Glands on the Market: Doctors, Drug Companies, and the Making of American Endocrinology, 1889-1919

By

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For Alex & George

Contents

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UMI Abstract

"Glands on the Market" investigates the emergence of clinical endocrinology in the U.S. with a special focus on the contributions of American physicians and pharmaceutical giant, Parke, Davis & Company, in shaping the bourgeoning field between 1889 and 1919. These first thirty years of endocrinology have received very little attention from historians of science and medicine because, as critics have been quick to point out, the field struggled to gain a scientific following in university spaces and was instead subjected to the vagaries and extravagances of the medical marketplace. It was also a period deficient in "blockbuster" drugs, such as insulin, estrogen, and testosterone, which all arrived in the interwar period and have claimed the lion's share of historians' attention. My dissertation shows, however, that in these first thirty years, endocrinology was nurtured and developed by clinicians and drug company employees who worked together to get high-quality endocrine products on the market and into clinics across the nation. Using drug company records, letters of correspondence, and medical periodical literature, I show how this new medical science was born and came of age in the clinic and on the medical marketplace.

Introduction: The Birth of a Clinical Field

The seeds of a new field of clinical medicine, later termed "endocrinology," were planted in Paris in June 1889, following the sensational claims of an eminent Franco-American physiologist, Charles Brown-Séquard, who suggested that testicular extracts from animals could be developed into a rejuvenating tonic for old men. His reasons for proposing this new therapy were simple, he explained in his inaugural address on the subject to the Société de Biologie in Paris. Conventional medical wisdom held that fully functioning testicles were critical to the health and vigor of young men. Building on this logic, Brown-Séquard figured that an underlying cause of the ageing process might be the diminishing function of the testicles. Might it be possible to correct this possible deficiency by injecting healthy testicular extracts in old and decrepit *malades*, he wondered?[1]

Brown-Séquard's shocking idea was made more shocking when he explained to the Société that he had already tested this therapy on himself, and that it worked wonderfully. He was 72 years old, in poor health, and in desperate need of a physical and mental reboot, so it made sense to Brown-Séquard to volunteer himself in this way. After some promising preliminary experiments on old rabbits, he was ready for the needle. First, he crushed up testicular extracts from young guinea pigs and dogs and passed it through a paper filter to remove the pulpy bits. Then, he injected himself into the arms and legs with the filtrate, several times over a three-week period. The good effects he felt from these injections were almost immediate and incredible. He explained that he could mount his stairs more quickly, stand for many more hours at his laboratory bench without tiring, and work well into the

[1] Charles Brown-Séquard, "Des effets produits chez l'homme par des injections sous-cutanées d'un liquide retiré des testicules frais de cobaye et de chien," *Comptes rendus des séances de la Société de biologie et de ses filiales*, June 15, 1889, 415–19. Brown-Séquard explained this reasoning in his first paper on the subject, and the many papers that came after. He made it clear that he was not attempting to reverse the ageing process, or become immortal-- this he thought was impossible--but rather to stave off some of the ill effects of old age, and to perhaps live a little longer.

evening on his manuscripts. He could also urinate more powerfully and defecate with ease, which were feats that had escaped him for many years. All this he explained to his colleagues at the Société de Biologie—naturalists and physicians who had a deep respect for Brown-Séquard's earlier work on nervous physiology, but who were taken aback by the strange direction his work had taken. Brown-Séquard was undeterred by their stunned silence during his address.[2] "I hope that other physiologists of an advanced age will repeat these experiments and demonstrate whether the effects that I have obtained on myself depend or not on my own personal idiosyncrasies."[3]

There was a mixed reception of Brown-Séquard's new therapeutic idea, which was noticed and taken up all around the scientific world within just weeks of his June announcement in Paris. He was an internationally acclaimed physiologist, which facilitated the quick spread of news about his radical therapy. But his foray with testicular extracts left some of his scientific and medical colleagues both scandalized and outraged. Was he being serious, they wondered? Had he completely lost his mind? Others, especially practicing doctors in search of new medicine for clinical use, found his ideas to be compelling and full of promise. As many historians have noted, the "method of Brown-Séquard" was trialed in the clinic by physicians all around the world who were eager to experiment.[4] It began with

