice to relax and minimize the stress caused by the pace and pressures of modern life.\textsuperscript{49} \textit{Saturday Night} emphasized Selye’s caution that stress could be beneficial as well as harmful, and that we must therefore learn to strike an appropriate balance to minimize injurious stress.\textsuperscript{50} \textit{Coronet} claimed that stress “will be a major reason for one out of every ten persons eventually developing some form of mental illness,” and that according to Selye, it is “the ultimate cause of the average person’s death.” However, thanks to Selye’s work on the chemical foundations of disease—and the research that it allegedly inspired—thirty different stress-induced diseases had been identified, including rheumatoid arthritis, leukemia, asthma, high blood pressure, hardening of the arteries, enlargement of the heart, and cancer. And as a result, approximately 200,000 patients in the United States alone received crucial medical care helping them to restore the chemical balance caused by their disease. Given the remarkable effects of such hormonal therapies, \textit{Coronet} referenced Selye’s claim that if pharmaceutical treatment were accompanied by his behavioral and dietary recommendations, average life expectancy might easily increase by thirty years.\textsuperscript{51}

As an important aspect of his publicity campaign, Selye also authored articles outlining his theory and philosophy of stress in numerous magazines reaching diverse audiences including,


\textsuperscript{50} Robertson Davies, “Stress as Angel and Devil,” \textit{Saturday Night}, January 5, 1957, folder: I: “Newspaper clippings,” HSC.

in such articles, Selye invariably strove to appeal to readers’ conceptions of stress as virtually synonymous with anxiety, by emphasizing psychological and emotional stressors. In the Fall of 1956, Selye contributed an article to one of Canada’s most popular magazines, *Maclean’s*, in which he advised readers to carefully budget their limited “bank account” of vitality and to strive to recognize their individual thresholds for stress and unique desires for self-expression on the grounds that “most of our tensions and frustrations stem from compulsive needs to act the role of someone we are not.”

Five years later, in IBM’s employee magazine *Think*, he identified the broad range of individuals suffering from stress that might benefit from his book, including

…the soldier who sustains wounds in battle, the mother who worries about her soldier son, the gambler who watches the races—and even the horse and jockey he bet on…the beggar who suffers from hunger and the glutton who overeats, the shopkeeper with his constant fears of bankruptcy and the millionaire struggling for yet another million…the housewife who tries to keep her children out of trouble, the child who scalds himself—and especially the particular cells of the skin over which he spilled the boiling water.

As this list suggests, Selye placed great emphasis on the influences of psychological stressors in his popular writings, arguing that stress fundamentally arises from social interactions. He explained that a “clashing of interests” produced an initial stressor, exacerbated by conflicting “impulses for resistance and submission which meet the stressor from within.” In order to diminish the harmful effects of such turbulent personal conflicts Selye advised indulging in self-

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expression and individualization—finding a pace of life and stress-relieving tactics to which one is best suited.\textsuperscript{54}

For Selye, individuality and self-expression were of the utmost importance in alleviating stress. Selye’s emphasis on individuality paralleled changes in the postwar medical marketplace that promoted individual consumerism as a principal therapeutic intervention. Individuals could claim mastery over their own health by implementing behavioral changes that reduced their risk for chronic disease—behavioral changes that often involved changing consumer habits, like reducing the consumption of alcohol, tobacco or fatty foods. They could also elect to take new pharmaceutical drugs to manage their health. North American patient-consumers’ preference for pharmaceutical therapy was strongly encouraged by the growth of the pharmaceutical industry in the postwar era.

\textbf{III. The Consumer Orientation of the Postwar Medical Marketplace}

North Americans’ perceptions of their own health changed as living standards increased. In the two-decades after the Second World War, manufacturing for personal consumption became the driving force of the US economy and enhanced purchasing power to acquire mass-produced goods became an index of national prosperity.\textsuperscript{55} In the midst of the Cold War, scientific innovation to improve mechanized production and develop new consumer goods became


\footnote{\textsuperscript{55} Medical consumerism in the United States predated the postwar rise of pharmaceutical firms. Nancy Tomes has documented how patient-consumers influenced the development of therapeutic practice and medical marketing in the United States in the first few decades of the twentieth century, giving rise to a normalized culture of medical consumerism and increased access to pharmaceutical drugs by the beginning of the Second World War. See Nancy Tomes, “Merchants of Health: Medicine and Consumer Culture in the United States, 1900-1940,” \textit{Journal of American History}, 88, no. 2 (September 2001): 519-547.}
essential to assert capitalist dominance over communism. The politicization of consumerism and scientific innovation inspired faith in the power of democratic capitalism to guarantee a higher standard of living that would protect against discomfort and disaster. Paradoxically, as more and more Americans benefitted from improved living standards and material comforts, they also embraced the medical concept of stress and the psychiatric concept of anxiety, both of which jeopardized their productive and pro-social capacity to perform as citizens.

Following a brief postwar recession, the US began two-decades of unprecedented economic growth, predicated upon the strength and privileged position of US manufacturing and favorable international trade agreements. By 1947, the US led the world in exports and manufacturing, supplying over fifty percent of all manufactured goods in the world, over sixty percent of the international oil supply, and over eighty percent of all automobile sales. Americans enjoyed an increased standard of living measured in their increased access to luxury consumer goods. In the words of medical sociologist Paul Starr, “prosperity gave Americans the opportunity to worry about their health, and it also changed the health problems they worried about.”

Wartime mass-production initiatives helped Americans to escape from the depression that had plagued the country for over a decade, and implicitly vindicated the Keynesian economic philosophy that called for government investment to stimulate private spending. The achievement of full employment by 1944 was perhaps the most powerful indicator of the effects of government spending—with unemployment plummeting from 25 percent in 1933, to 17.2 percent in 1939, to 1.2 percent in 1944. However, because the war production effort also stood


testament to the productive collaboration between government and business, the postwar era was conspicuously marked by a corporatist ethos. Industrial statesmen’s increased influence on economic policy transformed the Keynesian model to emphasize spending rather than saving and encouraging consumption rather than production.\textsuperscript{58} The passage of the 1946 Employment Act created a federal mandate to “promote maximum employment, production and purchasing power.”\textsuperscript{59} To meet this demand, two newly created federal boards privileged the recommendations of economic experts hailing from academia and industry. The President’s Council of Economic Advisors and the Congressional Joint Economic Committee shaped the commercial Keynesianism of the postwar era to focus above all else on increasing purchasing power by influencing the business cycle. Federal economic policies, combined with the end of wartime rationing, and the fact that Americans were able to spend their savings for the first time in a decade and half, increased purchasing power so effectively that between 1941 and 1946 personal consumption rose seventy percent.\textsuperscript{60}

The role that private industry played in the war effort, turning their manufacturing facilities to aid in the production of necessary war materials, did wonders to improve its public image and escape the anti-capitalist criticism the coursed throughout 1930s public debate. During the war, many corporations employed advertizing and marketing tactics to portray themselves as patriotic, productive, icons of American values for enterprise and industriousness.


\textsuperscript{60} Gary Cross, \textit{An All Consuming Century: Why Commercialism Won in Modern America} (New York: Columbia University Press, 2000), 88.
that were themselves, valuable natural resources. As a result, corporations emerged from the war as protagonists, rather than villains.

Postwar US and Canadian economic and trade policies were closely allied and strikingly similar in their commitment to develop a strong manufacturing sector to strengthen international trade and stimulate domestic consumption. Despite Canadian efforts to achieve greater national independence, the two countries developed what Canadian trade historian Dimitry Anastakis has described as “interdependent” industrial and economic structures. Canadian manufacturing and extraction industries benefited a great deal from contracts with the US Department of Defense and postwar military-industrial complex, especially following the Korean War.”

As the United States was by far the most powerful national economy in the world during the postwar period, Canadians benefitted from a close alliance with their southern neighbor as they distanced themselves from their former dependence on Britain in the aftermath of the war. Between 1947 and 1957, Canadian exports to the United States nearly tripled from $1.061 billion to $2.931 billion, while at the same time, goods imported from the United States to Canada increased from $1.951 billion (77 percent) to $3.878 billion (70.7 percent).

Bound together by trade agreements and a shared material and capitalist culture, the US and Canadian economies


bore striking similarities in their consumer-orientation and dependency on mass production and mass markets for economic prosperity.

The wealth of consumer goods stood testament to the benefits of a capitalist democracy, and as such, took on political significance in the context of the Cold War. As consumerism emerged as a primary index of economic prosperity, corporations also gained a newly important role as pillars of American productivity, tamed by their corporatist relationship with the federal government and balanced influence with their counterpart labor statesmen. Once viewed as villains that had plummeted the nation into economic catastrophe guided by their own greed, postwar corporations enjoyed a gilded image. Pharmaceutical companies in particular, benefitted from an improved reputation as the public became aware of their patriotic service in aid of wartime production efforts. As pharmaceutical production improved, making penicillin more affordable, it became a commonplace therapeutic option for more and more Americans—and a symbol of the great value that the pharmaceutical industry had contributed not only to the war effort, but to the improvement of civilians’ quality of life.

Postwar corporate growth depended on the capacity to influence consumer choice. Consequently, the advertising industry became a powerful economic actor in its own right, as it shaped patterns of consumption and manipulated consumer desire for material and psychological satisfaction. Again, the pharmaceutical industry emerged as an icon of the influence of advertising on consumerism in the postwar period. Increased revenues were directed towards marketing and public relations campaigns, with advertising expenditures more than doubling, from 3 to 7.4 percent of sales between 1950 and 1960.64 Pharmaceutical marketing targeted both the public and medical professionals. Yet, because the ethical impropriety associated with

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64 Temin, *Taking Your Medicine*, 83-84.
marketing drugs to the public still discouraged direct-to-consumer advertising, physicians were targeted as the primary means for increasing pharmaceutical sales to patients. At the 1954 midyear meeting of the American Pharmaceutical Manufacturers Association, G.B. Burrus, president of Peoples Drug Stores, Inc., pointed out that the 1951 Durham-Humphrey Amendments to the Food, Drug and Cosmetic Act of 1938 improved communication between the pharmaceutical industry and doctors as it essentially, “made it mandatory for a pharmacist to call a physician every time a legend drug is to be refilled.” Pharmaceutical firms began hiring “detail men” to visit doctors’ offices and hospitals and to develop personal relationships with physicians to encourage them to prescribe specific products. At the same time, pharmaceutical companies drew manpower and political rent from the relationships that they had developed with academic scientists and institutions, as well as state and federal agencies.

Historian Peter Temin argues that the pharmaceutical industry was poised for growth in the postwar period, due to three factors: new technology, patent protection, and patent monopolies held by vertically integrated companies. Together, these three factors contributed to unprecedentedly high profits and rapid growth. The pharmaceutical industry grew substantially after 1938 with the protection (and collaboration) of state agencies, namely the Food and Drug Administration, which took a new role in mediating patients’ relationship with the drug industry by inspecting the safety and approving the sale of penicillin batches as of 1945 (following a model set in place by the federal oversight of insulin production), created a distinction between


67 Temin, Taking Your Medicine, 75.
over-the-counter and prescription drugs, and required a prescription for medications that could be potentially harmful if misused. The 1951 Durham-Humphrey Amendments further curbed self-medication, and increased government oversight of the drug industry. At the same time, “quality control may have increased the costs of new and small firms more than those of established manufacturers and functioned as a partial barrier to entry,” which further empowered big companies by driving out smaller competitors. From 1948 to 1963, the number of pharmaceutical firms worth $1-10 million in assets rose from 82 to 138, the number of firms worth $10-100 million in assets rose from 22 to 31 and the number of firms worth more than $100 million in assets rose from 1 to 14.

<table>
<thead>
<tr>
<th>COMPANY</th>
<th>1939</th>
<th>1945</th>
<th>1950</th>
<th>1954</th>
<th>1956</th>
<th>1960</th>
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<tbody>
<tr>
<td>Parke, Davis</td>
<td>9.25</td>
<td>--</td>
<td>7.76</td>
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<td>17.86</td>
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</tr>
<tr>
<td>Abbott Laboratories</td>
<td>2.05</td>
<td>--</td>
<td>3.16</td>
<td>--</td>
<td>6.92</td>
<td>73.51</td>
</tr>
<tr>
<td>E.R. Squibb</td>
<td>2.06</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>8.06</td>
<td>87.54</td>
</tr>
<tr>
<td>Merck</td>
<td>1.86</td>
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<td>9.94</td>
<td>60.83</td>
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<tr>
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<td>--</td>
<td>--</td>
<td>--</td>
<td>15.20</td>
<td>145.24</td>
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<tr>
<td>Eli Lilly</td>
<td>--</td>
<td>--</td>
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<td>--</td>
<td>11.34</td>
<td>122.26</td>
</tr>
<tr>
<td>G.D. Searle</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>4.18</td>
<td>16.33</td>
</tr>
<tr>
<td>Smith, Kline &amp; French Labs</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>4.86</td>
<td>39.04</td>
</tr>
<tr>
<td>Schering Corp.</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>1.56</td>
<td>19.43</td>
</tr>
</tbody>
</table>

Table 1: Net Profits and Sales of Major Pharmaceutical Firms, 1940-1960, in millions of dollars. Data drawn from corporate annual reports filed with the SEC.

The Durham-Humphrey Amendment’s bifurcation of pharmaceuticals into prescription and over-the-counter drugs required the oversight of licensed medical professionals in the

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administration of potentially harmful and/or intoxicating medications. This increased the marketing valence of scientific authority, while also giving pharmaceutical companies a decided advantage over pharmacists in determining which medications were most commonly sold. In 1947, pharmaceutical sales accounted for only sixteen percent of drugstore sales, but rose to 25 percent by 1958.\textsuperscript{70} Overall, from 1939 to 1952, drugstore prescription sales increased from $166 million to $815 million, vitamin sales increased seven fold and antibiotic sales rose from nothing to $267 million.\textsuperscript{71} By the early-1950s, the pharmaceutical industry was growing at a rate of approximately nineteen percent annually.\textsuperscript{72}

As the industry grew, so did the public’s reliance on pharmaceutical therapies. From 1947 to 1955 US consumer expenditures on drugs and sundries increased 133 percent.\textsuperscript{73} Total US consumer expenditures on prescription drugs alone rose from $190 million in 1929, to $940 million in 1949, and $5.395 billion in 1969, an overall increase from 32\% to 85\% of all medicines sold.\textsuperscript{74} From 1935 to 1951, total US drug sales increased from $291.7 million to $1.4 billion, while investment in research increased from $10 million to $100 million, with this

\textsuperscript{70} Tone, \textit{The Age of Anxiety}, 37-38.


\textsuperscript{72} Bohmfalk, “The Modern Pharmaceutical Industry,” 3052-3057, data derived from Stanford Research Institute study of pharmaceutical industry.


marked growth largely concentrated in the development of wide-spectrum antibiotics, chemotherapeutic compounds and sulfa drugs.\textsuperscript{75} By 1953, the annual sales volume for pharmaceutical drugs was approximately $1.5 billion (about $13.3 billion in 2015 dollars), while overhead for marketing, research, and employee salaries approached one-third of a billion dollars annually (about $3 billion in 2015 dollars).\textsuperscript{76} Yet, while innovation in the industry increased the volume of pharmaceutical sales and diversity of products, intense competition limited the financial dominance of any one firm. For instance, from 1952 to 1953, total sales of pharmaceutical drugs rose from 50.8 to 54.2 million pounds, while the dollar value of these sales declined from $429.8 million to 409.1 million.\textsuperscript{77} (See Table 2)

<table>
<thead>
<tr>
<th>DATE</th>
<th>PRODUCTION</th>
<th>SALES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1941</td>
<td>34,199,000</td>
<td>29,024,000</td>
</tr>
<tr>
<td>1942</td>
<td>41,181,000</td>
<td>36,739,000</td>
</tr>
<tr>
<td>1943</td>
<td>55,695,000</td>
<td>51,803,000</td>
</tr>
<tr>
<td>1944</td>
<td>38,751,000</td>
<td>36,212,000</td>
</tr>
<tr>
<td>1946</td>
<td>40,747,000</td>
<td>40,402,000</td>
</tr>
<tr>
<td>1947</td>
<td>49,656,000</td>
<td>41,587,000</td>
</tr>
<tr>
<td>1948</td>
<td>43,635,000</td>
<td>38,240,000</td>
</tr>
<tr>
<td>1949</td>
<td>41,497,000</td>
<td>35,522,000</td>
</tr>
<tr>
<td>1950</td>
<td>49,330,000</td>
<td>37,011,000</td>
</tr>
<tr>
<td>1951</td>
<td>73,543,000</td>
<td>59,000,000</td>
</tr>
<tr>
<td>1952</td>
<td>66,815,000</td>
<td>50,783,000</td>
</tr>
<tr>
<td>1953</td>
<td>N/A</td>
<td>54,200,000</td>
</tr>
</tbody>
</table>


\textsuperscript{76} Harry Stenerson, “Behind the Markets” Chemical & Engineering News 31, no. 38, (September 21, 1953): 3926.

Industry insiders cheered the trend of corporate growth for encouraging more efficient production, as well as creating a competitive environment between sizable companies that would naturally increase innovation in the industry. Harry Stenerson, the associate editor for Chemical & Engineering News celebrated the vertical integration of the pharmaceutical industry “from test tube to physician” as a representation of “free enterprise at its very best.” Intense competition and diminishing profits stimulated an industry-wide quest for new, patentable products. From 1947 to 1958, as American pharmaceutical revenues from world-wide sales increased from $30 million to $2.7 billion, the industry’s investment in research and development increased from $30 million to $170 million. The intensification of research for product development led to the development and commercialization of a vast number of new and copycat drugs. In the 1940s, an average of approximately 20 new drugs were introduced to the medicinal market each year, whereas in the 1950s the average rose to approximately 50 new drugs per year. (See Table 3) By 1953 there were no less than 8,500 different ethical products marketed in the United States.

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78 Stenerson, “Behind the Markets,” 3926.

79 Tobbell, Pills Power and Policy, 35.

80 “Drug Product Research Speeded Up As Competition Becomes Intense,” Chemical & Engineering News 31, no. 38 (Sept, 21, 1953): 3856-3858. “Ethical” products, as defined by the AMA’s original Code of Ethics, includes all medicines requiring a medical experts’ instructions for use.

The pharmaceutical industry’s investment in research programs contributed markedly to innovation in the field. In the postwar period, industrial research helped to develop synthetic vitamins, hormones, sulfa drugs, antihistamines and antibiotics.\(^8\) According to Randolph Majors, vice president and scientific director of Merck, in 1951, 41 percent of pharmaceutical sales were antibiotics, 15 percent were vitamins and hemanitics, and 9 percent were endocrine preparations.\(^8\) The development of these new medicinal preparations was driven, in part, by the therapeutic needs of changing patient demographics. As noted by John McKeen, the president of Chaz. Pfizer & Company, by the early 1950s “the whole spectrum of illness which physicians are called upon to treat [was] shifting. New therapeutic agents [were] needed for the treatment of heart disease, arteriosclerosis, and hypertension.”\(^8\) Firms competed for market power by patenting (in many cases) subtly distinct products, particularly in the sale of antibiotics and sulfa drugs. For instance, Hoffman-La Roche marketed the sulfadrug Gantrisin, which offered 

\(^8\) “Drug Product Research Speeded Up As Competition Becomes Intense.”


\(^8\) “Drug Product Research Speeded Up As Competition Becomes Intense,” 3856.
of the same therapeutic benefits of Lederle’s Diamox. In other cases, firms developed unique products which helped them to corner a specific group of patient-consumers, such as with Merck’s diuretic drug Diuril, and Smith, Kline & French’s major tranquilizer, Thorazine. On average, by 1960, patented antibiotic, sulfa derivatives and tranquilizers accounted for 15-39% of any given pharmaceutical companies’ annual sales. Diuril, and the closely-related Hydrodiuril, represented 39% of Merck’s sales, while Thorazine accounted for 18% and its closely-related major tranquilizer Compazine comprised another 15% of Smith Kline & French’s sales.

But given the intense competition within the pharmaceutical industry, the development of new products was not sufficient to improve sales. Pharmaceutical drugs had to be effectively marketed to appeal to American patient-consumers. The American Pharmaceutical Manufacturers Association’s 1954 mid-year meeting focused on the increasing importance of public relations strategies in promoting pharmaceutical sales through popular education. Arno Johnson, Vice President and director of research for the advertising firm, J. Walter Thompson Company, advised his audience that 34 million Americans were walking around with a disease without knowing it. He urged the pharmaceutical industry to take an active role in promoting pharmaceutical consumption by “raising our sights in education, because it is education of people that changes consumer habits.”

Gerard Piel, the publisher of Scientific American

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84 Major tranquilizers (neuroleptics) differ from minor tranquilizers (anxiolytics) in their potency and are typically used as antipsychotics to treat severe mental disorders, such as schizophrenia and bipolar disorder, whereas minor tranquilizers are used as sedatives. Where not specified, hereafter the term “tranquilizer” will refer to minor tranquilizers.

85 Temin, Taking Your Medicine, 78-80.

stressed that pharmaceutical manufacturers must work with the popular science press to promote public health literacy about pharmaceutical drugs.\textsuperscript{87}

Wallace Werble, the editor of \textit{F-D-C Reports}, attributed the increase in pharmaceutical companies’ investment in public relations, in part, to growing public interest in scientific information and inordinate faith in science. He argued that throughout the Second World War the AMA pursued a publicity campaign to increase popular appreciation of the scientific content of medicines and the prestige of the individual doctor in prescribing medications in order to encourage the association of medical progress with the medical profession and discourage passage of national health insurance.\textsuperscript{88} With the development of the atom bomb, as well as antibiotics, vitamins and hormones, Werble claimed that “the public quickly became conditioned to the idea that science and scientists can do anything.” As a result, “the public began to expect … relatively safe specific medication for all human ailments,” and the use of terms like “miracle cure” and “wonder drugs” created an unrealistic “standard of achievement in the public’s mind.”\textsuperscript{89}

G.B. Burrus, president of Peoples Drug Stores, Inc., pointed out changing consumer demographics were changing market potential for pharmaceutical companies. He pointed out that Americans “are getting older and there are more of them,” so that by 1953 there were 42 percent more senior citizens and 65 percent more children under the age of five than there had


\textsuperscript{89} Werble, 201-203.
been in 1940, representing “a new market with over twice the population of Canada,” composed of the two age groups that provide the bulk of pharmaceutical business. Moreover, he explained that the American people had become better educated, with 4.5 times more high school graduates as in 1930, enabling higher standards of living and increased homeownership in growing suburbs. As a consequence, Burrus argued, Americans were also becoming more family-oriented, creating a large market of “people with an abiding interest in the welfare of their families [who] are tremendously health conscious.”90 The pharmaceutical industry had only to cater their marketing strategies to appeal to these demographic trends in order to keep pace with postwar prosperity.

**The Medicalization of Anxiety**

By the mid-1950s, the pharmaceutical industry also capitalized on a new demand for psychiatric medication generated by the postwar medicalization of anxiety. As discussed in Chapters Two and Three, neuropsychiatric research and the diagnosis of combat stress during the war helped to raise awareness, especially among servicemen and their families and neighbors, of the concept that “everyman has his breaking point.” When applied in civil society, this shared understanding promoted the universalization of a dynamic model of mental illness, and an awareness of the potential danger of untreated mental and physical stress. This not only created a sympathetic consciousness among US citizens, but also a growing professional interest in assessing and documenting the widespread existence of mental illness in society that gave rise to a number of community-based sociological and psychological studies which provided further support for the deinstitutionalization of neurotic patients.

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During World War II, the Neuropsychiatric Division developed a system of classification outlining the symptoms, etiologies and recommended treatments for a diverse array of psychiatric illness. *War Department Technical Bulletin, Medical 203,* was used as a common manual for all psychiatrists and medics serving in the Medical Corps. Under the substantial influence of psychoanalysts in the Neuropsychiatric Division during World War II (discussed in Chapter Two), *Medical 203* adopted a dynamic model of mental illness that placed normal and abnormal behavior on a continuum, linking neurosis (not psychosis) and normality. When military practitioners returned to civilian life, many of them retained the classification system outlined in *Medical 203,* and when the World Health Organization was founded in 1948, it too adopted *Medical 203*’s diagnostic schema. Consequently, by the end of the 1940s, the vast majority of practicing psychiatrists were familiar with and commonly used the system outlined in *Medical 203.* In 1952, this system was officially adopted by the American Psychiatric Association, and enshrined in their first *Diagnostic and Statistical Manual.*

The DSM-I contained 102 psychiatric “reactions,” evidencing the psychobiological terminology popularized by Adolf Meyer. Meyer used “reaction” to call attention to the subjective and dynamic nature of mental illness. In his terminology, a “reaction” denoted an adverse personal response when confronted with an external demand conditioned by one’s life history—essentially, a failure to adapt to one’s environment. The definition of an “anxiety reaction” outlined in the DSM-I emphasized individual difference and environmental maladjustment. Thus, clinically speaking, anxiety constituted a range of maladroit behaviors that

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arose from an inability to acclimate to one’s social or physical environment. By vastly expanding the medically-recognized range of disease symptoms and pathological behaviors, the DSM-I’s description of anxiety helped to advance a broad and continuous pathological model of anxiety that could be applied to a vast number of unhappy North Americans.

While the medicalization of anxiety helped to promote popular belief in a dynamic model of mental illness, psychiatric epidemiological research called attention to the previously under-recognized prevalence of psychiatric disorders amongst the general population. In the late-1940s and 1950, several population studies conducted by prominent Cornell psychiatrists and sociologists documented the widespread existence of mental illness in North American society. Beginning in 1948, Alexander Leighton, a member of Cornell’s Sociology and Anthropology Department and former student of Adolf Meyer, conducted a study of the natural occurrence of mental illness in Stirling County, Canada, an economically depressed community in Nova Scotia. While the Stirling County Study continues to this day, when Leighton first published his research in 1959, he reported that consistency and community control over sociocultural factors were found to offer protection against mental illness. Leighton also took a leadership role in a study nominally directed by Leo Srole, that examined the incidence and distribution of mental illness amongst individuals not receiving psychiatric treatment in the natural environment of midtown Manhattan. Published in 1962, Mental Health in the Metropolis, reported that Srole’s team found a correlation between psychiatric morbidity and low socioeconomic status,

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minority racial and ethnic background, as well as gender and marital status. Together, these studies suggested that there was a much higher rate of mental illness among the general population than previously recognized, and that community dynamics were critical to fostering rehabilitation.

The movement for community-based treatment of mental health also generated a vast new market for anxiolytic pharmaceuticals to enable psychological stabilization through outpatient treatment programs. In addition to the growing awareness of the widespread presence of mental illness in society, the deterioration of mental hospital care over the course of the early-twentieth century created the perception that mental hospitals were not therapeutic institutions, butoubliettes in which torturous therapies were inflicted on helpless victims. In the late-1940s and early-1950s, the outpatient treatment of schizophrenic and bipolar patients became more feasible with the commercialization of antipsychotic drugs, like Thorazine.

While the Second World War provided the funding, organization and interest for medical research that ultimately gave rise to the medicalization of stress, the Cold War helped to popularize this new disease concept. An academic-industrial complex that funded stress research grew alongside public fear of nuclear war and communist sedition. Even though Americans became painfully aware of the potential destructive power of science, they also came to defer to scientific expertise more and more. These competing tendencies worked together to marshal popular opinion to validate the psychosomatic theory of disease, as Americans became more conscious of their own susceptibility to “degenerative” and “psychological” diseases. By the end

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95 Grob, Mental Illness in America Society, 1875-1940.
of the 1950s, it had become a common assumption that, when forced to bear undue psychological tension, any man could develop not only a psychological disorder, but physiological problems, as well. Advertising and the new consumer-oriented medical market helped to spread this creed, while surreptitiously, the medicalization of anxiety created a vast market of anxiolytic pharmaceuticals that stood testament to growing public faith in the destigmatization and legitimacy of varying degrees of psychological disease.

The development of pharmaceutical tranquilizers in the mid-twentieth century was a direct outcome of the medicalization and popularization of anxiety. The very fact that Americans sought medical treatment for their anxiety indicated that they believed they were suffering from a legitimate medical disorder. In her examination of the development and marketing of anxiolytic drugs since the 1950s, Historian Andrea Tone argues that Americans’ choice to medicate their anxiety with pharmaceutical drugs reveals not only their desire for quick and economic therapy, but also the cultural power of physicians, the sovereignty of scientific research, the successful marketing strategies of pharmaceutical companies, and the preeminence of consumer culture. Underlying all of these factors was a value system that accepted stress as a ubiquitous exigency of modern life, yet sought to control it in order to achieve maximum productivity and sociability.96

The American fascination with tranquilizers began in 1955—one year before Selye’s publication of *The Stress of Life*—with Carter Products’ introduction of Miltown.97 The


97 Tone argues that the consumer demand for anti-anxiety medication began with the popularity of patent medicines in the late-nineteen and early-twentieth centuries—many of which derived their seeming efficacy from unlabeled narcotic ingredients—which indoctrinated the
development of meprobamate—named “Miltown” to conjure an association between the tranquilizing effects of the drug and the serenity of suburban life—grew out of an incidental discovery in the course of the pharmaceutical industry’s frenzy to mass-produce penicillin during WWII. Frank Berger, a talented chemist who fled his native Czechoslovakia when the Nazis invaded, participated in the Allied quest to mass-produce penicillin as an assistant bacteriologist in a British Public Health Laboratory outside of Leeds. Searching for an effective preservative for penicillin, Berger tested the toxicity of a disinfectant derivative, mephenesin, which unexpectedly produced powerful muscle-relaxation without disturbing the consciousness of his experimental mice. After the war, Berger moved to northern New Jersey to take a position at Carter Products, where he developed this minor tranquilizer for the commercial market.

Carter marketed Miltown to treat not only anxiety, but a breadth of physical complaints that might be exacerbated by anxiety, including heart disease, allergies, menopause and prepartum depression. Carter also licensed meprobamate to American Home, which marketed it as Equanil in much the same way. Complimenting an aggressive marketing strategy, published clinical trials of meprobamate defended its efficacy and safety in treating anxiety, tension and fear, as well as headaches, depression, “menstrual stress,” stomach disorders, skin ailments, patient-consumer with an expectation for pharmacological remedies for mental duress. While patent medications lost their cultural currency following the enactment of the Pure Food and Drug Act of 1906 (requiring the clear identification of a product’s ingredients), they were soon replaced with barbiturates, such as Veronal and Phenobarbital, which were also widely used for their analgesic, anesthetic and anticonvulsive properties (prescribed for physical complaints, such as ulcers, hyperthyroidism, anesthesia and obstetrics), as well as for recreational purposes. During World War II, barbiturate production rose dramatically from 531,000 pounds in 1941 to 900,000 pounds or 1.5 million doses by 1947, fueled, in part, by the increasing numbers of soldiers and veterans suffering from neuropsychiatric disorders. By the late 1940s, pharmaceutical companies produced 1,500 different kinds of barbiturates. See Tone, *The Age of Anxiety*, 22-23.
insomnia and alcoholism. Such broad therapeutic usefulness suggested that Miltown and Equanil could tap into an astoundingly vast market. At the 1955 meeting of the American Pharmaceutical Manufacturer’s Association, Howard D. Fabing, Chief of the Neuropsychiatric Department at Christ Hospital in Cincinnati noted that though Miltown was not yet commercially accessible, clinical experiments showed very promising results, offering the hope that “it might be used by general practitioners in one of every four or five patients who come through his door, because this is one of the most common ills of man.” Moreover, Fabing argued that “when all the psychotic and psychoneurotic and neurological patients are lumped together, they constitute more than half the sick in this country,” and therefore represent fertile “rich unbroken fields” from which to reap tremendous “potential harvests.” Carter and American Home plundered these virgin fields, and within its first year of sales, as Miltown and Equanil spiked from one percent to 70 percent of the tranquilizer market, Carter’s sales nearly tripled from $15 million to over $40 million, and between 1955 and 1957 American Home’s sales jumped from $90 million to $160 million.

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100 Herzberg, Happy Pills in America, 25-26.
Image 7: Miltown Advertisements, 1959101

Carter’s marketing of Miltown unleashed a popular phenomenon in which patient-consumers demanded prescriptions for tranquilizers. In turn, tranquilizers became a status marker—a testament that one’s lifestyle was so fast-paced and demanding that they required pharmaceutical therapy, and that they were well-adjusted and affluent enough to take such cutting-edge medicine. At the same time, research into the actions of neurotransmitters lent credence to the primacy of brain chemistry as a fundamental cause for anxiety and recommended pharmacological treatment of mental illness. As Tone argues, the proved efficacy of tranquilizers “encouraged biological explanations for mental illness while providing practitioners with a broader mandate to treat [anxiety] pharmacologically.”

102 As evidence that tranquilizer use became ubiquitous in American culture, Tone cites the Senate Subcommittee on Antitrust and Monopoly’s investigation of price fixing by tranquilizer manufacturers and its discriminatory affect on lower-income groups in depriving them of their right to a “necessity.” See Tone, *The Age of Anxiety*, 115. Yet, the fact that predominantly middle- and upper-class consumers used tranquilizers suggests that the cultural belief in the omnipresence of anxiety and the efficacy of its pharmaceutical treatment was a class-based phenomenon and calls for further research into the socioeconomic character of anxiolytic prescriptions and the use of alternative methods of therapy across classes.

103 Tone, *The Age of Anxiety*, 165, 27. Tone also argues that the prominence of biological psychiatry led to changes within the psychiatric discipline, most notably the symptom-based etiology of the DSM-III.
The immense popularity of tranquilizers inspired Hoffman-La Roche to develop a new class of anxiolytics, the benzodiazepines, most notably, Librium and Valium. Though chemically different from tranquilizers, benzodiazepines were also used to treat a vast range of medical conditions and maladaptive behaviors thought to be induced or exacerbated by anxiety—such as asthma, ulcers, insomnia, headaches, arthritis, PMS, frigidity, et al. Valium and Librium were also aggressively marketed—with Roche spending $400 million on advertising in one year (about $3.2 billion in 2015 dollars). As a result of its popular appeal

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105 Tone, The Age of Anxiety, 154.
and effective marketing, Valium became the first $100 million prescription drug, and according to Tone, was so popular that it became a “staple in medicine cabinets, as common as toothbrushes and razors.”

IV. Catering Research to the Medical Market: Anxiety, Aging, Lifestyle Diseases

Selye responded to the increased prevalence of anxiety, as well as the demand for pharmacological interventions for heart diseases and arthritis, by catering his research to appeal to pharmaceutical firms and their clients. The media coverage of Selye’s research following the publication of *The Stress of Life* highlighted three dynamics which Selye incorporated in the disease model of stress. He emphasized the psychosomatic foundations of stress, indicting the frenzied demands of modern civilization as well as overwrought emotional tensions as primary stress risk factors. He also connected stress with the rise of chronic heart disease, and recommended behavioral modifications—primarily, dietary changes and increased physical exercise—as the most critical intervention to reduce stress-related heart disease. And he spoke directly to the changing patient demographics arising from the increase in life expectancy by depicting aging itself as a pathological condition caused by stress. The fact that the mainstream media latched onto these three aspects of stress in their coverage of Selye’s work speaks to his prowess at highlighting the practical importance of his research, in spite of his disdain for applied research.

*Psychosomatic Stress*

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Press coverage of *The Stress of Life* frequently fixated upon the mental and emotional implications of Selye’s theory—despite the fact that his clinical experiments did not seek to evaluate the psychological impact of physical stress or the physiological impact of psychological stress. In a grand interpretive leap that displayed an increasingly common muddling of biological and psychological stress, *Coronet* reported that “continued stress on Dr. Selye’s laboratory rats had produced marked mental illness,” when treated with cortisone and ACTH. However, these effects could be corrected by administering that antagonist DOC, which induced a tranquil state in the rats, even lulling them to sleep.\(^{107}\) Despite *Coronet*’s claims, these experiments did not strive to evaluate the experimental animals’ psychological health, for Selye interpreted his use of panic and exhaustion as physical stressors.

Selye overtly encouraged the media’s focus on the psychological implications of his stress research. One magazine’s assertion that “if you know what is causing your migraine or indigestion… you are less likely to worry yourself into worse mental and physical illness,” implicitly suggested that patients’ mental state and confidence in their own diagnoses had a direct impact on their physical health.\(^{108}\) *Vogue* conveyed this message to its female readership throughout North America, cautioning that “only by dissecting our trouble can we clearly distinguish that part played by the stressor.” *Vogue* further reinforced the psychosomatic nature of disease by reminding its readers of the increased release of adrenaline and corticoids during anxiety. Selye taught that it was the patient’s responsibility to recognize when they reach their

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\(^{107}\) Fromer, “What Makes You Tense?”

\(^{108}\) Beresford-Howe, “Men of Action: Hans Hugo Bruno Selye.”
“stress quota” and take appropriate steps—via diversion or rest—to “tune-down” when they became overly “keyed-up,” or risk the inevitable consequence of poor physical health.  

Popular interpretations of Selye’s theory of stress often reinforced the undercurrent of individualism by alluding to different personality types that responded to stressors differently. Notably, the media frequently contrasted the stresses suffered by a “businessman” with those suffered by a “housewife,” indicating a glaring gender bias in the popular discourse of stress etiology. Reifying archetypal characters of an idealized postwar American society, Reader’s Digest reporter John Drury Ratcliffe cautioned that “the florid, hard-driving plant manager has his coronary,” while the “always-tired, always overworked housewife may become diabetic.” And conjuring images of a stereotypical film noir maladroit, he further warned that “the thin, quiet type, who keeps his worries bottled up within himself, becomes the victim of high blood pressure.” While this is no doubt an oversimplification of Selye’s theory of stress, Selye himself endorsed the press’s tendency to construct stress personality profiles in his insistence that each person must learn their own threshold for enduring stress. Ultimately, he too would invoke personality profiles in his descriptions of stress, calling for slower, calmer “turtle” types and harried, excitable “race horse” types to respect their own internal drives, and not force themselves to incur unnecessary stress by defying their own ‘natural’ optimized pace.