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[2] According to one editorialist writing in *Le Figaro*, "the greatest silence reigned" in the room in the wake of Brown-Séquard's initial address, as the Parisian scientific elite attempted to compute what had just transpired. See Gaston Calmette, "L'art de ne pas vieillir," *Le Figaro*, June 13, 1889, 2. Second-hand accounts of Brown-Séquard's announcement usually note the "skeptical" reception, but some enthusiastic reporters, including Jean Frollo, a journalist for *Le Petit Parisien*, stated that Brown-Séquard's speech concluded with "a thunder of applause," which casts some doubt on the entirely skeptical reception of Brown-Séquard's initial presentation. See Jean Frollo, "Rajeunissement," *Le Petit Parisien*, June 15, 1889.

[3] Brown-Séquard, "Des effets produits chez l'homme par des injections sous-cutanées d'un liquide retiré des testicules frais de cobaye et de chien," 418.

[4] Merriley Borell, "Brown-Séquard's Organotherapy and Its Appearance in America at the End of the Nineteenth Century," *Bulletin of the History of Medicine* 50, no. 3 (1976): 309–20; Bert Hansen, "America's First Medical Breakthrough: How Popular Excitement about a French Rabies Cure in 1885 Raised New Expectations for Medical Progress," *The American Historical Review*, April 1, 1998, 414–17; Chandak Sengoopta, *The Most Secret Quintessence of Life: Sex, Glands, and Hormones, 1850-1950* (Chicago: University of Chicago Press, 2006); Elizabeth Siegel Watkins, *The Estrogen Elixir: A History of Hormone Replacement Therapy in America* (Baltimore: Johns Hopkins University Press, 2007).

injections of testicular extracts, but soon extended to all manner of extracts sourced from diverse glands of the body, such as the thyroid, thymus, testicles, ovaries, adrenals, spleen, brain, and pancreas. This was following Brown-Séquard's own theory, extended in 1891, that possibly all glands and all tissues of the body—not just the testicles—secreted something "special" into the blood that could be used therapeutically.

Brown-Séquard's story is legendary among historians of endocrinology, who have been as shocked and amused by his therapies as contemporaries from the fin-de-siècle. Yet, despite the international hullabaloo that Brown-Séquard's therapies generated, historians have yet to make a close and careful study of his movement. They acknowledge that his therapeutic idea did spark an interest in the therapeutic potential of the glands of the body, and that many physicians did use his therapy. But historians of endocrinology have preferred to focus instead on the 1920s and 1930s, when clinical endocrinology really took off. In this period clinicians and scientists had a clearer idea about the system of glands in the body, termed "endocrine glands." Interwar clinicians knew that these glands made up an integrated and carefully orchestrated physiological system that secreted potent chemical messengers, termed hormones, into the bloodstream, and that these hormones affected critical functions in bodily processes as diverse as metabolism, development, growth, and aging. It was a more enlightened era compared to the days of Brown-Séquard, commentators have argued, when physiologists and physicians were still working out how the glands of the body functioned, what exactly they secreted into the blood, and how it related to health and disease.

The 1920s and 1930s was also a period when endocrinology became an indisputably powerful force in the clinic. There was a "goldrush" of discoveries of new hormones of medical relevance, which were processed into powerful chemical drugs.[5] It began in the early

[5] This "goldrush" term comes from Alison Li, "J. B. Collip, A. M. Hanson and the Isolation of the Parathyroid Hormone, or Endocrines and Enterprise," *Journal of the History of Medicine* 47 (1992): 406.

1920s with the discovery of insulin, which was a seemingly miraculous treatment for the once-fatal diabetes.[6] This was followed by many other hormone discoveries, including estrogen, progesterone, testosterone, and human growth hormone in the late 1920s and early 1930s.[7] As historians have explained, interwar endocrinology was a confident and seemingly unstoppable force; it promised to revolutionize medicine, redefine the natural history of disease, and even provide insights into the secrets of life itself.[8]

What we know less about, and what this dissertation closely investigates, is the period that came before the goldrush. How did clinical endocrinology develop from Brown-Séquard's quirky idea, and the questionable therapeutic movement that followed, into its confident interwar form? What important clinical developments occurred in the thirty-year period that elapsed from 1889 to the dawn of the 1920s? Who was responsible for laying down the medical and commercial infrastructure that allowed ground-breaking hormone discoveries to occur? Perhaps most pertinent to this historical recovery mission: why do we know so very little about the period between Brown-Séquard and the discovery of insulin?