The pathological view of the “businessman” gained cultural currency with the publication in the late-1950s of Walter Reed Army Institute of Research scientists John W. Mason and

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Joseph Brady’s psychoendocrine research on “executive monkeys.” Mason and Brady administered electric shocks to monkeys restrained in specialized chairs. One monkey was given a lever that would prevent the shock from being delivered, while the control monkeys were not. They found that the monkey with the power to prevent the shock developed peptic ulcers as adrenocortical hormones flooded their stomachs following the experimental period. As the control monkeys did not suffer the same rate of ulceration, Mason and Brady deduced that conditioning the monkeys to both anticipate the shocks and learn they had the power to prevent them increased their stress levels. This led to the presumption that those with more powerful jobs—executives—were more prone to stress-induced ulceration. At the same time, two San Francisco cardiologists in private practice, Meyer Friedman and Ray Rosenman began studying the relationship between personality and heart disease. Categorizing personality types by letter, they found that the “type A” profile—characterized by competitiveness, hostility and time urgency—were more prone to cardiovascular disease. By the 1970s, the “type A hypothesis” became a household euphemism for high-stress individuals suffering poor psychosomatic health.


Selye did not pursue his own medical research on personality as a conditioning factor for diseases of adaptation, nor did he reference the work of contemporary researchers who were substantiating the concept with clinical evidence. However, given his published comments, he implicitly accepted the notion, and encouraged popular faith in the importance of individual personality and lifestyle decisions in the etiology of disease. By the end of the 1950s, Selye’s suggestion that anxiety could induce physical disease was indeed becoming increasingly widespread. The Metropolitan Life Insurance Company published a pamphlet to promote healthy habits in its policy holders which claimed that “studies show that almost half the people who seek medical attention are suffering from ailments brought about or made worse by prolonged emotional stress—too much worry, anxiety, or fear.” Moving beyond Selye’s emphasis on individual expression, yet still embracing the individual’s responsibility for their own health, Met Life advised that in order to diminish the harmful effects of stress we must begin with “understanding ourselves and those around us,” but also to strive to strike a healthy balance between work with play, to rest, to exercise and to be emotionally open about our troubles.  

Selye’s work was further distanced from its biological focus by putting it into conversation with that of psychiatric and psychosomatic researchers. In discussing Selye’s work, Redbook quoted former director of the Neuropsychiatric Division in World War II, Dr. William C. Menninger’s bald statement that “at least half of the patients who go to medical doctors…have complaints caused by or intimately related to emotional disorders,” cited Helen Flanders Dunbar’s Emotions and Bodily Changes for documenting the ways in which “the effects of fear could be actually measured in bodily response,” and noted Stewart Wolf’s “What is Stress?” (New York: Metropolitan Life Insurance Co., 1959), folder: I: “Newspaper clippings,” HSC.
experiments with electrocardiograph measurements of fear amongst heart patients. Indeed, it had become commonplace to claim that “few doctors now deny that there is a link between emotional stress and certain types of illness, and every doctor knows how some patients worry themselves sick, or at least predispose themselves, through worry, to illness… disease cannot be diagnosed and treated as if it were an entity divorced from the patient’s life, home, job and personality.” Yet, while some proponents of psychosomatic theory embraced the popularization of this concept which they had long proselytized, others held fast to the tenets of Freudian psychoanalysis, fundamentally rooted in a belief that personal experiences and memories, rather than physiochemical changes governed psychological expressions. Representing the steadfast Freudian psychosomaticians, Franz Alexander and his Chicago School were directly challenged by Selye’s research—even though they shared a belief in the etiological importance of personality—as well as that of psychiatrists, like Harold Wolff and Stewart Wolf. The Montreal Gazette reported that Selye’s report was profoundly “startling” to doctors who “have operated for years on theories that attribute most mental illnesses to early childhood experiences and to inability to cope with ‘emotional’ problems.”

Furthermore, despite the fact that he actually had little expertise in evaluating psychological stress, Selye played quite a significant role in the ascendance of a neuro-chemical paradigm in psychiatric treatment. Speaking at the 112th annual meeting of the American

115 “Psychosomatic Ills, Real or Imagined?” Redbook, October 1960, 53, folder: I: “Newspaper clippings,” HSC.


117 Brian Inglis, “Stress.”

Psychiatric Association in Chicago on April 30, 1956, Selye announced that recent research provided evidence that the overproduction of steroids, mineralocorticoids and prophlogistic hormones can generate psychiatric disorders, including “pathological confusion or excitement, chronic fatigue, depression, convulsive seizures and pregnancy neuroses.” Time remarked that Selye’s announcement made it clear that the dominant trend in “psychiatry’s new direction… is the search for psychiatric answers and cures in the field of chemistry.”

While psychiatric wonder drugs, like chlorpromazine and meprobamate became increasingly popular treatments in the management of psychotic and neurotic conditions, respectively, there developed a broad increased faith in pharmaceutical solutions for mental disorders, large and small. Selye encouraged this trend by emphasizing the link between emotional stress and physical health, but also by speculating—beyond the scope of his expertise—that “the secret of schizophrenia may be some apparently harmless chemical which is quite naturally and normally produced in the brain by the working of the nerve cells,” but causes insanity in individuals with abnormal endocrine systems—possibly arising from excess or prolonged stress. Blurring the distinction between physical and psychological stress further, Selye also mused that one day medicine might “be able to develop a hormone with a generalized,
natural tranquilizing effect on the body,” and thereby enabling “repair for wear and tear everywhere.”

Such ponderings from the foremost authority on stress were a great advantage to pharmaceutical companies—both in the treatment of emotional and physical stress. Selye endorsed the use of cortico-steroids to treat endocrine disorders caused by stress, as well as tranquilizers for the control of anxiety and nervous tension. Selye’s research on the anesthetic effects of steroids also supported the development of a range of pharmaceutical drugs including Pfizer’s anaesthetic steroid Viadril, Schering’s anti-inflammatory and analgesic steroid Presurin, and the Wyeth Laboratories’ growth-stimulating anabolic steroid Norbolethone (which was never marketed due to fears of harmful toxicity).

While pharmaceutical companies exploited the marketability of stress, Selye did not personally recommend pharmaceutical treatment for emotional stress without reservations. He did not endorse the increasing fad of self-medicating with tranquilizers or hormones, and recommended that patients only take drugs prescribed by their physician. He cautioned that, “‘drugs may help control [stress], but the source of control rests with the individual.’” Thus, he encouraged those suffering from stress-related diseases to employ the stress-management


strategies that he explained in *The Stress of Life*. While he maintained that patient empowerment was a powerful remedy, he was wary of psychopharmacological medication. Yet, his dissent did little to deter pharmaceutical manufacturers from seizing upon the marketing power of “stress,” and by the mid-1960s Selye came to criticize the excess use of minor tranquilizers for diminishing the capacity to withstand stress. In 1967, Selye told an audience of York University students that “tranquilizers don’t let you liberate the energy needed to protect your body against damage, and may be reducing healthy aspects of stress.” In order to withstand stress, he insisted that people needed to increase their resistance through repeated exposure, not be numbed to it.

**Heart Disease, Life-Style Risks & Aging**

In addition to Selye’s efforts to make his theory of stress relevant to the increasing concern over the widespread prevalence of anxiety, Selye also strove to market his research as a means of controlling chronic disease through the contemporary fad of nutritional therapy. In the wake of *The Stress of Life*’s great success, Selye released news of his latest scientific breakthrough in the treatment of heart disease. He had found that mineral metabolism, particularly the administration of potassium and magnesium salts helped to protect against cardiac infarcts or accidents in experimental rats, rabbits and monkeys, especially when the animals were first sensitized by treatment with cortisone. However, when the animals were treated only with cortisone and exposed to stress, or if they were treated with sodium salts and cortisone, they

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developed damaged heart tissue similar to that present in humans with heart disease. Potassium and magnesium were even found to be effective in diminishing the damage caused by sodium salts in the heart, coronary arteries and kidneys.\(^{129}\) Consequently, these experiments offered hope that potassium and magnesium pharmaceuticals may be helpful in treating patients predisposed for cardiac accidents.\(^{130}\) The recent introduction of Diuril (chlorothiazide) and tetrahydrozoline to treat hypertension and high blood pressure suggested that there might also be a market for Selye’s proposed mineral therapy.\(^{131}\) According to *Newsweek*, Selye claimed that “‘in [his] 30 years of stress experiments, this discovery is the one most immediately practical, most likely to help ailing human beings.’”\(^{132}\)

While laboratories in Mexico, Canada and Europe performed clinical trials on humans\(^{133}\) to test Selye’s hypothesis, he planned additional animal experiments in his own lab, which he anticipated would cost approximately $100,000 per year over the next five years (about $800,000

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\(^{130}\) Gerald Freeman, “Medical Scientists Make Advance in Heart Disease,” *The Sarnia Observer*, February 18, 1958, folder: I: “Newspaper clippings,” HSC.


\(^{132}\) Brian Cahill, “Dr. Hans Selye Lauded for Heart ‘Discovery,’” folder: I: “Newspaper clippings,” HSC.

per year in 2015 dollars). Among other things, he suggested that ideally such research might lead to the development of “a harmless drug that could be given to any person likely to suffer a heart attack…to restore the body’s balance before stress worked mischief.” While the ultimate cause of heart disease was not yet known in the late-1950s, medical experts generally recognized that about fifteen percent of patients who suffered a heart attack were likely to suffer a repeat attack within twelve months. Selye’s research offered a means of diminishing the likelihood of a repeat attack by prescribing potassium and magnesium pills following a heart attack. He estimated that administering such post-attack treatment might reduce the incidence of repeat heart attacks to five percent.

By the fall of 1960, Selye had struck upon yet another medical breakthrough in the prevention of heart disease. He found that when he conditioned rats with regular physical exercise, they were better able to withstand both the stress of exercise, as well as other stressors, such as extreme cold and chemically stimulated stress (injections of noradrenaline). Maclean’s claimed that since Selye’s “stress theories have shaped many of the medical ideas of our century,” he was qualified to advise how “a man can train his heart to overcome weaknesses that cause it to fail.” His prescription was simple enough to allure even suspicious readers: “‘careful and controlled exercise is the best possible defense against heart failure,’” provided that


135 “Heart Failure Made to Order,” Columbia, June 1958, 21, 36, folder: I: “Newspaper clippings,” HSC.


one’s health is not already so compromised that exercise could cause further complications. Selye explained that by the phenomenon of cross resistance, regular exercise helped to condition experimental rats to withstand stress caused by extreme temperatures, physical strain and artificial stimulation by noradrenaline injections. By the principle of crossed-resistance, calisthenic exercise might protect against both physical and emotional stress, “the kind of stress that arises when a man has gone bankrupt or been told of a death in the family… like the White Knight’s Armor, which shields him equally well against the Black Knight’s sword and the dragon’s breath of fire.” Conditioning with exercise, just as with salts, was an effective means of preventing cardiac accident because “pretreatment with stress offers protection,” and “only unaccustomed stress triggers cardiac accidents.”

Selye’s research on exercise and crossed-resistance led him to infer that heart attacks may in fact be caused by a weakened capacity to withstand stress, among other contributing factors. Speaking before a meeting of the Wayne County Medical Society in April 1961, Selye suggested that a high standard of living and habitual inactivity were both powerful conditioning factors in the development of heart disease. Selye further alleged that by the theory of crossed-resistance, exercise could protect against emotional stress, basing his claim on his own personal experience, rather than empirical, clinical evidence.

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139 “Potassium, Magnesium Salts May Prevent Heart Lesions,” *Medical Tribune*, (July 20, 1964, folder: I: “Newspaper clippings,” HSC.


Selye’s indictment of life-style choices, such as a high-fat diet and lack of physical exercise, as risk factors for stress and disease, led him to argue that such risky personal behaviors caused premature aging and death. Differentiating between stress—the “rate of wear and tear on the body”—and aging—the use of the body—he insisted that old-age need not inevitably lead to death. He projected that increasing life expectancy might be increased by an estimated 30 years through lifestyle modifications aimed to minimize exposure to stress and stress-induced chronic diseases. Selye insisted that disproportionate wear and tear on certain systems or organs ultimately caused death. Teaching by analogy, as he so loved to do, Selye would often explain that “like the tires on a car,” or “the rug on the floor, the human body wears longest when it wears evenly.” In order to ensure that we did not overuse any one body part, he recommended variation in activities, something which he believed the body naturally craved. By ensuring even deterioration of the body’s systems, one might not only live longer, but live to enjoy better quality health in their old age and perhaps even escape death by disease.


143 Julian Hartt, “They’ll Eye Every Heart Beat as X-15 Nudges Outer Space,” Los Angeles Examiner, April 28, 1959, folder: I: “Newspaper clippings,” HSC.


Selye’s interest in the connection between aging and stress led him to develop a series of experiments on tissue regeneration in rats. With funding provided by the NHI and NSF, he implanted a tube under the skin of the rat using his granuloma pouch technique. Following implantation, Selye observed that a protein-rich fluid similar to blood plasma and rich in the blood-clotting agent fibrin, began to fill the tube and support the growth of living tissue beginning at both of its ends and gradually growing to meet at its middle—essentially

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regenerating non-living tissue. This cord would die within ten or fifteen days, unless the fluid that surrounded it was constantly refreshed. The fibrin cord provided a model of growth and degeneration that permitted longitudinal scientific study of human aging in “real time.” The “lifespan” of a fibrin cord could be observed in just a few weeks, whereas aging studies in rats took many months, and in humans took decades.

Based on the results of his fibrin experiments, Selye set out to test the extent to which various tissues were capable of regeneration. He sensitized rats with a Vitamin D derivative (which catalyzes calcium absorption) for 24-48 hours before injecting them with a solution of egg white (known to produce allergic reactions in rats). Within three weeks the animals’ fur became hard like a shell and molted, like snakes or crustaceans shed their exoskeletons. The new coat of skin and fur underneath the molted shell showed none of the original scars or other distinguishing features of the animal’s original coat of skin, indicating that it had completely regenerated its external cutaneous layer. Subsequent experiments involving sensitization with a calcium-producing agent (administered orally), followed by intravenous injections of chromium chloride, caused similar hardening of the parathyroid gland, the pancreas and the uterus, respectively. Selye named this process “calciphylaxis,” and hoped that it might lead to a

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greater understanding of the role of calcium in inflammatory collagen (also known as connective tissue) diseases, such as rheumatic fever, rheumatoid arthritis, lupus erythmatosus, et al., and that it might also be a useful means of treating diseased organs by mimicking a natural defensive reaction to selectively harden the organs instead of surgically removing them.\textsuperscript{153}


The calciphylaxis experiments led Selye to believe that abnormal calcium deposits in joints, tissues and organs accelerated the aging process. He deduced that by preventing calcium drift aging might be slowed-down and longevity extended. The \textit{Journal of the American}

Medical Association quoted Selye’s statement that, “‘while we cannot be sure that this is true aging, it is nevertheless a very good model of aging’… when the form of calciphylaxis that deviates calcium is used in the experimental animals, the aging symptoms are completely inhibited.”¹⁵⁴ A 1963 report in Reader’s Digest suggested that Selye was on the verge of discovering the elusive “fountain of youth.”¹⁵⁵ Similarly, Science Today claimed that Selye’s calciphylaxis studies offered the revolutionary possibility of preventing aging and disease.¹⁵⁶

Selye’s interests lay not only in lengthening life expectancy, but improving the quality of health in old age. He proclaimed that “we should not think only of making life more tolerable for senile people, we should attack the process of senility itself on a biological level,” combining compassion and scientific understanding.¹⁵⁷

Selye’s calciphylaxis research was a part of a rising trend of research on human senescence. In November of 1963, Pageant remarked on the increasing scientific interest in the process of aging especially in the past two years, attributing it in part to the drastic increase in the number of elderly Americans, noting that “in the past 50 years the number of Americans over 60 has jumped from 4.9 million to 23 million.” However, they found that scientific confidence was an even more significant catalyst, as more and more “scientists now believe that we can penetrate the mystery of death—and, furthermore, that we may finally learn the secret of

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prolonging human life.” Increased funding for research on disease and aging attracted scholarly attention to gerontological research—as evidenced by the recent publication of a great many scientific papers on aging, as well as several conferences dedicated to research on aging organized by the American Association for the Advancement of Science, and the American Chemical Society, as well as the first White House Conference on Aging in 1961, among others.\footnote{On the pathologization of aging see Park, “Refiguring Old Age.”} In 1962 alone, the NIH reportedly invested over $30 million (about $236 million in 2015 dollars) on 800 separate studies on aging.\footnote{James L. Collier, “Must We Die?” \textit{Pageant}, November 1963, 6-15, folder: I: “Newspaper clippings,” HSC.} Of the expanding cannon of stress research, \textit{Pageant} assessed Selye’s research to have been the most beneficial to understanding the relationship between age and disease.

In the fall of 1964, the University of California-San Francisco hosted the “Man Under Stress” Conference, with support provided by the Ford Foundation and Smith Kline and French, and featuring many of the most notable names in stress research, including Harvard microbiologist Rene Dubos, Harvard psychiatrist Dr. Jack R. Ewalt, former Director-General of the World Health Organization Brock Chisholm, the Chairman of the NYC Med Center Department of Rehabilitation and Physical Medicine Howard A. Rusk, and the Harvard and Massachusetts General Hospital anesthesiologist Henry K. Beecher.\footnote{“Why Stress in Man’s Life is Good, Even If It Means a Lot of Worry,” \textit{The National Observer}, November 18, 1963, folder: I: “Newspaper clippings,” HSC.} The general tone of the conference celebrated the prospect that science might soon discover a means of extending the average human life span to the age of one hundred. Selye proclaimed “that he and his associates have cracked the ‘chemical code,’ and have learned to combine certain carriers with drugs in
order to selectively destroy, through calcification, almost any organ of the experimental animal’s body,” which he predicted “may eventually lead to the prevention of calcium changes in humans, and may thus stop, the ravages of senility.” Making it explicitly clear that this could not be accomplished by attempting to avoid stress, he insisted that “a certain amount of stress is good for you,” just as a “reasonable number of fleas is good for a dog—keeps him from broodin’ over being a dog.”161

**Conclusion**

By marketing his research as relevant to the disease concerns of patient-consumers and pharmaceutical companies regarding widespread anxiety, chronic diseases, and age-related degeneration, Selye promoted the popular assimilation of his theory of stress. Due to his savvy use of the popular media and self-branding, Selye earned scientific authority in the public sphere, despite his refusal to take a leadership role as a scientist statesman. While Selye shunned professional and public service, and administrative and advisory appointments, he used his cache as a revered scientific authority to gain control over the popular discourse of stress, and used his discursive power to promote his own individualistic and reductionist disease model and philosophy of stress. By endorsing the mass cultural perception of stress as an analog of anxiety, Selye also used his expert authority to promote a psychological theory of stress that departed from his own biological research, yet supported his “philosophy of gratitude”—which he would come to call “altruistic egotism.” Invoking his individualistic theories of stress-reducing lifestyle modifications, Selye used his scientific expertise and public reputation to criticize national research policy and endorse the political and economic interests of private enterprise.

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Chapter 6: Naturalizing Individualism and Politicizing Stress Research

Introduction

In the early-1960s, Selye was faced with new funding challenges following a devastating fire at the IMCE that destroyed laboratory space and a large portion of his library’s holdings. Already harboring a deep-seated resentment of his perpetual need to compete for funding, Selye undertook new measures to gain lasting security and autonomy for his research. Frustrated by the lack of funding opportunities for basic research in Canada, Selye used the media to vent his grievances and attract new financial supporters. He acerbically criticized Canadian participation in the arms and space races as a foolish and wasteful use of limited national resources. Rather than attempt to compete with Cold War powers, he argued that the millions of dollars allocated for aeronautical and military innovations be redirected to investment in medical research that may make a greater difference in improving the quality of life and health of Canadians, and citizens of other nations. Calling on the government to cultivate a culture of “scientism,” Selye vociferously encouraged federal sponsorship and planning of medical research.

Yet, while on one hand Selye advocated greater centralized federal control of research, he also paradoxically criticized governmental regulations aimed at improving public health. Selye’s frustrated pursuit of funding led him to develop an extremely lucrative relationship with the North American tobacco industry. Beginning in the late-1950s, he began soliciting financial support from the Council on Tobacco Research, the public relations and political face of the powerful tobacco industry trade association, the Tobacco Institute, Inc. As a spokesman for the CTR, Selye lent his authority as an expert on stress to support the commercial interests of the tobacco industry, testifying against proposed tobacco regulations before the Canadian Senate,
and explaining the stress-alleviating “diversionary” aspects of smoking in numerous radio and film interviews.

By the late-1960s, Selye’s philosophy of stress had become so deeply entwined with his scientific research that he was able to present his self-help credo as a principle of nature. Selye claimed that his theory of “altruistic egotism” was inspired by the behavior of multi-cellular organisms, in which individual cells prioritize their own survival for the good of the entire organism. This naturalization of individualism offered a powerful indictment of the potential dangers of governmental intervention in personal health, since only through negative liberty—freedom from externally imposed restraints—could individuals adequately respond to their unique health concerns. At the same time, Selye formalized his theory that stress can never be eradicated but must be balanced, by proposing two opposing qualities of stress, eustress (or “good stress”) and distress (or “bad stress”). Selye theorized that individuals responded to stressors differently, and therefore must hone their own ability to gauge harmful or productive stress in order to maintain health. Thus, while one person may find smoking relaxing, for example, another may find it aggravating. Moreover, those who relied on smoking to alleviate stress, might suffer worse health consequences than those potentially caused by smoking, were they to force themselves to endure the stress of quitting.

As Selye gained popular influence through his ties to industry, he lost influence among his peers. Paradoxically, Selye lost control over the academic stress discourse to the increasingly dominant voice of psychiatrically-trained researchers, while at the same time he gained power over the public perception of “stress.” Consequently, popular understandings of stress

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1 Negative liberty is often associated with limited state-imposed restrictions on citizens. In contrast to negative liberty, positive liberty involves personal empowerment—which may require state protections—to achieve their potential.
retained the individualistic focus of Selye’s disease model, while academic research began to pursue questions examining stress-inducing factors in the psycho-social environment. By promoting an individualistic and pro-corporate concept of stress, Selye offered a disease model that obscured the extent to which larger social, economic and political forces affect the distribution of stress burdens on particular population groups. Ironically, at the same time that he was mobilizing this theory to support industry and manipulate popular opinion, psychological stress researchers were paying more attention to psycho-social risk factors for stress. Even as psychologists sought to develop more sophisticated scientific means of assessing personal differences in evaluating stress—assessing appraisal and coping strategies, ranking the impact of stressful life events, and analyzing role ambiguity and conflict—they did so by examining individuals in the context of social situations. Whether it be in the family, community or workplace, interpersonal relationships became the paramount factor in determining psychological stress reactions.

Similarly, biologists and epidemiologists also emphasized the social environment as a primary determinant of stress. Primate studies helped to identify the role of social hierarchies in distributing stress, and the cumulative effects of constant internal imbalance, or allostatic load (which generates wear and tear), or weathering that damages certain biological mechanisms, decreases immunity and ultimately causes disease. Population studies on white-collar workers, ethnic minorities, and socioeconomically disadvantaged groups corroborated the biological theory that social status, social disorganization, and a lack of social capital ultimately confer susceptibility to stress. Evidence uncovering the social determinants of stress contributed to a larger recognition that stress is a political and economic construct, and not only a product of individual behaviors that can be controlled through lifestyle modifications. The disease model
that Selye fathered has now been shown to be much more complex and dynamic than his reductionistic and individualistic framework acknowledged.

I. Politicizing Research

Despite the autonomy he enjoyed as the head of his own institute and despite the international acclaim he received for revolutionizing modern medicine, by the late 1950s Selye was facing potential bankruptcy. By 1957 the IMCE operated on an average annual budget of approximately $250,000 (just over $2 billion in 2015 Canadian dollars), half of which was supported by grants from US sources.² Maclean’s remarked that “although Canada’s been taking most of the credit for Dr. Hans Selye’s medical findings at the University of Montreal, the United States has been providing most of the cash,” with the dominion government providing an annual grant of $30,000 (about $250,000 in 2015 Canadian dollars).³ While the US Department of Defense also gave Selye an annual grant of $30,000 (about $262,000 in 2015 dollars)—perhaps as compensation for his service as an Expert Consultant to the Surgeon General of the US Army since 1947,⁴ the PHS and the NSF provided much more substantial support.⁵

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² Beresford-Howe, “Men of Action: Hans Hugo Bruno Selye.”


⁴ “Pen Portraits of Distinguished Fellows of the International College of Surgeons,” Journal of the International College of Surgeons 25, no. 11 (1956), folder I: Newspaper clippings, HSC.

⁵ The IMCE also received philanthropic aid from the Gustavus and Louise Pfeiffer Foundation in New York, which contributed $62,400 to the IMCE every year since 1955 (and $30,000 in 1954), and the Abraham J. Gipsberg Foundation of New York, which issued a $23,000 to IMCE in 1959. “$23,000 Grant Made for Diapulse Research,” Montreal Star, July 30, 1959, folder I: Newspaper clippings, HSC.
As Canadian journalists warned of a specter that “research on the greatest killer of Western man may stop for lack of funds,” Selye estimated that he would need at least $100,000 per year for the next five years (nearly $850,000 in 2015 dollars) in order to continue his research on heart disease and aging. In his desperation to obtain support for his ongoing research, Selye went “begging” to private funders. He carefully selected forty philanthropic organizations and the 100 most influential Americans to whom he sent letters explaining the dire nature of his situation and requesting $5,000 grants. He had hoped to secure 100 donations, however in response he initially received only $20 from US foundations and absolutely no support from Canadian funders. Ultimately, the PHS came to his rescue, with an emergency grant of $8,000, followed by two five-year grants of $170,000 each (about $1.44 million per year in 2015 dollars) for research on heart disease, as well as arthritis and bone disease. The experience—certainly not his last in soliciting funding for his research—left Selye resentful of the need to pursue grantsmanship for taking valuable time away from his research. Moreover, the fact that he received far more support from the US government than his own, in his mind stood testament to a fundamental problem in Canadian health and scientific research policy. As he emerged from the verge of bankruptcy with a profound bitterness against grantmakers’ preference for applied research, prioritization of expenditures for aeroscience, and the inefficiency of grant application process in general, Selye vented his grievances in the press. He penned numerous op-eds and


7 Arnie Myers, “Chance, Not Logic, Key to Medical Discoveries,” *The Vancouver Sunday Sun*, April 11, 1964, folder I: Newspaper clippings, HSC.

articles in US and Canadian newspapers and magazines complaining of the unfair preferences that applied sciences received from public and private funders. In an op-ed in *The New York Times*, Selye bemoaned the lack of appreciation or funding for original discoveries and proposed that grantmakers provide scholarships and fellowships for senior researchers, who might very well prove to be a better investment given their experience and records of achievement. By thus, “ridding the creative spirit of the elite among a nation’s scientists of the shackles of predetermined routines,” the quality of research and the nation might benefit, and accomplished scientists might excel with less meddling supervision. To that end, in an interview with *Newsweek* Selye suggested that the current political economy of research might hinder truly revolutionary discoveries, suggesting that if Darwin, Pavlov, Pasteur or Fleming had been forced to prove the applicability of their research to achieve funding they might never have been able to discover evolution, behavioral conditioning, bacterial contagion or penicillin—each of which, he claimed, had been “accidental discoveries, made by men with the rare talent of noticing the unexpected.”

Selye warned of a critical change that transformed the social role and professional responsibilities of scientists. In the *Saturday Evening Post*, he echoed British polymath Bertrand Russell’s prediction that in the postwar era, scientists will bear the responsibility of not only uncovering the secrets of nature, but of persuading the world that their discoveries are worthwhile. Claiming that “the future welfare of humanity depends largely upon the recognition of first rate basic research in its earliest stages,” Selye insisted that because scientific knowledge

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10 “Toward Sounder Hearts.”
belongs to all citizens of a democracy, it falls to the scientist “to translate his problems into a language meaningful to the layman,” while the general public “will have to realize that, however simplified, the essence of basic research cannot be assimilated without mental effort.”

Claiming scientific discovery as a public interest, Selye directed his criticism at the Canadian federal government. While in 1959, Canadian defense expenditures were approximately $80 million and CNRC projects were about $21 million, only $10 million per year (about $81 million in 2015 Canadian dollars), or $.63 per person per year (about $5 in 2015 Canadian dollars) was spent on medical research. However, if the government were to increase medical research expenditures to $3 or $4 per person, Selye projected that better use might be made of national intellectual and institutional resources in the fight against disease, aging and death. Estimating federal funds for medical research to amount to only one percent of defense expenditures, Selye questioned whether it was “any longer necessary to put so much effort into war?” Or, for that matter, whether it is “so very important to go to the moon’” when the money could be better spent on cancer or heart disease research.

Selye’s jealousy of the moon and defense industry aside, his calls for enhanced federal support for medical research resonated in the postwar atmosphere of international competition in

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13 Peterson, “1,000 Yr. Life Span Seen Possible.”


15 Fred Poland, “Research Fund Lack Hamstrings Scientists,” Montreal Star, July 17, 1959, folder I: Newspaper clippings, HSC.
which quality of life was interpreted as an index of national prestige. On the eve of Queen
Elizabeth II’s visit to Canada in 1960, McGill psychiatrist Wilder Penfield and the Canadian
Association of Medical Colleges led a national campaign to establish a central, federal medical
research institute, modeled after those of the United States and Britain.  Selye celebrated the
Dominion Government’s creation of the Medical Research Council (MRC) and its $1 million
research fund (about $8.1 million in 2015 Canadian dollars) as a worthy and important gesture of
Canadian nationalism, remarking that “‘nothing could be a finer example of mature patriotism
than wholehearted support for Canadian research directed toward the alleviation of human
suffering far beyond the borders of this country.’”  Yet, given the astronomical expenditures on
defense and space research, even this improvement seemed insufficient.

Despite Selye’s widely publicized distaste for grantseeking, in the winter of 1962 he
found himself forced to undertake the largest fundraising campaign yet in his career. At
10:30am on February 20th, a spark from construction on the floor above caused a fire to break
out on the seventh floor of his institute, killing 200 of his experimental animals, destroying
research records, and severely damaging his world-renowned library.  Over the past 30 years,
Selye had built the library to consist of approximately 400,000 items, some of which dated back

16 Fred Poland, “Medical Research Held One-Body Role,” *Montreal Star*, July 14, 1959,
folder I: Newspaper clippings, HSC; Fred Poland, “Penfield Proposal Stirs Controversy,”
*Montreal Star*, July 16, 1959, folder I: Newspaper clippings, HSC.

17 “Need for Medical Research,” *The Newsletter of the Canadian Arthritis and
Rheumatism Society* 8, no. 3 (September 1959), folder I: Newspaper clippings, HSC.

18 “Costly Research Files Believed Lost in Blaze,” *Montreal Star*, February 21, 1962,
Star*, May 21, 1964, folder I: “Newspaper Clippings,” HSC.
centuries and were simply irreplaceable. Between 150,000 and 200,000 of these holdings were destroyed, as was the entire library catalogue, making it impossible to determine exactly which items were lost. Selye projected that though the library quarters would be repaired by the fall, it would take about three years to rebuild what was lost from its collection.

Since the total financial loss of the fire was estimated at $550,000 (about $4.35 million in 2015 Canadian dollars), exceeding the $281,000 covered by the IMCE’s insurance, Selye was compelled to “go begging” once more to help rebuild his labs and his library. He printed appeals in medical journals in several countries, asking his peers to send reprints to help rebuild the library—by the summer he had receive a total of 60,000 pieces from around the world and Selye was able to microfilm thousands more thanks to the US Library of Congress, the Canadian National Library and McGill University’s gracious offers to allow Selye to borrow materials from their library. In addition, Selye received $200,000 (about $1.6 million in 2015 Canadian dollars) in contributions to offset the cost of construction repairs. The NHI issued Selye a grant of $25,000 a year for three years (nearly $200,000 per year in 2015 dollars) and the Gustavus and Louise Pfieffer Research Foundation issued an emergency grant of $62,000 (about $490,000 in 2015 dollars).

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19 “University of Montreal’s Tragic Loss,” Montreal Gazette, February 23, 1962, folder I: Newspaper clippings, HSC.


21 Wardwell, “30 Years of Scientific Work Lost in U of M Library Fire.”

22 “$500,000 and Three Years Needed to Restore Library,” Medical Tribute (1962), folder I: Newspaper clippings, HSC. The Gustavus and Louise Pfieffer Research Foundation was founded in 1942 to support research in medicine to improve public health outcomes.
Selye estimated that repairs would cost at least $250,000 and would take a minimum of seven years. Yet, when the library reopened in 1964, he had received over $700,000, 200,000 reprints and 4,000 books. In total, $431,000 was donated in addition to the $281,000 in insurance compensation. Foundations and pharmaceutical firms provided the most substantial donations at $287,400 (about $2.26 million in 2015 dollars), augmented by support from private individuals and governmental agencies, all but $70,000 of which was contributed by American sources. Once again, Selye was left with a sense of shame that his own country did not sufficiently value his work.

**National Research Policy and the Canadian Brain Drain**

The fire marked a turning point in Selye’s career, after which he exerted a newly politicized public voice. Drawing on his esteemed professional reputation and acerbic Cold War rhetoric, Selye sought to shame the Canadian government into reforming medical research policy by warning that “‘the excellence of the international name of a country depends on scientific accomplishments.’” At a meeting of the American Association for the Advancement of Science in January 1965, Selye questioned whether national investment in space exploration was truly in the national interest. Given Canada’s limited resources compared to other “first world”

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23 Wardwell, “30 Years of Scientific Work Lost in U of M Library Fire.”


26 “Better Understanding Required Between Scientists, Politicians.”

countries, he insisted that Canada could not match the United States in its development of nuclear arms or space exploration, but it could make significant progress in conquering the most deadly diseases of modern man. Selye declared the “‘race to the moon… picayune compared to helping a man who is choking with cancer of the lungs,’” and suggested that “‘Canada should stop putting up little Alouettes,’” in a farce to compete with other nations in science and industry, and instead invest in worthy, feasible projects in the field of medicine.\(^{28}\)

Not only was Selye critical of Canada’s space and defense expenditures, but he also took aim at the US space research program for monopolizing the most talented scientists and thereby diminishing the quality of medical research professionals.\(^{29}\) Though he received 80-90 percent of his annual budget from the PHS, the US Army, and private US donors, he nevertheless felt that priority should be given to medical research over all other scientific projects.\(^{30}\) While Selye conceded that “there may be something worth having on the moon,” he nevertheless found “it very difficult to imagine that any treasure found on another planet could be more conducive to gratitude and prestige than the cure, say of cancer or insanity.”\(^{31}\)

Selye overtly questioned whether it was in Canada’s best interests to “follow other nations in the current astrophysical and arms race,” when such money and talent could be more


\(^{31}\) Hans Selye, editorial to *Montreal Gazette*, December 10, 1965, folder I: Newspaper clippings, HSC.
effectively invested in trying to find a cure for cancer, heart disease or aging. He advocated the country adopt an ethos of “scientism” and “culturalism” in order to encourage the cultivation of scientific expertise for the good of the nation.\textsuperscript{32} As a self-described “perpetual immigrant” who since the fall of his native Austria-Hungary, “always felt a profound urge to belong to a nation that [he] could be proud of,” it is likely that Selye’s efforts to influence national research policy were tantamount to asserting a national identity. Moreover, in the dissolution of the Austria-Hungarian Empire Selye lost not only his nationality but also his elite class identity, which had been secured by his father’s rank in the Imperial Army as well as a substantial estate, all of which had been in invested in Austrian crown bonds rendered worthless after the war. Thus, it is likely that in advocating a national policy of “scientism” Selye on some level sought to promote a new social order in which he would be awarded a respected status for his scientific expertise.\textsuperscript{33}

\textit{Maclean’s} called Selye’s proposal for science-oriented cultural planning a “genuinely radical idea,” but one worthy of attention given the increasing migration of Canada’s scientific professionals to the United States, drawn by the abundance of jobs generated from the US military-industrial complex.\textsuperscript{34} According to the Canadian Technical Service Council, approximately 11,300 Canadian graduate scientists and engineers emigrated to the United States...


\textsuperscript{33} Selye, \textit{The Stress of My Life}, 47.

between 1951-62 with more than 1,000 per year leaving between 1957 and 1960. In the twelve months before July 1, 1963, 1,583 trained professionals left Canada for the United States, including 894 engineers; 115 university professors and instructors; 148 scientists, and 467 physicians and surgeons.\textsuperscript{35}

Emphasizing the critical problem of scientific “brain drain,” Selye complained that half of his own students left for the United States after graduating because there was a shortage of jobs in Canada, they could stand to earn more in the United States, and “talent will go wherever talent is.”\textsuperscript{36} However, in August of 1964, due to the inauguration of President Johnson’s Great Society programs and the escalation of the US military presence in Vietnam, US federal agencies were forced to decrease grants for international research. From 1963-1965, the NIH spent a total of $5 million in Canada (about $38.4 million in 2015 dollars)—$2 million in 1963, $2 million in 1964 and $1.4 million in 1965. During the same time period, Canadian research on heart disease received a total of $1.2 million from U.S funders (about $9.2 million in 2015 dollars).\textsuperscript{37} Canadian researchers as a whole stood to lose $1.8 million a year in support from NIH alone, and Selye faced the loss of one-third of his entire research budget and the prospect of having to lay off 40 of his 120 workers. Indeed, though he had received two grants totaling $130,000 (approximately $1 million each in 2015 dollars) from HEW in 1964, the following year one of these grants was reduced to $75,000 and the other was completely eliminated.\textsuperscript{38}

\textsuperscript{35} Bogdon Kipling, “We Lose Too Many of Our Bright Men,” \textit{Financial Times of Canada}, March 16, 1964, folder I: Newspaper clippings, HSC.