Historians of endocrinology Victor Cornelius Medvei and Merrily Borell who wrote the first histories of the field in the late 1970s and early 1980s, are two of the few scholars to have worked closely on the period between 1889 and 1919. Their scholarship is focused on the scientific contributions of physiologists, chemists, and physicians who laid down important scientific foundations for the emerging field.[9] This included, among others, British

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[6] See Michael Bliss, *The Discovery of Insulin* (Chicago: University of Chicago Press, 1982).
[7] Nelly Oudshoorn, *Beyond the Natural Body: An Archaeology of Sex Hormones* (New York, London: Routledge, 1994); Watkins, *The Estrogen Elixir*; Aimee Medeiros, *Heightened Expectations: The Rise of the Human Growth Hormone Industry in America* (Alabama: The University of Alabama Press, 2016); Rebecca M. Jordan-Young and Katrina Karkazis, *Testosterone: An Unauthorized Biography* (Cambridge, Massachusetts; London, England: Harvard University Press, 2019).
[8] Sengoopta, *The Most Secret Quintessence of Life*; Oudshoorn, *Beyond the Natural Body*; Celia Roberts, *Messengers of Sex: Hormones, Biomedicine, and Feminism* (Cambridge, New York: Cambridge University Press, 2007); Lily E. Kay, *The Molecular Vision of Life: Caltech, the Rockefeller Foundation, and the Rise of the New Biology* (New York: Oxford University Press, 1993).
[9] Victor Cornelius Medvei, *A History of Endocrinology* (Lancaster; Boston: MTP Press, 1982); Merriley Borell, "Origins of the Hormone Concept: Internal Secretions and Physiological Research, 1889-1905" (PhD Diss, New Haven, Conn., Yale University, 1976); Merriley Borell, "Setting the Standards for a New Science: Edward

physiologists George Oliver and Edward Schäfer, who discovered in the mid-1890s that adrenal gland extracts had vasopressor effects, and William Bayliss and Ernest Starling, two more British physiologists, who discovered "secretin" and coined the term "hormone" in 1902 and 1905 respectively. It also included American investigators Harvey Cushing, John Abel, and Walter B. Cannon, the first who worked closely on the pituitary gland and the latter two on the adrenal glands in the early 1900s.[10] Medvei's encyclopedic work draws attention to many other scientific investigators across Europe and America whose scattered contributions between Brown-Séquard and the discovery of insulin were the first preliminary steps in the "long and drawn-out procedure" of developing "endocrinology" as a body of scientific knowledge.[11]

Medvei and Borell's coverage of scientific advancements in endocrinology between 1889 and 1919, while important and admirable, has left us without a synthetic and analytic account of how endocrinology was operationalized on the ground as a clinical movement and as a pharmaceutical enterprise in this period.[12] By "clinical movement" I am referring to how Brown-Séquard's method was taken up, put to work, and improved by practicing doctors. And by "pharmaceutical enterprise," I mean the infant drug industry of glandular products that emerged in the wake of Brown-Séquard's initial address in 1889 and continued to grow throughout the 1890s and early 1900s, especially in America. As yet, we have only an incomplete account of the early history of endocrinology as a clinical and pharmaceutical

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Schäfer and Endocrinology," *Medical History* 22, no. 03 (July 1978): 282–90; See also Richard B. Welbourn, "The Emergence of Endocrinology," *Gesnerus* 49, no. 2 (1992): 137–50, https://doi.org/10.1163/22977953-04902003; See also D. Lynn Loriaux, *A Biographical History of Endocrinology* (John Wiley & Sons, 2016).

[10] See Merriley Borell, "Organotherapy, British Physiology, and Discovery of the Internal Secretions," *Journal of the History of Biology* 9, no. 2 (1976); Borell, "Origins of the Hormone Concept"; Welbourn, "The Emergence of Endocrinology"; Garabed Eknoyan, "Emergence of the Concept of Endocrine Function and Endocrinology," *Advances in Chronic Kidney Disease* 11, no. 4 (October 2004): 371–76.

[11] Medvei, *A History of Endocrinology*, 339.

[12] See p. 338 of Medvei in particular, where he describes the emergence of the "New Physiology" and its distinction with the earlier therapeutic enterprise.

phenomenon in America, and as it was experienced by working clinicians and drug company employees.[13] This dissertation aims to fill part of this lacuna.

Gaps exist in our historical knowledge in the case of clinical endocrinology, I suggest, because of how past historians have approached the field. Like some of Brown-Séquard's contemporaries in the 1890s (and beyond), historians have struggled to recognize his bizarre therapy, and the therapies that were practiced by his physician-disciplines, as real "scientific medicine." This was the age of bacteriology, after all, where innovative and effective vaccines and serotherapies were being developed in venerable academic institutions, including the Pasteur Institute in Paris and the Institute for Infectious Diseases in Berlin.[14] Brown-Séquard's drugs seemed to pale by comparison; they were often crude and elementary, and a far cry from the sophisticated hormone drugs that were to come. What's more, as historians have explained, Brown-Séquard's ideas also attracted "quacks" and "charlatans" who claimed that the "elixir of life"—a moniker used in the U.S. for Brown-Séquard's testicular extract therapy—could radically cure diseases, which functioned to taint the legitimacy of his movement. Even the serious followers of Brown-Séquard's method in these early years seemed to administer therapies on purely empirical grounds; absent were clear physiological principles guiding the use of glandular extracts in the clinic, and how they worked in the body. Indeed, it took until the late 1910s and early 1920s for the scientific community to gain more confidence in the endocrine system of glands and its therapeutic

[13] For another dissertation that draws attention to the clinical and pharmaceutical valences of early endocrinology, albeit in France, see André Marchand, "Opothérapie: émergence et développement d'une technique thérapeutique (France, 1889-1940)" (Conservatoire national des arts et métiers (CNAM), 2014).
[14] For literature on turn-of-the-century vaccines, see Jonathan Simon and Christoph Gradmann, eds., *Evaluating and Standardizing Therapeutic Agents, 1890–1950* (London: Palgrave Macmillan, 2010); Jonathan Simon, *Diphtheria Serum as a Technological Object: A Philosophical Analysis of Serotherapy in France 1894-1900* (Lanham: Lexington Books, 2017); Jonathan Simon, "Quality Control and the Politics of Serum Production in France," in *Evaluating and Standardizing Therapeutic Agents, 1890-1950*, ed. Christoph Gradmann and Jonathan Simon (Palgrave Macmillan, 2010), 89–104; Gerald L. Geison, *The Private Science of Louis Pasteur* (Princeton, N.J.: Princeton University Press, 1995); Evelynn Maxine Hammonds, *Childhood's Deadly Scourge: The Campaign to Control Diphtheria in New York City, 1880-1930* (Baltimore: Johns Hopkins University Press, 1999).

potential. For these reasons, and taking his cue from his interwar and postwar endocrinologists who reflected on the emergence of the field, Medvei described the first thirty years of endocrinology as a period of "drought" and of "crisis" and an era in which clinical endocrinology was in disrepute.[15] There were few scientific advancements relative to the interwar period, small buy-in from universities, and no landmark discoveries of blockbuster drugs until the arrival of insulin in 1921.

But should an absence of these conventional hallmarks of scientific progress be taken as evidence that "progress" did not occur in clinical endocrinology? Should we continue viewing the first three decades of clinical endocrinology for what it purportedly lacked in a scientific sense? In this dissertation, I argue that much can be learned from the first three decades of clinical and pharmaceutical endocrinology if it is approached with a new perspective. Rather than overlooking the empirical therapies employed by doctors, this dissertation asks: how did physicians develop a bourgeoning field of therapeutics? Instead of categorizing early endocrinology as a field led astray by commercially motivated actors, I ask: how did the medical marketplace, and especially manufacturing houses, shape the emergence of the clinical field? Rather than measuring glandular products against the yardsticks of vaccines and serotherapy, I greet those who used Brown-Séquard's therapies on their own terms. Why did doctors use these products? What did they do to develop his ideas?