\textsuperscript{36} “Selye Warns of ‘Brain Drain,’” \textit{Montreal Gazette}, March 6, 1964, folder I: Newspaper clippings, HSC.


\textsuperscript{38} “More Cutbacks Coming on Research in Canada.”
In response, Selye mounted a new campaign calling on the Dominion government to offset the decrease in US funding. Though the MRC’s annual budget had been increased from $5.3 million to $6.6 million from 1963 to 1964 (from about $41 million to about $50 million in 2015 Canadian dollars), the total still had to be divided amongst 12 medical schools and several other research institutions.39 Joined by the eminent discoverer of insulin, Charles Best, Selye made a widely publicized appeal to increase the MRC’s budget.40 Speaking before the Parliamentary voluntary committee on health at the invitation of the Health League of Canada, Selye insisted that “‘whether Canada is to be a first-rate or a second-rate nation depends largely on its research potential… to develop this potential, and to stop the brain drain to other countries, ‘we shall have to revise our whole attitude towards the support of research.’”41 He boldly claimed that “Canada could not hope to reach the moon in space research, but it could concentrate its effort in certain fields of medicine, where Canada already has achieved an international reputation.” To that end, Selye recommended that increased funding for medical research be directed towards the study of aging and chronic disease.42

At a time when there was widespread concern in Canada about economic dependence on the United States, and the stymied development of Canadian industry due to the overpowering influence of US manufacturing, the fear of losing Canada’s intellectual capital to the United


40 “Sponging on Uncle Sam,” *Toronto Star*, February 25, 1964, folder I: Newspaper clippings, HSC.

41 Norman Campbell, “Doctor Urges More Medical Research,” *Ottawa Citizen*, May 7, 196), folder I: Newspaper clippings, HSC.

States was a particularly troubling prospect—both to government and to business interests. Yet, rather than seek outright competition, many industrial sectors—such as automotive, scientific and tobacco industries—cultivated cooperative relationships across the US-Canadian border. Medical science, in particular, promised to benefit from bi-national collaboration and the pooling of intellectual and industrial resources.

Selye pitched an appeal to the bi-national business community to help develop uses for basic research, pleading that “’businessmen and scientists must work shoulder to shoulder,’” for each other’s mutual benefit: business needed scientists to make new medical discoveries, and scientists needed businessmen to provide the “know-how” to “’develop beneficial discoveries so that they will be available to the greatest number of people.’” Because the scientist’s “’place is in the laboratory,’” Selye claimed, “’we have neither the knowledge nor the time to organize and develop beneficial discoveries.’” It was imperative that science and business partner in pursuit of improving the quality of health for as many people as possible. Selye’s interpretation of this mission paradoxically led him into an alliance with an industry that actually impaired public health, and contributed to the increase in deaths from cancer and cardiovascular disease.

III. Selye’s Philosophy of Stress and the Naturalization of Individualism

Selye claimed that he found “’stress’ has always been a difficult question to define for public consumption,’” because “’the more a concept deviates from the conventional, the harder it is to


44 “Heart Ills From Stress Respond to New Method,” *Montreal Star*, August 20, 1958, folder I: Newspaper clippings, HSC.

sell.”

However, certainly by the late-1950s, stress had proven its marketability—he was nevertheless prescient in seeking to recruit the marketing savvy of trained business professionals to help him brand his discovery. Selye’s theory of stress was especially attractive to industrial investors, as it lent itself to commercialization in a marketplace oriented towards individualistic consumption. In 1956, Selye had originally outlined what he called the “philosophy of gratitude” in *The Stress of Life*, promoting the credo to “fight always for the highest attainable aim; but never put up resistance in vain.” Since then, he had been surprised that his credo seemed to attract more attention than the physiological implications of the theory of stress. He was recruited to speak before diverse non-scientific audiences—including religious, self-help, community, and business groups—which offered him the opportunity to further expound on his philosophy of stress. Selye offered glimpses of his evolving philosophy in various interviews for popular periodicals, as well as his own publications.

In his 1964 monograph, *From Dream to Discovery*, Selye offered to aspiring scientists on why, when, where and on what subjects to do research, as well as how to behave, work, think, read, write and speak like a scientist. Selye opened with a hypothetical letter to an admiring young scientist, “John,” whom he encouraged to pursue basic research—regardless of what criticism his peers may level against him—for the sheer fact that the study of natural laws “brings us peace, serenity and happiness.” Furthermore, he argued that John should feel no shame in working for his own satisfaction, since “egotism is the most characteristic, the most ancient, and the most essential property of life,” shared by “all living beings, from the simplest

46 “Better Understanding Required Between Scientists, Politicians.”

47 Selye, *The Stress of Life*, 300.

amoeba to man.” Selye insisted that “selfishness is natural,” and beneficial to society as a whole, because the entire community can benefit from the hardwork and talents of each member, and thus, seemingly self-centered behavior may in fact inspire gratitude and respect in others, and their desire to protect you. In other words, doing what you do best is the best way of supporting your fellow man, and ensuring your own safety and survival.49

In 1974, Selye published yet another self-help guide for popular audiences, Stress Without Distress, outlining his now much more fully developed philosophy of “altruistic egotism.” Claiming that he derived the principles underpinning his philosophy from natural law, he argued that “the rules which act so efficiently at the level of cells and organs could also be the source of a natural philosophy of life, leading to a code of behavior based on scientific principles.”50 Observing that multicellular organisms operated on a principle of self-preservation, each performing its own specialized task for the good of the entire being, Selye argued that this model of “cellular egotism” should govern human social interactions, as well. Selfishness, not selflessness offered the greatest benefit to your fellow man, therefore, rather than “love thy neighbor as thy self,” one should strive to “earn thy neighbor’s love” by expressing his or her talents to the best of their ability.51 Selye explained that, “the aim of life is to maintain its own identity and express its innate abilities and drives with the least possible frustration.”52 To do otherwise “only leads to guilt feelings and mental stress for us to be ashamed of and to suppress

49 Selye, From Dream to Discovery, 11-12.


51 Selye, Stress Without Distress, 64-65.

52 Ibid., 102.
natural drives that cannot be avoided.” He insisted that “the most frequent causes of distress in man are psychological—that is to say, lack of adaptability, not to have a code of behavior.”

While Selye had outlined the basis of these principles in *The Stress of Life*, by the mid-1970s he had developed a more elaborate philosophy of individual stress management. According to Selye, in order to relieve stress one needs to seek out an appropriate diversion that suits his or her own lifestyle. There is no single thing that alleviates all individuals’ stress equally, just as there is no single thing that initiates the same magnitude of stress response in all individuals. It is critical that each person strive to understand what causes and what alleviates his or her stress, and to take appropriate steps to disrupt patterned stress responses, or stress *grooves*. Moreover, it is incumbent on each person to strive to maintain a reasonable balance of productive stress, or *eustress*, but to avoid or reduce negative stress, or *distress*. Selye believed that his philosophical advice was in many ways of greater import than his decades of clinical research, at least in terms of improving individual health, and he relished the opportunity to help improve people’s lives. Towards the end of his life he told a reporter for *Macleans*—with no awareness of his own arrogance—that he liked for people to tell him, “You saved my life. I was going to commit suicide until I read your book.”

In attempting to naturalize selfishness, and frame it as a socially beneficent behavior, Selye presented stress-therapy as a commercially appealing prospect. While Selye professed: “there is a biological basis for what I say, I am not moralizing or preaching,” there was an

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implicit moral message in his code.\textsuperscript{56} Undergirding Selye’s ethical code was a belief in negative liberty that individuals should be free from legal restraints—whether protective or not—that impeded their ability to regulate their own health. This perspective of disease meshed well with the nascent neoliberal backlash against centralized state regulations that might limit both personal liberty and private enterprise, which was emerging in the early-1970s. Selye’s emphasis on individualism in disease appealed to the business community that spearheaded the early neoliberal movement, and he was quite receptive to requests for speaking engagements from business schools, trade associations, corporations and Chambers of Commerce.\textsuperscript{57} Charging $5,000 per lecture and requiring first-class air fare, Selye profited from the coordinated organization of business interests in the early 1970s, just as the business community reciprocally benefited from his expert endorsement of pro-industry antiregulatory policies.\textsuperscript{58}

\textbf{II. Authenticating Anti-regulatory Policy for Big Tobacco}

The epitome of Selye’s pro-industry stance was his increasingly close relationship with the tobacco industry.\textsuperscript{59} Since the mid-1950s, the Tobacco Institute had staged a marketing offensive to counter the mounting evidence correlating cigarette smoking with increased risk for lung

\textsuperscript{56} Selye, “Secret of Coping with Stress.”

\textsuperscript{57} See untitled list of Selye’s Speaking Engagements, especially 1970-1979, Folder: “Speaking Engagements,” HSC.


cancer, heart disease, emphysema and other diseases. Headed by the Tobacco Institute—the trade association for the tobacco industry, essentially run by the heads of the three big tobacco companies, Lorillard, R.J. Reynolds and Philip Morris—the two main strategies of this campaign were first, to frame smoking as an expression of individual choice and liberty, and secondly, to mobilize industry-friendly scientific evidence that refuted the allegation that cigarettes contributed to the development of cancer and heart disease. To that end, the Tobacco Institute sponsored in-house research and recruited medical experts to endorse the position that there was no conclusive evidence that cigarette smoking actually caused cancer.⁶⁰

In 1964, the US Surgeon General released a Report on Smoking and Cancer that outlined the scientific evidence linking tobacco smoking with lung cancer, cardiovascular disease, bronchitis, emphysema and psycho-social issues. The Surgeon General’s report carefully distinguished between “factors,” “determinants,” and “causes” of disease, explaining that “while a factor could be a source of variation, not all sources of variation are causes.”⁶¹ However, statistics revealed a strong correlation between tobacco smoking and disease. Per capita consumption of cigarettes rose from 138 in 1910 to 2,986 in 1961. Meanwhile, deaths from lung cancer increased from less than 3,000 in 1930 to 41,000 in 1962, deaths from arteriosclerotic, coronary and degenerative heart disease increased from 273,000 in 1940 to 578,000 in 1962, and deaths from bronchitis and emphysema increased from 2,300 in 1945 to 15,000 in 1962. By the early 1960s, nearly 70 million Americans—68 percent of men and 32.4 percent of women over

⁶⁰ For a detailed history of the tobacco industry’s efforts to manufacture doubt regarding the causal relationship between cigarette smoking and cancer. See Allan Brandt, The Cigarette Century (New York: Basic Books, 2007).

age of 18—were regular smokers. Given the statistical evidence that the risk of developing lung cancer increases 9- to 10-fold for cigarette smokers, and 20-fold for heavy smokers, the Surgeon General’s Report concluded that “smoking is associated with a 70 percent increase in the age-specific deaths rates of males, and to a lesser extent with increased death rates of females,” and that “cigarette smoking is causally related to lung cancer in men… [and] far outweighs all other factors.”

Following the publication of the Surgeon General’s Report, organized public health campaigns in the United State and Canada sought to impose regulations on tobacco sales and advertising in order to decrease cigarette smoking. And in response, the tobacco industry escalated their efforts to raise doubt as to the causal relationship between smoking and disease. The mobilizing of expert opinion in defense of smoking was a critical component of this pro-industry propaganda. Since the Surgeon General’s Report had drawn attention to the stress-alleviating qualities of cigarette smoking, it offered yet another line of defense for the tobacco industry to pursue. And as an internationally renowned, expert on stress physiology, Hans Selye was an ideal spokesperson for their cause.

In October of 1959, Selye prepared a memorandum on the relationship between cigarettes and lung cancer for the New York law firm, Davis, Polk, Wardwell, Sunderland & Kiendl to be used as scientific evidence that the statistical correlation between smoking and cancer does not


63 Smoking and Health, 31.

64 The Surgeon General’s report explored many factors influencing the psychological drive to smoke, including type A, or “coronary type” personalities and high levels of anxiety, which it pointed out may not only drive individuals to smoke to alleviate psychological tension, but also predispose them to develop cardiovascular disease. The report actually named stress as corollary etiological factor in heart disease (p. 327), and noted that stress seemed strongly associated with increased frequency of smoking (p. 377). Smoking and Health.
necessarily establish a causal relationship. Selye’s memorandum emphasized four points: 1) that the induction of disease in experimental conditions is phenomenal rather than causal, 2) that cancer arises from a complex relationship which cannot be attributed to any single factor, 3) that cigarettes are no more dangerous to public health than automobiles, alcohol, animal fat or even sunshine, and 4) that cigarettes offer benefits that may outweigh their risks.\(^{65}\) He also prepared a subsequent, more concise memorandum in which he stated that “the ‘personal equation’ or ‘clinical impression’ of the practicing physician cannot lead to the identification of any one factor as the cause of a disease unless all possible other factors have been eliminated—this is obviously not feasible in the case of a smoker who develops lung cancer, since we do not know what factors other than smoking may have been involved.”\(^{66}\) Selye was compensated $1,000 for the first and $500 for the second memoranda (respectively, approximately $8,000 and $4,000 in 2015 dollars). While these payments were hardly sufficient to support the IMCE, this work signified to the tobacco industry that Selye was sympathetic to their position and amenable to offer his expertise and reputation to manufacture doubt about the alleged harmfulness of the tobacco industry’s products. Consequently, these two brief memoranda provided a fertile foundation for what would become a strong alliance between Selye and the North American tobacco industry by the end of the 1960s.

In the fall of 1966, Frank Decker of Cambell, Medinger, Fosyth & Decker, head counsel for The Council for Tobacco Research (CTR), the purportedly-independent research wing of the


powerful tobacco industry trade association, obtained the memos that Selye wrote for Davis, Polk, Wardwell, Sunderland & Kiendl in 1959. Sharing it with Bill Shinn and Alex Holtzman, fellow CTR representatives, all three men agreed that Selye’s subtle admission that cigarette smoke had carcinogenic properties could be a liability, but nevertheless saw great potential in developing a relationship with Selye. Decker, Shinn and Holtzman flew to Montreal on December 21, 1966 to meet with Selye and discuss the possibility of recruiting him as an expert witness and spokesperson for the CTR. They found that Selye was extremely receptive to the CTR’s scientific public relations problems. He offered that even though there was likely some link between smoking and cancer, this was not much of an indictment against cigarettes since “you can produce cancer with anything… [and] almost anything will be toxic to some people under some circumstances.” He also noted that experiments showing cigarette smoke to induce cancer in animals do not establish a strong causative relationship, just as experiments which showed that alcohol was harmful for dogs did not establish that it was also a danger to human health. Most of all, Selye emphasized that there were in fact benefits to smoking that in some cases might outweigh its risks. For example, he offered, “a very stressful individual is better off for smoking because, if the person did not smoke, he ‘might pop a blood vessel.’” In such a case,

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cigarette smoking was a ‘reasonable risk to take,’” compared to further mounting stress, or to other riskier deviations.70

Selye proposed a “five-step project for advancing the concept that stress is related to disease, that ‘deviation’ of stress is necessary, and that cigarette smoking is an acceptable deviation.” This plan consisted of a change in the tobacco industry’s defensive strategy from attempting to refute the evidence linking smoking and cancer, to instead focusing on the “prophylactic and curative” nature of smoking. To that end, Selye would prepare a memorandum outlining how cigarettes served as an effective deviation or diversion for alleviating stress, emphasizing the importance of personal choice in selecting appropriate diversions, and explaining the way in which crossed-resistance worked as a deviation. Thirdly, the industry was to undertake a large-scale public education campaign via mass media in order to popularize the concept of stress and the idea that deviation was necessary to reduce potential damage from stress. He suggested that “there would be no great problem in convincing the public of the importance of stress in disease because the public already has been conditioned to accepting it.”71 Selye would lend his scientific authority to this effort by sitting for interviews with freelance writers, selected and arranged by the CTR. And in addition, he would write one or two articles for publication in medical journals regarding the use of cigarettes as a diversion from stress. And finally, Selye would offer testimony before Congress or Medical Associations in support of the beneficial attributes of tobacco smoking, and against regulatory efforts to


restrict tobacco marketing. In return, Selye asked that the CTR make a generous, unrestricted contribution to his institute to continue their work on stress, deviation, and chronic diseases—though not necessarily on tobacco.

Decker, Shinn and Holzman were all “quite impressed” with Selye’s “forthrightness,” professional reputation, and willingness to support the industry’s position. Agreeing that, “it is doubtful that we could find a man better able to develop the benefits of smoking as a deviation from stress,” they paid him a $5,000 commission (about $35,600 in 2015 dollars) to write the memorandum outlining the beneficial diversionary aspects of cigarette smoking by mid-January 1967. While they did not make any immediate arrangements to undertake the rest of Selye’s plan, they envisioned that he might be extremely useful to the CTR in at least 6 areas: 1) by emphasizing the causal relationship between stress and disease; 2) offering scientific credence to the possible constitutional predisposition to both adapt poorly to stress and choose to smoke; 3) refuting the causal relationship between smoking and cardiovascular disease; 4) establishing the applicable parameters for animal experimentation in assessing human disease; 5) promoting the theory that stress might be equally (or more) accountable for deaths attributed to smoking; and 6) validating the perception that smoking offers certain benefits in alleviating stress by deviation.72

By February of 1967, the CTR had decided to develop Selye as a potential witness for industry, even though they doubted whether he could be ready in time for that year’s Congressional hearings on tobacco regulation.73 However, despite their auspicious beginnings,


two years passed after Selye initially wrote his memo for the CTR, without him receiving any further assignments, or substantial funding from the CTR. When Decker contacted Selye in March of 1969 regarding his pending testimony in upcoming Canadian Senate hearings on tobacco regulation, Selye made it clear that without financial support he was less than eager to offer his help to the CTR. Had the CTR come through with the funding he had initially requested, he suggested that he would have likely already completed the proposed research on stress and deviation and would have something to report to the Senate. Nevertheless, Selye offered that he would still be willing to perform research on the beneficial effects of nicotine under a contract with the CTR, if they could supply $80,000 annual costs (about $518,000 in 2015 dollars) for expenses plus overhead.74 In light of the upcoming Canadian Senate hearings, as well as Selye’s scheduled appearance on a one-hour television program on ‘Science and Conscience,’ the CTR felt that “if Selye is working on this project, he will be inclined to say so both in testimony and on the telecast and will probably take a position that the critics of tobacco lack proof.” The CTR agreed to split the cost of Selye’s proposed research—which had now risen to $100,000 per year for three years (nearly $650,000 per year in 2015 dollars)—with the Canadian Tobacco Manufacturers Council.75 All publications produced from this research were to recognize the CTR’s support by stipulating that they arose from a “Special Project of the


On June 12, 1969, Selye delivered testimony the Canadian Senate worthy of his fee. Using tones of scientific authority as well as popular appeal, he carefully explained the importance of diversionary activities to alleviate stress, and how smoking, much like exercise, hot or cold baths, or cocktails, can thereby offer significant benefits to individuals suffering stress. But he went further in outlining the state’s responsibility in responding to the health threats posed by stress and smoking. Claiming that “man will always seek gratifying relief from stress,” Selye warned that “our responsibility is not to lock up all avenues that may be dangerous, but to determine as objectively as possible which are the most and which are the least dangerous in proportion to their benefits.” He claimed that closing off certain avenues may lead individuals to choose even riskier diversions, as children scared that they may get cancer from smoking cigarettes, might turn to illegal drugs instead. Because every person is different in their response to stress, they also gain relief from very different diversions. Selye insisted that personal choice was key in determining the appropriate method of release, therefore, the government must not delimit the available methods of relief available to individuals unless there was substantial proof that they were harmful. Selye opined that he did “not think that government should mix into the private predilections of individual citizens… if somebody wants to smoke, despite the fact that he knows what dangers may be or may not be involved, that is his private business.” Since cigarette smoke was no more harmful than industrial smog or automotive exhaust, he claimed that “singling out of this particular activity seems to me not to be based on logic.” Finally, he

took the opportunity to repeat a favorite admonition, speculating that “if we had put all the money that has been wasted on this [smoking] controversy into medical research on diseases of stress it would do much more for humanity than doing what is being done now.”