"Glands on the Market" thus unearths the voices of doctors and drug companies from the archive to learn more about how endocrinology grew up between 1889 and 1919. It also pays close attention to Brown-Séquard himself, who has received superficial attention from many historians but not yet sustained analysis.[16] Focusing first on France, where Brown-

[15] Medvei, *A History of Endocrinology*, 385.

[16] Other than his various biographers, Merriley Borell is the historian who has given the most attention to Brown-Séquard. Her doctoral dissertation and articles served as my entry point into this project. See Borell, "Origins of the Hormone Concept"; Borell, "Brown-Séquard's Organotherapy"; Borell, "Organotherapy, British Physiology, and Discovery of the Internal Secretions"; Merriley Borell, "Organotherapy and the Emergence of Reproductive Endocrinology," *Journal of the History of Biology* 18, no. 1 (1985): 1–30.

Séquard launched his ideas, and then shifting to the U.S. context, where the glandular product drug industry was very active, I show that not all doctors who practiced Brown-Séquardian therapeutics were "quacks" and "charlatans." There was a small but growing community of serious investigators who exerted considerable efforts to reform Brown-Séquardian remedies into workable therapies that were effective in the clinic. I show that by 1900, this community of doctors came to rely on the expertise of high-end manufacturing houses to produce new glandular products. I focus especially on the relationship that emerged between American doctors and Parke, Davis & Co.—a Michigan-based company which was one of America's largest pharmaceutical manufacturers at the time, and a leader in glandular product development.[17] Between 1900 and 1919, Parke, Davis and doctors worked together to continue developing the new field of glandular therapeutics, which involved detailed experimental work in the Parke, Davis laboratory, as well as a coordinated system of clinical testing of drugs-in-development, which took place in thousands of clinics across the nation.

I argue that these doctors and drug company employees brought the clinical field to life between 1889 and 1919. Their successes were not expressed in the publication of new physiological theories, or by unveiling stunning new techniques in the clinic. Rather, they shaped endocrinology by performing ordinary and extraordinary labor, in clinics and in corporate laboratories, to develop Brown-Séquard's original therapy into something that was workable. It was through their efforts, I suggest, that a new therapeutic method, once so

[17] Parke, Davis & Co. were the most active in the glandular market, with the possible exception of Armour & Company, who were also mentioned frequently by physicians in medical periodical literature. I have found evidence that physicians also bought glandular products from Merck & Co. and the New York Pasteur Institute (under Paul Gibier's directorship), and Britain's Burroughs Wellcome & Co. Eli Lilly & Co. started to invest heavily in the field in the 1910s. H. K. Mulford, a leader in vaccine manufacturing in the 1890s, were much slower to than their competitors to develop glandular products. According to the trade literature that exists at the Kremers Reference Files at the American Institute for the History of Pharmacy, H. K. Mulford did not get into the glandular product game until the 1910s at the earliest. Note that there were smaller companies that sold glandular products, such as Frederick Stearns & Co., Bovinine, G. W. Carnrick & Co., and Shering & Glatz, evidenced by advertisements that they placed in medical periodicals. However, I have not seen strong evidence in the medical periodical literature that these smaller companies were regularly patronized by orthodox physicians.

marginal and odd, matured into mainstream American medicine that came to be practiced in clinics all across the nation.

Historiographical Contributions: Clinical Endocrinology as Scientific Medicine

The rise of scientific medicine at the turn of the century is often explained through the achievements of medical scientists in elite laboratories, such as Louis Pasteur and Robert Koch, who formulated groundbreaking vaccines and forever changed the way infectious disease was treated in the clinic.[18] We hear and read far less often, and sometimes not at all, from doctors and drug companies.[19] How did they experience the rise of scientific medicine at the turn of the century? In what ways were they involved in shaping the emergence of new scientific and clinical fields?