Selye’s testimony did not thwart the proposed tobacco advertising regulations, however, it did perpetuate the veneer of scientific authenticity supporting the tobacco industry’s position. It also paid handsomely, supporting at least six years of research at the IMCE that produced overtly pro-industry results. Between 1969 and 1974, Selye received $50,000 annually (an average of about $280,000 per year in 2015 dollars) for two research projects on “Cross-Resistance and Beneficial Effects of Deviation,” and “Stress and Relief from Stress,” leading to at least two scholarly publications on behalf of the CTR, and four others for the Canadian Tobacco Manufacturers Council. Under contract with the CTR, Selye began research on the catatotoxic effects of the steroid pregnenolone-16a-carbonitrile (PCN) on nicotine metabolism. Selye also received funding for this project from the PHS Child Welfare Department. He published the results of this research in the *Journal of American Geriatric Society*, suggesting

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that this mechanism may offer insight in evaluating the detrimental effects of aging.\textsuperscript{80} The potential use of PCN in ameliorating the destructive effects of nicotine was beneficial to the CTR not only for public relations purposes, but also as a potential marketing opportunity.\textsuperscript{81} While PCN was never actually commercially developed for these purposes, Selye readily lent himself to the public relations and marketing interests of the CTR by announcing on a national radio broadcast that he was in the process of developing a “cancer preventive pill for smokers,” that might offer a means of developing immunity to lung cancer. However, he claimed, the Federal Food and Drug Directorate was impeding the necessary clinical tests on humans, which he estimated would take an additional five years.\textsuperscript{82}

In late-July of 1969, H. Wakeham, [Director of Scientific Research For the CTR] met with Selye in his Montreal lab, where Selye renewed his recommendation that the CTR undertake a mass education campaign to raise awareness of the “importance of relief from stress,” coordinated through university-based adult education programs.\textsuperscript{83} The stress-awareness campaign also utilized mass media exposure as a complimentary channel for influencing public opinion. To that end, Selye participatd in radio, television and documentary interviews, including a televised broadcast on Washington’s WETA in early September 1969, examining


\textsuperscript{82} “Quotes Dr. Selye,” [WTOP News Radio broadcast], May 1, 1972, Bates No. 1005136283, UCSF Legacy Tobacco Archive, accessed July 24, 2013, http://legacy.library.ucsf.edu/tid/yjt54e00/pdf.

philosophical and scientific issues in the smoking debate. Selye claimed that the controversy surrounding cigarettes, was turning smokers into “neurotics” as they tried to quit or “spend the rest of their life feeling sinful about it.”

In the fall of the 1970, the CTR began planning a “Conference on the Motivational Mechanisms of Cigarette Smoking” to be held in St. Maarten in January 1972 and supported by all 6 major tobacco companies. They invited experts in the life, behavioral and social sciences to mount “a renewed scientific attack upon a question that in recent years has not been accorded the priority that it rightfully merits.” The industry’s intention was to overshadow the health controversy, which had become intensely politicized as a result of the regulatory debates over the past decade, by rationalizing the questions through scholarly scientific discussion. Noting that domestic consumption of cigarettes had actually risen nine percent from 1960 to 1969, the CTR’s invitation to prospective participants asked them to ponder reasons that might explain this “remarkable intractableness of cigarette smoking in face of the resourceful anti-smoking campaigning that has characterized the decade of the sixties?”

Selye gave the St. Maarten Conference’s keynote address on “Smoking as a Defensive Response to the Effects of Stress,” in which he explained that diversionary methods may “vary in degree of disruptiveness or intrusiveness upon ongoing life styles, ranging from innocuous mannerisms such as pencil or foot tapping at the one extreme to devastating heroin or alcohol

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addiction at the other.” He went on to explain that when one selects smoking as a diversionary tactic, he is not deciding whether,

‘to smoke or not to smoke,’ but whether to smoke, or to overeat, to drink, to drive on polluted and crowded highways, formerly to fret and bite our fingernails to avoid boredom and give vent to our pent-up energy. Man must weigh the pros and cons of any diversional activity; he must undertake his own benefit/risk analysis, and act accordingly. If you take aspirin, you accept its potentially dangerous effect on platelet adhesiveness in exchange for the relief of pain. A woman using contraceptives accepts their undesirable side effects in exchange for protection against an unwanted pregnancy and the risks of childbearing. The value of diversion has been well shown by various forms of ‘nonspecific therapy,’ many of which (insulin shock, metrazol shock, electroshock, extreme hot or cold bath, etc.) are unpleasant or even highly dangerous.

Selye’s message set the tone for the rest of the conference, and afterward brought the conference’s message to a public audience when the conference proceedings were published as a monograph entitled, *Smoking and Behavior: Motives and Incentives* the following year.86

Having repeatedly proven himself a powerful spokesperson for the tobacco industry, following the St. Maarten conference, the CTR also explored the possibility of further strengthening their relationship with Selye by hiring him to fill the then vacant position of Scientific Director. During the conference, Selye expressed great interest in the position to Bill Dunn, indicating that he intended to retire from the University of Montreal in 1976, at which point he would like to find a new position in the United States. While at the time, Dunn felt that “Selye’s world eminence makes his name a most valuable commodity,” and that the “association of his name and presence with a research institute or foundation would be a most beneficial arrangement for all concerned,” ultimately the CTR never brought him in-house.87 They did, however, continued to sponsor his research at the IMCE—renewing his $150,000 grant (about


$854,000 per year in 2015 dollars)—and to rely on him for public relations projects. 88

Over the course of the 1970s, Selye was featured in a number of films sponsored by the tobacco industry, as well as non-industry projects, where he consistently presented the theory of smoking as a beneficial diversion to relieve stress, and emphasizing the importance of personal choice in determining appropriate stress releases. 89 Selye was apparently a very persuasive voice. A 1972 test-screening of the Tobacco Institute’s, “Smoking and Health: the Need to Know,” found that Selye was rated the most “believable” of all experts featured in the film. 90

Yet, Selye’s cache only lasted so long, and by the end of the 1970s, he had fallen out of favor with the tobacco industry. After retiring from the University of Montreal and leaving the IMCE


in 1976 and starting the new International Institute for Stress, Selye sought additional funding from the CTR for his new institute. However, his request was denied on the reviewers’ sense that his budget was more than twice the necessary amount, that Selye’s request was inspired by hubris rather than genuine need, and that it was no longer wise to invest in his work as he seemed “to be showing some signs of advancing senility,” and “has contributed very little new to the study of stress over the past 10 or 15 years.”

III. Psychological Stress Research in the 1960s and 70s

Though harsh, the CTR was at least correct in their criticism that by the late-1970s Selye was no longer significantly contributing to the development of the medical understanding of stress. Having spent the past decade trying to achieve financial security for the IMCE and the IIS by pandering to private funders, he had failed to produce any substantial research of his own. He yet sought to maintain control over the academic discourse of stress, by publishing two digests of current research, entitled Selye’s Guide to Stress Research, volumes 1 and 2. In his absence, psychologists had come to dominate the field of stress research, and their etiological theories of stress came to acknowledge broader ecosocial factors.

Psychologists did not entirely abandon an individualistic focus in stress research. In the 1960s, psychological stress research began to emphasize the subjective nature of stress, and call for unique, personalized therapeutic interventions. In many ways, this vein of research complemented Selye’s individualistic view of stress. Yet, while Selye espoused the need to resort to personalized diversions to disrupt endocrinological stress “grooves,” in contrast,

psychologists, psychiatrists and occupational health researchers were developing standardized, systematic means of assessing individual interpretations of their own stress levels, in order to determine appropriate psychological interventions.

For most of the twentieth-century, a modified behavioralist, stimulus-response model dominated psychological stress research. This uni-directional perspective viewed psychological stress as a natural response to an adverse external stimulus, and therefore, left little room for evaluating individual difference to stressors. Franz Alexander’s “specificity theory,” and Helen Flanders Dunbar’s personality profiles typified this etiological model, which applied psychoanalytical theory to diagnose individual personality types and traits as prone to specific diseases. The quintessential example of this paradigm may be Friedman and Rosenman’s model of the Type A, coronary-prone personality. But, by the mid-1960s, the “new-look” movement in psychological stress research drew attention to the subjective and dynamic nature of stress reactions, promoting a stress-organism-response model that acknowledged individual variation in response. “New-look” stress research placed great importance on idiosyncratic attitudes, beliefs, expectations, and motives in determining differences in the interpretation of stressful situations, and variations in response to stress. In this model, the individual is recognized as the critical relational factor in mediating stress reactions, yet environmental influences are fundamental in stimulating a stress reaction.92

In the 1960s and 70s, psychological stress researchers began to pay greater attention to the catalytic influence of stressful life events, such as the loss of a loved one, a traumatic injury or disease diagnosis, divorce, bankruptcy or unemployment. The concept of stressful life events placed great emphasis on individuals’ own perceptions of stress, building on Harold Wolff’s

emphasis on individual assessment in determining stress-inducing threats and conflicts. In an attempt to quantify stress by objective measurement, in 1964 researchers at the University of Washington headed by Thomas Holmes and Richard Rahe developed the Schedule of Recent Experiences (SRE), which asked interviewees to rank stressful events according to intensity. Three years later, they developed the Social Readjustment Rating Scale (SRRS), which differentiated between individual occurrences or acute episodes of stress, as opposed to lifestyle factors that contributed to stress load. The SRRS also evaluated the intensity of experiences, and was also measured by self-assessment questionnaires and interviews. The SRRS’s reliance on participant assessment meant that its results were decidedly subjective, and potentially confounded their intended measurement of symptoms with inadvertent measurement of subjects’ perception of their own health outcomes. Yet despite their drawbacks, the SRRS and the SRE advanced psychological stress research by providing a common metric for evaluating individuals’ stressful experiences.

In May of 1965, Mortimer Appley Chair of York University’s Department of Psychology, and Richard Trumbull of the Psychological Sciences Division of the US Office of Naval Research, organized a conference on psychological stress at York University. The aim of the conference was to present the latest research on physiological, psychological and social factors influencing stress reactions, and to come to a consensus as to the meaning of the word stress. In the published conference proceedings, Appley and Trumbull noted that since Selye had

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93 Harold Wolff, *Stress and Disease.*


introduced the biological concept of stress, it had grown in popularity, often being used as a “substitute for anxiety, conflict, emotional distress, extreme environmental conditions, ego-threat, frustration, threat to security, tension, arousal,” and so on. While on one hand, the inconsistent and widespread use of the term “stress” generated confusion as to its meaning, at the same time, it offered great possibilities for identifying relationships between psychological and physiological health.\textsuperscript{96} Appley and Trumbell argued that while physiological indexes, such as heart rate, adrenal weight, and galvanic skin response, could be helpful in measuring stress, nevertheless “the first necessary step in such studies is to determine how the subject perceives the stimulus or situation presented.”\textsuperscript{97} Because stress is a responsive phenomena, in order to understand why a stress reaction occurs it is more important to identify the environmental factors to which an individual was sensitized by their prior experiences. Therefore, “in addition to emphasizing the role of the individual… attention must also be given to social factors—the influence of other individuals or of the social and cultural milieu in producing or relieving stress.”\textsuperscript{98}

Richard Lazarus stood at the forefront of this new relational model of psychological stress. Having participated in military combat stress research during World War II, Lazarus was profoundly influenced by Roy Grinker and John Speigel’s psychoanalytic perspective of stress reactions as determined by individual life histories. In the late-1950s and early-1960s, Lazarus created a new stress research initiative at the University of California-Berkeley that would become known as the Stress and Coping Project, which emphasized cognitive mediation as the

\textsuperscript{96} Psychological Stress, 1-2.

\textsuperscript{97} Ibid., 9.

\textsuperscript{98} Ibid., 11-12.
critical pathway by which stress responses were determined. Lazarus was particularly critical of
Selye’s insistence that the GAS was initiated by a physiological first mediator, which Lazarus
claimed, ignored the “psychological signaling system” of the stress response. Furthermore,
Lazarus questioned the extent to which stress was truly a non-specific syndrome, given its
limitless variation in scope and intensity from person to person and situation to situation. From
1964-1966 he outlined a theory of personal appraisal of stress, which placed great emphasis on
individual cognitive mediation in determining the force and type of psychological stress
responses to various stressors. Essentially, Lazarus’s concept of appraisal held that individuals
reacted differently to the same stressors based on how threatening or benign they perceived them
to be. In the late-1960s and early-1970s, Lazarus expanded his work on variations in individual
interpretation of stress by examining different ways in which people tolerated stress, a
phenomenon to which he referred as coping.99

In contrast to Lazarus’ insistence on the importance of individual perceptions of and
responses to stress, by the mid-1970s, Bruce and Barbara Dohrenwend at the Columbia
University School of Public Health, urged an objective evaluation of stressful life events
independent of individual assessment. The Dohrenwends’s proposition that stress could be
evaluated as an independent factor in a natural environment stood in direct opposition to Richard

    Hill, 1966); Lazarus and Raymond Launier, “Stress-related Transactions Between Person and
    Environment,” in Perspectives in Interactional Psychology, L.A. Pervin and M. Lewis, eds.
    Coping Dispositions and Recovery From Surgery,” Psychosomatic Medicine 41 (19730: 109-
    181; Lazarus and S. Folkman, Stress, Appraisal and Coping (New York: Springer, 1984);
    Lazarus and Folkman, “Transactional Theory and Research on Emotions and Coping,” European
    Lazarus: An Analysis of Historical and Perennial Issues (Mahwah, NJ: Lawrence Erlbaum
Lazarus’s theory of individual appraisal and coping strategies.\textsuperscript{100} These competing theories gave rise to at least a decade of what one researcher has described as “stress wars” in which stress researchers identified with the subjective perspective or the objective camp.\textsuperscript{101} Both fields gave rise to fruitful research, with the subjective theorists developing more sophisticated means of assessing personal evaluations of stress, and coping strategies, while the objective theorists documented evidence of the universal threat of certain stressful life events.

Also in the mid-1960s, a group of Swedish stress researchers based at the Karolinska Institute in Stockholm, began to expound upon the psycho-social influences on stress reactions. Early in the decade, physiologist Ulf von Euler developed a method for measuring stress levels according to the urinary concentration of adrenaline and noradrenaline (rather than ketosteroids), for which he won the 1970 Nobel Prize in Physiology and Medicine. Von Euler’s colleagues applied his metric for assessing stress, to a broad range of social situations. In 1959, Lennart Levi, created the Stress Research Laboratory within the Karolinska Institute, which later gained recognition as a World Health Organization center for psychological research and training. Under Levi’s leadership, the Stress Research Lab advanced research regarding psychological influences on physical health, particularly with regard to the workplace.\textsuperscript{102} Levi’s colleague, Marianne Frankenhaeuser used biological indices to document the Progressive Era concept that

\begin{itemize}
\item \textsuperscript{101} Francine Deutsch, “Calling a Freeze on ‘Stress Wars’: There is Hope For Adaptational Outcomes,” \textit{American Psychologist} 41 (1986): 713.
\end{itemize}
technological innovation far outpaced human biological development, and consequently created a relationship of discordance in which humans were ill-equipped to physiologically respond to the demands of modern society.\(^{103}\)

Partly inspired by the work at the Karolinska Institute’s Stress Research Lab, an auxiliary field of stress research began to emerge in the late-1960s which focused primarily on occupational health and organizational psychology. Growing out of the earlier fields of human resources and industrial hygiene, occupational health psychology sought to improve the quality of workers’ health by removing environmental hazards and developing ergonomic practices, but primarily focused on improving relationships within the workplace, amongst coworkers and between employees and management. In the late-1960s and early-1970s, occupational stress research also focused on the individual as the primary variable in determining the onset of stress, by evaluating worker satisfaction and empowerment. Guided by research at the University of Michigan Institute for Social Research concentrating on the extent to which workers understood what was expected of them (role ambiguity) and felt capable of performing all of their duties (role conflict),\(^{104}\) occupational psychologists also began to place great emphasis on the extent to which an employee felt overly challenged (role overload) or bored (role underload) in their work.


Similarly, in the late-1970s Robert Karasek found that workers who performed highly demanding jobs in which they felt disempowered to make critical decisions that affected their own job performance, reported high rates of exhaustion, depression, anxiety, and insomnia. Critical to this interpretation of stress is the extent to which an individual feels poorly matched with the demands of their position, which promotes a transactional model of stress between the individual and their psychosocial environment. In a much broader sense, the field of occupational health psychology was predicated upon an understanding of stress as a substantial economic and social cost to an employee and employer, as well as to the individual and society.

Collateral to the field of occupational stress research, military stress research also contributed significantly to the changing disease model of stress in the late-1960s and 1970s. The Vietnam War renewed interest in combat stress research, and transformed the medical understanding of stress by validating the reality of post-combat enduring trauma. Retaining the lessons of the Second World War, the War Department implemented psychological screening and neuropsychiatric therapy as close to the front as possible. As a result, the incidence of war neuroses was shockingly low, with an average of twelve neuropsychiatric casualties per 1,000


soldiers, even in the intense fighting following the Tet Offensive in January of 1968. Compared to the rate of 37 casualties per 1,000 in the most intense periods of combat during the war in Korea, this was a drastic decrease.\textsuperscript{107} However, the fact that fewer soldiers were breaking down during combat did not mean that they were unaffected by the trauma of war.\textsuperscript{108} The media coverage of the war increased public awareness of the severe strain under which soldiers fought—from the anxiety of guerilla warfare, to the neurological damage caused by exposure to chemical weapons—as well as some of the more horrific scenes of total war, epitomized by the My Lai Massacre. Moreover, the reproach of returning veterans generated by the antiwar movement, may have inhibited soldiers’ capacities to readjust to civilian life. For an abundance of reasons, Vietnam veterans exhibited a high rate of psychological suffering long after they returned from service, and as such, placed new therapeutic demands on the psychiatric profession.\textsuperscript{109}

When the second edition of the American Psychiatric Association’s \textit{Diagnostic and Statistical Manual} was published in 1968, the diagnosis of \textit{gross stress reaction} was omitted. University of Iowa neuropsychiatrist, Nancy Andreason attributes the removal of the stress diagnosis from the DSM-II to the fact that this was a period of relative peace, however military psychologists who served in Vietnam at the time attribute it to the effective implementation of

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screening, preventive and therapeutic strategies.\textsuperscript{110} When the Task Force on Nomenclature was assembled to prepare the third edition of the DSM, its director, Robert Spitzer, appointed Andreason to head the Committee on Reactive Disorders and to work closely with the Vietnam Veterans Working Group, an organized group of Vietnam veterans that had been campaigning for the DSM-III to include a “Post-Vietnam Disorder” diagnosis reflecting the continuing psychological effects of combat stress in civilian life.\textsuperscript{111} As an expert in the psychological trauma suffered by victims of burn injuries, Andreason was already familiar with a well-established late-onset syndrome induced by exposure to severe physical and emotional stress, and expressed in a battery of physiological, cognitive and emotional symptoms. Andreason wrote the definition for Post-Traumatic Stress Disorder (PTSD) to apply to not only veterans, but victims of a vast range of traumatizing experiences, including survivors of physical and emotional abuse, natural disasters, horrific accidents and human rights violations.\textsuperscript{112} As it was published in the 1980 DSM-III, the primary qualification for a PTSD diagnosis was that the stressor had to be “outside the range of normal human experience,” and outlined three principal symptoms of re-experiencing, numbing, and cognitive or autonomic reactions.

The creation of a new diagnostic category substantially increased the reporting of stress-related disorders, so that by 1987, when the DSM-III was revised, the definition of PTSD came to emphasize psychological stressors, and diminish the influence of physical etiological factors.


The DSM-IIIR definition also included chronic conditions and collateral mental disorders, such as dissociative states, which soon led to professional backlash against the concept of PTSD on the grounds that it had become so overbroad that it strained its diagnostic utility. Since then, the APA has thrice revised the definition of PTSD, generally aiming towards greater specificity and therapeutic applicability. Recently, victims and researchers of PTSD have spearheaded a campaign to categorize PTSD as a disease rather than a disorder, signaling a desire for more austere medicalization that would reduce the stigma associated with suffering from a “disorder.” At the very least, the development of the diagnosis of PTSD over the past forty years indicates that it is both contested and socially useful. Yet more importantly, the rise of PTSD stands testament to the need to distinguish between normal and abnormal reactions to stress, as well as the increasing recognition of the psycho-social environment as a major determinant of stress.

IV. Stress and Society

As psychological studies of stress began evaluating environmental influences on individual stress conditioning, so too did physiological studies. A quintessential example of this can be seen in a population study of an Italian-American community in eastern Pennsylvania conducted by Stewart Wolf, who had formerly revolutionized psychosomatic stress research with his collaborative studies with Harold Wolff on the emotional stimulation of gastric secretions. In the early-1960s, Wolf and his colleague at the University of Oklahoma, John Bruhn began studying the shockingly low rate of heart disease in the town of Roseta, Pennsylvania. Despite the fact that the residents of Roseta were exposed to the same traditional risk factors for heart disease as their neighboring communities of Nazareth and Bangor—diets high in animal fat, relatively

113 Andreason, “Post-traumatic Stress Disorder: A History and Critique,” 70.
sedentary lifestyles, cigarette smoking, and average incidences of hypertension and diabetes—they were somehow insulated against the development of heart disease. Wolf and Bruhn determined that counter to the prevailing scientific theory that heart disease was primarily biologically determined, Rosetans were ultimately protected by sociological factors, including a close-knit, insular community that prescribed clearly defined gender and social roles and a relatively homogeneous value system maintained by the centrality of the Catholic church and “old world values.” Wolf and Bruhn won grants from the NHI and the NIMH to conduct a prospective longitudinal study of Rosetans, which served to confirm their original hypothesis. Over time, as Rosetans became increasingly Americanized—which Wolf and Bruhn measured by an assimilation of materialistic and middle-class values, liberalized gender and social relationships, and a decreased influence of the Catholic church and Italian folk traditions—the prevalence of heart disease gradually rose.114

The Roseta Study indicated that the increased prevalence of coronary disease in the United States since the turn of the twentieth-century

…coincided with a loosening of family cohesion and a diminished reliance on religion, together with increased emphasis on individual freedom, self-reliance and self-fulfillment. People became more competitive, more litigious and less concerned with the welfare others. Not only was there a decline in the influence of churches and teachers, but of parents as well. By the late 1960s, the urgency of free self-expression had all but crowded out deference and considerateness and, in some quarters, even civility.

Wolf and Bruhn argued that social cohesion protected against heart disease, while social confusion contributed to it.115 Moreover, the increased prevalence of individual behavioral risk factors, such as smoking, decreased physical activity/exercise (due to occupational change from


hard labor to middle class service jobs) and consumption of less-healthy fats (lard vs. olive oil) are less significant contributors to the increased prevalence of heart disease than the “loss of social stability, as reflected in the loosening of family ties and the weakening of community cohesion,” which it seems generated “a sense of uncertainty about the future among Rosetans, with a variety of accompanying apprehensions and emotional conflicts and perhaps undue variability in vital homeostatic systems.”\textsuperscript{116} Thus, while individual conditioning factors certainly played a significant role in the onset of stress, broader social forces ultimately shaped the extent to which individuals were protected or put at risk for disease.

In the 1970s, the World Health Organization organized a series of conferences on \textit{Stress and Society}, each examining topics regarding stress and the psychosocial environment, childhood and adolescence, gender relationships, occupational health, and aging.\textsuperscript{117} The first of these conferences, dedicated to exploring psychosocial environmental influences on psychosomatic disease, was held in April of 1970 in Stockholm, drawing illustrious presenters such as Stewart Wolf, Richard Lazarus, Lennart Levi, and none other than Hans Selye. While the majority of presentations focused in one way or another on adaptational challenges to the psychosocial environment, Selye delivered a highly technical report on the etiological development of cardiovascular-stress research, epitomizing his aloofness from the other presenters. Richard Lazarus articulated the growing disjuncture between Selye’s biological model and the social turn in stress research by offering that,

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if we were to use the word ‘stress’ to refer, say, only to Selye’s adaptation syndrome, then its meaning would be restricted entirely to physiological stress, and in fact to an even narrower
\end{quote}

\textsuperscript{116} Wolf and Bruhn, \textit{The Power of Clan}, 109.

concept, namely the ‘non-specific’ adaptation response of tissue systems to any type of noxious stimulation. In so narrowing our focus we are then permitted to deal only with a limited portion of the total problem of society, stress and disease, that is, noxiousness to tissue systems. This could eliminate what I think are more serious, stress-induced, adaptational problems at the level of behavioural [sic] maladjustment, including the functional psychoses, the character disorders (e.g. of criminals, alcoholics and drug addicts), the neuroses, and the countless varieties of subclinical problems of people who live with psychological malaise while not necessarily suffering from a tissue damage.118

As Lazarus reveals, by the beginning of the 1970s, the broad usage of stress required a much broader etiological model than Selye’s conceptualization allowed. Yet, Selye remained austerely committed to his view of biological stress, suggesting that he was perhaps blithely unaware that he was becoming a marginal influence in a field he purportedly ‘fathered.’

By the end of the 1970s, biologists, as well as psychologists, were turning their attention to uncovering social determinants of stress. Relying on population studies of primates, researchers have identified sociological factors influencing stress distribution patterns, including hierarchical rank, gender, and age. Pursuing Bruce McEwen’s theory of allostatic load—a normative, constant deviation from homeostasis resulting from perpetual exposure to stressors—to explain how chronic exposure to stress forces a perpetual deviation from homeostasis, Robert Sapolsky has documented the neurological health risks of low rank in primate hierarchies and Carol Shively has uncovered a correlation between subordinate stress and increased risk for metabolic, cardiovascular, endocrinological and reproductive diseases.119


Similarly, epidemiologists, sociologists and public health researchers have examined stress at the population level, rather than the individual level, and have uncovered a range of social determinants of stress, or what Bruce Link and Jo Phelan have described as “fundamental causes” of disease—conditions that put people “at risk for risk.”

Since the late-1970s, public health researchers have focused on the role of the social environment in fomenting or alleviating stress—particularly to the extent that social networks can provide support to individual, as well as the effects of social hierarchy on emotional health. Sir Michael Marmot's famous studies of British civil servants revealed a correlation in humans between social rank and health—particularly that subordinate office workers register much higher risk for adverse health symptoms due to performance-based stress. Leonard Pearlin and Gary Evans, among others, have documented the socioeconomic risks for increased stress and compromised health, respectively including chronic economic hardship and exposure to discrimination, as well as limitations of the built environment that foment social isolation. Since the early-1990s, a substantial body of research has documented that racial minority and low-socio-economic status

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strongly correlate with high rates of heart disease and mental illness.\textsuperscript{123} University of Michigan sociologist Arline Geronimus’ “weathering hypothesis” explains this phenomenon as a result of cumulative exposure to stressors that progressively weaken immunity and physiological resilience.\textsuperscript{124} As Geronimus has shown, the experience of chronic racial or gender discrimination alone can be so stressful that over time it will predispose an individual to disease.

In the past twenty years, public health research has focused on the extent to which “social capital”—or, the value generated from social networks, for both individual and collective benefit—protects against the development of disease.\textsuperscript{125} Since the mid-1970s, Stanford University sociologist Mark Granovetter has argued that casual and informal social interactions, what he calls “weak ties,” help to establish a safety net that provides therapeutic resources, and


inspires confidence in one’s capacity to access support. More recently, Columbia University psychiatrist Mindy Fullilove has documented the nurturing quality of emotional ecosystems within stable neighborhood communities—and the disastrous consequences of uprooting and destroying these supportive community resources. Similarly, echoing the premise of Jane Jacobs’ germinal theory that community interaction offers support and protection to its members, Harvard University political scientist Robert Putnam has argued that civic activism promotes social cohesion, which is supportive of mental and physical health.

When we recognize the extent to which stress risk factors are determined by political and economic forces often beyond the individual’s control, we gain a perspective of stress as a distinctly ecosocial construct. Calling for a broad understanding of disease as a political problem, historian of medicine and public health Simon Szreter has argued that “we literally create our public health, our understanding of it, and our capacities to monitor and improve it through a continuous historical practice of acts of political will to bring about, fund, and support

this area of knowledge and to act on what we learn about it.”

To that end, the prevalence of stress is more profoundly determined by social structures than by individual behavior, as social status, state policies and economic forces often determine the latitude of personal choices available to different individuals. University of Toronto Professor of Health Sciences, David Coburn has extensively documented how privatization and anti-regulatory policies have contributed to increased income inequality and decreased access to health resources for lower-socioeconomic groups. As a result, domestic and international neoliberal policy has directly contributed to an increased burden of stress-related mental and physiological disease for disadvantaged members of local and global populations.

Conclusion

While Selye was instrumental in laying the foundation for our current understanding of stress—by showing how physiological health is affected by environmental and psychological agents—his disease model was severely limited in its etiological perspective. Guided by a professional standard for reductionist methodology, and catering to a political economy oriented around medical consumerism and state and corporate sponsorship, Selye developed a concept of stress that focused on individual risk and responsibility for disease, to the exclusion of larger social


forces. Striving to retain viability as a researcher, he lent his expert authority to endorse the commercial and anti-regulatory interests of his corporate supporters by proselytizing the central importance of personal choice in stress conditioning and reduction. In doing so, he supported a competitive market economy that distributed disproportionate stress burdens on under-privileged and under-represented members of society, while at the same time telling them that they bore responsibility for alleviating their own stress.

Ironically, Selye actively promoted this individualistic model of stress while the field of stress research was increasingly turning towards an examination of sociological and psychosocial risk factors for stress. Thus, Selye ended up promoting a disease model that was at odds with contemporary theory. Yet, despite its deficiencies, Selye’s theory of stress gained popular endorsement because Selye commanded public attention through his own self-promotional strategies and publicity appearances on behalf of his supporters, and because it resonated with patient-consumers conditioned to seek individualized therapy in the medical marketplace. As a result, from the mid-1960s until Selye’s death in 1982, the popular understanding of stress was at variance with the contemporary academic disease model. In fact, to this day the medical concept of stress retains the markings of individualism assigned to it by Selye as he struggled to keep his own research compatible with the corporate liberal ethos that guided state policy and medical consumerism in the postwar era.
Hans Selye died of a heart attack in 1982 at the age of 75. His obituary in Macleans credited him with promoting the term stress into “part of Everyman’s vocabulary, a buzz word for the cause of myriad maladies affecting modern man.”¹ In Macleans’ estimation, Selye’s main legacy was in impacting popular understandings of health, more so than medical knowledge. Two years earlier, a biographical piece on Selye in the same magazine reported that “having confirmed his place in the medical pantheon, Selye has in the past two decades turned to writing, lecturing and spreading the good news of stress’s constructive powers.”² Though he remained ardently dedicated to his research on stress, in the 1960s and 70s, Selye was increasingly marginalized in a field he purportedly fathered. By the mid-1970s, Selye complained that he had come to feel he was not respected for the worth of his research, but only superficially for his reputation as a “‘founding father’ of stress.”³

Hans Selye’s legacy reveals much about the enduring confusion and conflict in stress research. Selye contributed to our understanding of stress in three important ways: 1) by focusing on the significance of adrenocortical hormones in regulating disease, 2) by highlighting the influence of conditioning behavior and experiences, and 3) by emphasizing processes of adaptation in the formation of chronic diseases and aging. Consequently, Selye’s stress research introduced a new diagnostic category capable of responding to the mid-century rise of chronic, multicausal diseases. Yet, he is not remembered for his revolutionary contributions to etiological theory. Selye is remembered for being the first person to use the term stress to describe a

³ Selye, The Stress of My Life, 264.
specific physiological process. Yet, this is largely due to Selye’s own vociferous insistence that he was responsible for introducing the term “stress” as a physiological concept, despite the reality that he was one of many researchers involved in developing the disease concept of stress. In the history of endocrinology, Selye is remembered as a pioneer of research on the regulatory mechanisms of pituitary and adrenal steroids, the relationship between stress and inflammation, the cardiovascular effects of the stress response, and dynamics of multicausation, including cross-resistance and conditioning. Yet, in popular memory, Selye is not celebrated for his advancement of endocrinological science. Nor is he remembered for his theory of the GAS or for his dogma that stress is the root of all disease. Rather, his legacy as “the father of stress” is associated with his contribution to substantiating the physiological basis of psychological stress—a reputation derived from his commercial relationships and promotional activities, rather than his scientific research.

Selye’s stress research reveals how the disease concept of stress was culturally and economically constructed. Selye’s methodology, funding relationships and self-promotional techniques advanced a disease model that conformed with mid-twentieth-century biomedical principles of objectivity, empiricism and reductionism, as well as the individualist consumer ethos of the medical marketplace. As a histologist, Selye focused on pathophysiology within the individual, emphasizing biochemical changes in cells, tissues and organs as critical etiological mechanisms. Selye did not examine the epidemiological implications of disease, and therefore failed to recognize etiological factors that operate at the population level. Arguably, this failure

actually resulted from Selye’s mastery of his own discipline, and that blame should be attributed to the culture of biomedicine which encouraged disciplinary demarcation as well as reductionist methodology. The boundaries of Selye’s vision as a histologist offer an important lesson about how disciplinary perspective can both empower and limit scientific knowledge.

Yet, it was not biomedical culture alone that encouraged Selye’s individualistic focus. Selye’s commercial interests helped promote an individualistic disease model that obscured ecosocial pathways of disease. As a result, the medicalization of stress sought to naturalize a uni-dimensional model, when in fact stress is a multi-level phenomenon that is largely determined by social, economic and political structures. At the heart of Selye’s medical and philosophical theories of stress were a focus on individual interventions, whether through pharmaceutical treatment, self-medication, or behavior modification. Selye insisted that individuals could manage their own health, and discourage the onset of diseases of adaptation by controlling their exposure to conditioning factors and preserving their adaptation energy. Moreover, he insisted that they reduce their exposure to distress and instead incur eustress by practicing “altruistic egotism” and indulging in their own idiosyncratic wants. Thus, he promoted a popular understanding of stress that focused exclusively on individual causes and therapies that seemed to offer patients the power to improve their own wellbeing. By avoiding salt and red meat, exercising, indulging in stress-reducing diversions, and when necessary, taking stress relieving medications, individuals could take control of their own health. However, this perspective presumed that physical health is controlled by will power, reifying a belief in the psychosomatic nature of disease. Consequently, while the scientific validation, corporate endorsement and functional value of biological stress encouraged its social assimilation, its meaning remains contested and shrouded in ambiguity. This logic has not only contributed to
the ambiguous psychosomatic interpretation of stress, but also failed to account for multi-level and multi-directional social and environmental stress risk factors that are beyond individual control.

Selye helped to revolutionize our understanding of the causes of disease by substantiating the concept of attributable risk and multicausal disease, and thereby reconciling biomedicine with the mid-century rise of chronic disease mortality. His work on stress made a profound foray into the medical investigation of holistic health and helped to legitimate the scientific investigation of the relationship between the mind and the body. Yet, his individualistic and reductionist focus hindered the recognition of social determinants of stress. Indeed, his advocacy of consumer-oriented and behavior-centered therapeutic and diversionary interventions insulated and obscured commercial pathways that influence the distribution of stress. And, perhaps ironically, these same potentially harmful commercial pathways helped “stress” to gain cultural currency.

Appealing to consumer and corporate interests, Selye emphasized psychological anxiety as one of the most widespread risks for stress. In doing so, he blurred the distinction between the psychological theory of stress and what he insisted was a purely physiological response, but encouraged popular belief that psychological tension could induce physiological diseases and increased the marketability of anxiolytic and adrenocortical pharmaceutical drugs. By exploiting the marketability of stress in order to encourage its social assimilation, he promoted biased popular health literacy. Selye was able to manipulate popular health literacy based on his expert scientific authority. He earned this esteemed reputation not simply by producing innovative research, but by developing relationships with powerful research patrons in the US federal government and private industry. In spite of his considerable vested interests, Selye presented
himself as an objective, impartial authority imparting pure scientific knowledge. Moreover, he invoked his expert authority in attempts to manipulate public policy to promote a regulatory environment that favored his own basic research on stress, aging and chronic disease, as well as his patrons’ commercial interests. This reveals both how social forces can influence health literacy and how scientific knowledge can be used for political ends. Selye’s theory upheld the primacy of the market as the principal point of therapeutic access, promoting the assimilation of a disease model that favored consumerist and behavior-oriented treatments, and therefore failed to acknowledge a full spectrum of risk. Moreover, Selye’s formulation of stress was catered to appeal to a culture of medical consumerism that privileged the therapeutic priorities of middle class North Americans with access to primary health care and the means to purchase pharmaceutical remedies.

Stress, as Selye described it, offered patient-consumers a means of managing their own health. Yet, by advancing an individualistic and commercially-appealing theory of stress, Selye obscured the role of ecosocial pathways of disease that distribute stress risk beyond the control of individual interventions and disproportionately burden racial, ethnic and socioeconomic minorities. Stress was conceived as a disease of civilization. As such, it was commonly applied to the protagonists of civilization, not the victims. When it was first popularized, vernacular ideals of stress warned of the hazard of overwork and the frenzied pace of “the business man.” From the late-1940s to the late-1960s—the height of Selye’s career—stress operated as a middle class, white, and largely masculine diagnosis. Selye promoted a disease model that assigned responsibility for risk avoidance to the individual at a time when minority rights movements were fighting to dismantle discriminatory structures and enshrine new protections for social justice in North America. The civil rights, Chicano, American Indian and women’s liberation
movements drew attention to the disproportionate stresses placed upon racial minorities and women, while the War on Poverty exposed the harshness of poverty suffered by “other Americans.” Racial, gender and socioeconomic segregation limited these groups’ physical mobility and access to opportunity, while cultural boundaries impeded their social mobility and social capital. When women were acknowledged as victims of stress, they were only recognized as housewives, incurring trivial stresses from the trials of housekeeping and childrearing, denying the stress of working mothers, single women and other women that did not conform to the contemporary idealized American woman. Moreover, housewives suffering from “the problem that has no name” for feeling trapped in their idealized suburban homes, were prescribed tranquilizers to minimize their psychological stress—to such an extent that the stereotype of the psycho-medicated housewife became a public health concern in the mid-1960s. However, African Americans and the poor were commonly denied any medical intervention to manage their disproportionate burdens of stress. By ignoring social determinants of health, Selye’s individualistic concept of stress failed to recognize race, gender and ethnicity as fundamental determinants of health. As a consequence, the revolutionary therapeutic potential of stress etiology was limited to serve only more affluent members of North American society, and advanced a “victim-blaming” etiological theory that reinforced medical discrimination against minorities, women and the poor.

We now recognize that a lack of social capital and personal mastery contribute to stress. Poverty, limited educational and economic opportunities, geographic isolation, political impotence, pollution and cultural discrimination are all powerful stressors that cannot be controlled by therapeutic behavioral modifications. People living in food deserts cannot simply

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5 Metzl, Prozac on the Couch; Tone, The Age of Anxiety.
decide to make more nutritious choices to minimize the conditioning influence of salt and fat. People living in isolated, low-income high-rises—or people who are working multiple jobs and raising children—may not have access to space or leisure time to prioritize physical exercise. Victims of environmental racism may not have the option to minimize their exposure to harmful toxins. Moreover, people who lack access to health care or channels of health literacy may not know how to make health-wise decisions. And people who have become accustomed to any of these circumstances may have internalized feelings of a limited horizon, or a lack of options for growth or mobility, which can contribute to stress.

The medicalization of stress changed how we perceive health and mortality. Stress informs how we understand aging, risk management and patient responsibility for healthcare. Because we have culturally assimilated a disease model of stress, we recognize the cumulative weight of strenuous experiences, or “wear and tear,” as a weakening force that renders us more vulnerable to disease and physical degeneration. We interpret various excesses as a threat to our health—excessive work, rest, emotion, toxins, exercise or poor nutrition may all disrupt our delicate homeostatic balance and create an opportunity for disease to manifest. While the social indictment of the pace of modern life and overwhelming sensory stimulation for depleting precious vital energy predates the medicalization of stress, the biochemical evidence that prolonged adrenocortical excitement can induce disease offers positivist justification for condemning the wages of civilization. The scientific legitimization of stress promoted the perception that it is a natural force to which everyone is susceptible. Yet, the universalization and naturalization of stress has obscured the reality that the disease model of stress is a manmade construct, influenced by economic and cultural interests, and moreover, that risk for stress is not truly universal as it is not evenly or equitably distributed throughout society.
Appendix A: Glossary of Abbreviations

**US Federal Agencies**
AHCS - USNRC Ad Hoc Committee on Stress
CMR - USNRC Committee on Medical Research
DMS - USNRC Division of Medical Sciences
NCI – National Cancer Institute
NHI - National Heart Institute
NIAID - Institute for Allergy and Infectious Diseases
NIAMD - the National Institute of Arthritis and Metabolic Diseases
NIDR - National Institute for Dental Research
NIH - National Institutes of Health
NIMH – National Institute of Mental Health
NIHDB - National Institute of Neurological Diseases and Blindness
OSRD – Office of Scientific Resource and Development
PHS - Public Health Service
USNRC - National Research Council

**Canadian Federal Agencies**
ACMR - Associate Committee on Medical Research
CNRC - National Research Council
DMR - Division of Medical Research
MRC - Medical Research Council
SSBS – Subcommittee on Shock and Blood Substitutes

**Professional Organizations**
AMA – American Medical Association
APA – American Psychiatric Association
ARNMD – Association for Research on Nervous and Mental Diseases
ASRP - American Society for Research in Psychosomatic Problems
CTR – Council for Tobacco Research
GEB – Rockefeller Foundation General Education Board
IMCE - L’Institut de Médecine et de Chirurgie Expérimentales
LHC – Laurentian Hormone Conference
WFEB – Worcester Foundation for Experimental Biology

**Scientific Terms**
ACTH – adrenocorticotropic hormone
COL - cortisol
DOC (DOCA) – desxocorticosterone (desxocorticosterone acetate)
DSM – *Diagnostic and Statistical Manual* of the American Psychiatric Association
GAS – General Adaptation Syndrome
LAP – lyophilized anterior pituitary extract
PTSD – Post-Traumatic Stress Disorder
SRRS - Social Readjustment Rating Scale
STH – somatotrophic hormone
Appendix B:
The Etiological and Nosological Development of Selye’s Research on Stress

I. The General Adaptation Syndrome (GAS), 1936
Selye explains his unified theory of non-specific disease: when exposed to diverse agents (including extreme temperatures, excessive physical exercise, immobilization, surgical trauma, toxic poisoning) experimental rats developed 1) adrenal hypertrophy, 2) thymic-lymphatic involution, 3) gastro-intestinal ulceration. Reaction occurs in tri-phasic pattern: Alarm Reaction, Stage of Resistance, Stage of Exhaustion. Selye does not use the term stress to describe the GAS.

Key Publications:

II. Crossed-Resistance, Crossed-Sensitization & Adaptation Energy, 1937
Selye explains how exposure to a unique antagonist can induce heightened resistance to all harmful stimuli during the Alarm Reaction (crossed-resistance), yet during the Stage of Resistance, the body loses its crossed-resistance, and instead develops a heightened sensitivity to all stimuli except for the original antagonist (crossed-sensitzation). He argues that over time, repeated demands for adaptation diminish an organism’s capacity for future adaptation due to decreased “adaptation energy.”

Key Publications:

III. Glucocorticoids and Mineralocorticoids, 1937-1944
Selye classifies adrenocorticoids into two primary groups: glucocorticoids (such as cortisol, cortisone and hydrocortisone) decrease inflammation, whereas mineralocorticoids (such as aldosterone and desoxycorticosterone) increase inflammation.

Key Publications:

IV. Shock and Counter-shock, 1940
Selye discovers two phases of Alarm Reaction: Shock (characterized by general adrenal insufficiency and impaired immunological function), and the counter-shock phase (characterized by an increase in adrenocortical secretions, blood volume, blood sugar and chlorides, and body temperature, as well as decreased size and activity of the thymus and other lymphatic organs). Signifies his primary interest in the early stages of the GAS.

Key Publications:
V. Diseases of Adaptation and Conditioning Factors, 1941-1945
Selye finds that the adrenal cortex is primarily responsible for producing chronic degenerative “diseases of adaptation,” such as arthritis, hypertension nephrosclerosis and gastric ulcers. He also finds that certain “conditioning factors,” including temperature, fasting, rest, salts, sugars and proteins (over time, he would add exercise and psychosocial factors to this list, as well as stress, itself) can weaken or strengthen tissues to resist stress.

Key Publications:
“Production of Nephrosclerosis by Overdosage with Desoxycorticosterone Acetate and Sodium Chloride,” Canadian Medical Association Journal 49 (1943).
“Production of Nephrosclerosis and Cardiac Hypertrophy in the Rat by Desoxycorticosterone Acetate Overdosage,” American Heart Journal 27 (1944).

VI. Introduction of Term “Stress” as Cause or Effect of GAS, 1946
Selye adopts use of term “stress” to describe conditions that cause the GAS, as well as the GAS, itself. Defines the GAS as “the sum of all non-specific, systemic reactions of the body which ensue upon long continued exposure to stress.”

Key Publications:

VII. Interhormonal Tension and Pathological Situations, 1947-48
Selye expounds on Walter Cannon’s theory of homeostasis to argue that an imbalance between glucocorticoids and mineralocorticoids contributes to tissue damage and the onset of diseases of adaptation. He also argues that individuals’ “pathological situations”—i.e., personal exposures to stressors, sensitization by conditioning factors, expenditures of adaptation energy, and learned capacities for resistance—affect how they respond to the GAS.

Key Publications:

VIII. Use of term “Stress” as Synonym for the GAS, 1950
Selye introduces the term “stressor” to denote an antagonistic stimulus that initiates the GAS, and begins using the term “stress” to refer to the “interaction between damage and defense,” and notes that “anything that causes stress endangers life.”

Key Publications:
IX. **Granuloma Pouch Technique, 1953**
Selye develops a contained environment for studying the effects of localized stress.

*Key Publications:*

X. **The Philosophy of Gratitude, 1956**
Selye argues that based on observances of cytological behavior, all living things should practice a “philosophy of gratitude,” in which they practice selfishness for the good of all—i.e., work to the best of their ability in pursuit of self-preservation so that society, as a whole, benefits from everyone’s talents and health. He contends that individuals should seek to inspire others’ gratitude. Notably, during this time he also comes to define stress as the “state which manifests itself by the GAS,” and the “rate of wear and tear.”

*Key Publications:*

XI. **Protective Effects of Magnesium and Potassium (and Destructive Effects of Sodium) on Cardiovascular Health**
Finds that conditioning factors of magnesium and potassium salts help to reduce risk for cardiac accidents, while sodium exacerbates them. Emphasizes dietary interventions—through pharmaceutical treatments and lifestyle modifications—to manage heart disease. Also advocates callisthenic exercise to increase resistance to stress.

*Key Publications:*
“Prevention by MgCl$_2$ and KCl of the Vascular Hypersensitivity Induced by Pretreatment with Dihydrotachysterol (DHT),” *International Archives of Allergy* 12 (1958).
“Prevention by MgCl$_2$ and KCl of the Myocardial Necroses Normally Produced by Papain,” *Cardiologica* 33 (1958).
“Production with Sodium Sulphates of an Electrolyte-Steroid-Cardiopathy Characterized by Necroses (ESCN), and its Prevention by MgCl$_2$ and KCl,” *Canadian Journal of Biochemistry* 36 (1958).

XII. **Fibrin and Caliphylaxis**
Selye discovers accelerated model for studying aging in his “fibrin” experiments, and develops means of regenerating cutaneous and glandular tissue by means of “caliphylaxis,” in which laboratory rats grew and molted hardened external shells. Leads him to believe that aging is largely a result of calcium drift, and with pharmacological interventions we might extend life expectancy by as much as thirty years.

*Key Publications:*
“Caliphylaxis and the Concept of ‘Vital Molting,’” *Perspectives of Biological Medicine* 9 (1962)

**XIII. Deviations, Diversions, Eustress & Distress**

Argues that in order to disrupt cycles of harmful stress “grooves” one should find deviations or diversions that help them to relax and distract them from their stress triggers. Selye argues that one should not try to avoid stress, but instead strive to balance good stress (eustress) and bad stress (distress).

*Key Publications:*

**XIV. Altruistic Egotism**

Builds on the concept of the “philosophy of gratitude” to naturalize an individualistic perspective of stress and disease.

*Key Publications:*

**Chronological List of Selye’s Major Publications**

       “Studies on Adaptation,” *Endocrinology* 21 (1937)
       Selye, “Experimental Evidence Supporting the Conception of ‘Adaptation Energy,’”
       *American Journal of Physiology* 123 (1938)
       “Pharmacological Classification of Steroid Hormones,” *Nature* 148 (1941)
       “An Attempt at A Natural Classification of the Steroids,” *Nature* 151, 662 (1943)
       “Role of Sodium Chloride in Production of Nephrosclerosis by Steroids,”
       *Proceedings of the Society for Experimental Biology* 52 (1943)
“Malignant Hypertension Produced by Treatment with Desoxycorticosterone Acetate and Sodium Chloride,” *Canadian Medical Association Journal* 49 (1943)


“Prevention of Gastric Ulcer Formation During the Alarm Reaction,” *American Journal of Digestive Disorders* 11 (1944)

“Influence of High Carbohydrate Diets Upon the Development of Experimental Nephrosclerosis and Allied Cardiovascular Phenomena,” *Canadian Medical Association Journal* 54 (1945)


Appendix C:
Selye’s Funders and Grants
*This is not a complete list of all of Selye’s funders, but is gleaned together from acknowledgements in his publications, as well as archival records.

**Philanthropies:**
Rockefeller Foundation
Josiah Macy, Jr., Foundation
John and Mary R. Markle Foundation
Commonwealth Fund
Banting Fund
Gustavus and Louise Pfeiffer Foundation
Irwin Strasburger Memorial Medical Foundation
Muscular Dystrophy Association of Canada
American Heart Association
Canadian Arthritis and Rheumatism Society
Quebec Heart Foundation
Life Insurance Medical Research Fund
Readers Digest Foundation

**Pharmaceutical Firms** (grants and gratis materials):
Frank W. Horner
Schering Corp.
Ciba
Des Bergers-Bismol
Merck
Smith, Kline & French
Pfizer
Hoffman-LaRoche
Warner-Chilcott Labs
Abbott Laboratories
Geigy Pharmaceuticals
Lederle Laboratories of the American Cyanamid Company
Nordic Biochemicals (ACTH)
Upjohn Company
Billhuber-Knoll Corporation

**State Agencies:**
Committee on Endocrinology, US National Research Council
Committee for Research in Problems of Sex, the Committee on Endocrinology, US National Research Council
Medical Research Board, Office of Surgeon General-US Army
Army Medical Research and Development Command, Department of the US Army
The Division of Medicine and Dentistry Research of the Office of Naval Research National Heart Institute
National Cancer Institute
National Institute of Neurological Diseases and Blindness
National Institute of Mental Health
The Division of Medicine and Dentistry Research of the Office of Naval Research
Subcommittee on Shock and Blood Substitutes, Associate Committee on Medical Research,
Canadian National Research Council
Quebec Department of Health
Canadian National Research Council
Canadian Medical Research Council

Miscellaneous Private Industry:
Council on Tobacco Research (US)
Canadian Tobacco Manufacturers Council
Davis, Polk, Wardwell, Sunderland & Kiendl, LLP (for tobacco industry)
The American Sugar Foundation
Gelatin Products

Notable Grants:
Note that this is not a complete account of all grants awarded to Selye, but a select account
coiled together from diverse sources, including 1) Records of the Associate Committee on
Medical Research, Library and Archives of Canada (ACMR); 2) Records of United States
National Research Council, Division of Medical Sciences, National Academy of Sciences
Archives (DMS); 3) Gregory Goodwin Pincus’s Collected Papers, Library of Congress (GGP); 4)
the University of California, San Francisco, Legacy Tobacco Archive (UCSF-LTA), 5) Figures
reported in popular news media featured in the Hans Selye Collection, University of Montreal
Library (HSC); and 6) Acknowledgements listed in Selye’s peer-reviewed publications.

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<td>“Effects of steroid hormones on the kidney and removal of certain endocrine glands on the actions of steroid hormones”</td>
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<td>1941</td>
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<td>Action of DOCA to delay uremia and inhibit rise in non-protein nitrogen content of blood after nephrectomy; Anaesthetic action of steroids;</td>
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<td>Subcommittee on Shock and Blood Substitutes, Canadian National Research Council. Lung edema and on the role of the adrenal cortex in shock. &quot;Proceedings of the Thirteenth Meeting and a Special Meeting of the Associate Committee on Medical Research,&quot; Mar. 17-18, 1944, Box 6, ACMR.</td>
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Chirurgie Expérimentales

Foundation Gives $150,000 for Psychiatry Department,” HSC.

“McGill Announces Grants of $215,148. Rockefeller Foundation Gives $150,000 for Psychiatry Department,” HSC.

“McGill Announces Grants of $215,148. Rockefeller Foundation Gives $150,000 for Psychiatry Department,” HSC.

“McGill Announces Grants of $215,148. Rockefeller Foundation Gives $150,000 for Psychiatry Department,” HSC.

“McGill Announces Grants of $215,148. Rockefeller Foundation Gives $150,000 for Psychiatry Department,” HSC.

“A Nation’s Health is a Nation’s Wealth. Industry Aids Research.” Montreal Star (Sept. 27, 1946), HSC.

“McGill Announces Grants of $215,148. Rockefeller Foundation Gives $150,000 for Psychiatry Department. Gland Research Aided. Work of Dr. Hans Selye on Adrenal Cortex is Supported by Large Donations” Montreal Daily Star (1944), HSC.

"Study of 'rheumatoid' changes produced by hormones"

"Proceedings of the Seventeenth Meeting of the Associate Committee on Medical Research,” Mar. 29, 1946, Box 6, ACMR."
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<td>Canadian Arthritis and Rheumatism Society</td>
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<td>&quot;$100,000 Gift to U of M For Research. Foundation Supports Famous Doctor’s Work” Montreal Star (Jun. 3, 1954), HSC.</td>
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<td>1952-53</td>
<td>$12,000</td>
<td>Associate Committee on Medical Research, Canadian National Research Council</td>
<td>Studies on the relationship between hormones and tumorigenesis</td>
<td>“Proceedings of the Twelfth Meeting of the Advisory Committee on Medical Research,” Mar. 7, 1952, p. 3 and Appendix A, p. 5, Box 33, folder 30.24, ACMR.</td>
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<td>&quot;Proceedings of the Fourteenth Meeting of the Advisory Committee on Medical Research,&quot; Oct. 6, 1952, p.6, Box 33, folder 30.24, Record Group: MG 30, B 91, ACMR.</td>
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<td>&quot;The interactions of corticoids and growth hormone&quot;; &quot;Studies concerning the mechanism of the General Adaptation Syndrome.&quot;</td>
<td>&quot;Proceedings of the Fifteenth Meeting of the Advisory Committee on Medical Research,&quot; Mar. 9-10, 1953, p. 9, Appendix B, p. 2 and Appendix F, p. 9, Box 33, folder 30.24, ACMR.</td>
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<td>Memorandum disputing causative relationship between cancer and tobacco smoke</td>
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<td>Arthritis and bone disease</td>
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<td>The Division of Medicine and Dentistry Research of the Office of Naval Research</td>
<td>Tissue growth and wound healing</td>
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<td>Memorandum outlining the beneficial diversionary aspects of cigarette smoking</td>
<td>William W. Shinn to David R. Hardy, Memorandum re: AD HOC (Dr. Hans Selye), Dec. 29, 1966, Bates No. 1005083923/3926, UCSF-LTA, <a href="http://legacy.library.ucsf.edu/tid/yiu88d00/pdf">http://legacy.library.ucsf.edu/tid/yiu88d00/pdf</a></td>
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<td>1969-1972</td>
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<td>Council for Tobacco Research &amp; Canadian Tobacco Manufacturers Council</td>
<td>Research on stress and cancer: “Cross-Resistance and Beneficial Effects of Deviation”; “Stress and Relief from Stress”</td>
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