"Glands on the Market" offers the history of endocrinology as an ideal case study for answering some of these questions. By showcasing the stories of doctors and drug companies and detailing why they were of particular importance to the rise of endocrinology, this dissertation hopes to create space for new questions about the revolution in scientific medicine at the turn of the century. Were medical scientists always the change-makers, as histories of bacteriology suggest? Did new medicine always get produced in labs? What roles

[18] There is an old and established literature that positions laboratories and medical scientists as central to the rise of scientific medicine at the turn of the century. See, for example, W. F. Bynum, *Science and the Practice of Medicine in the Nineteenth Century* (Cambridge, England; New York: Cambridge University Press, 1994); Andrew Cunningham and Perry Williams, *The Laboratory Revolution in Medicine* (Cambridge, England; New York, NY: Cambridge University Press, 1992); Harry M. Marks, *The Progress of Experiment: Science and Therapeutic Reform in the United States, 1900-1990* (Cambridge, England; New York: Cambridge University Press, 1997).

[19] Drug companies are almost always excluded from histories of the bacteriological revolution, and the revolution in scientific medicine in general. When we do hear about doctors, they are often presented as antagonists to the new bacteriological medicine. For literature on physicians' resistance to the new scientific medicine, see Gerald L. Geison, "Divided We Stand: Physiologists and Clinicians in the American Context," in *Therapeutic Revolution: Essays in the Social History of American Medicine*, ed. Morris J. Vogel and Charles E. Rosenberg (Philadelphia: University of Pennsylvania Press, 1979), 67–90; Russell C. Maulitz, "'Physician versus Bacteriologist': The Ideology of Science in Clinical Medicine," in *The Therapeutic Revolution: Essays in the Social History of American Medicine*, ed. Morris J. Vogel and Charles E. Rosenberg (Philadelphia: University of Pennsylvania Press, 1979), 91–108; Hammonds, *Childhood's Deadly Scourge*.

did physicians play in shaping the production of knowledge and medical products? How should pharmaceutical companies be factored into histories of scientific progress? [20]

The history of scientific medicine is ripe for critical histories about the commercial and clinical valences of the laboratory revolution. We already have compelling literature that shows there was an "invisible industrialist" behind the production of scientific knowledge, as argued by Jean-Paul Gaudilliére and Ilana Löwy, and others.[21] We also know that the turn of the century was a period when the pharmaceutical industry was growing in Europe and America and forming strong connections with medical communities.[22] This was particularly true of the self-styled "ethical" manufacturing firms, a segment of the market that sought to differentiate itself from "patent" or "proprietary" manufacturers by publicly professing to abide by the values of the orthodox medical community. This meant condemning the use of patents, decrying "profit-seeking" behaviors, and promising to commit to the production of medicine that was both honest and "scientific" –that is, produced in laboratories, without secret ingredients, and using uniform strengths.[23]

The attitudes of clinicians to drug companies were also changing in this period. As historian Joseph Gabriel has argued, clinicians started to accept (and even embrace) the

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[20] Indeed, similar questions have been asked of other scientific fields, especially natural history. See especially work by Lynn K. Nyhart, who has given close attention to how natural history, and natural historians, traversed the laboratory revolution. See especially Lynn K. Nyhart, *Modern Nature: The Rise of the Biological Perspective in Germany* (Chicago and London: University of Chicago Press, 2009); Lynn K. Nyhart, "Natural History and the 'New' Biology," in *Cultures of Natural History*, ed. Nicholas Jardine, James A. Secord, and E. C. Spary (Cambridge; New York: Cambridge University Press, 1996), 426–43. Another illuminating chapter in *Cultures*, which launches a similar argument about science taking place in non-university spaces, is Anne Secord, "Artisan Botany," in *Cultures of Natural History*, ed. Nicholas Jardine, James A. Secord, and E. C. Spary (Cambridge; New York: Cambridge University Press, 1996), 378–93.

[21] Jean-Paul Gaudillière and Ilana Löwy, eds., *The Invisible Industrialist: Manufactures and the Production of Scientific Knowledge* (Houndmills, Basingstoke, Hampshire; New York: Palgrave Macmillan, 1998).

[22] Jonathan Liebenau, *Medical Science and Medical Industry: The Formation of the American Pharmaceutical Industry* (Baltimore: Johns Hopkins University Press, 1987); Joseph M. Gabriel, *Medical Monopoly: Intellectual Property Rights and the Origins of the Modern Pharmaceutical Industry* (Chicago: The University of Chicago Press, 2014); Li, "J. B. Collip, A. M. Hanson and the Isolation of the Parathyroid Hormone, or Endocrines and Enterprise."

[23] Gabriel, *Medical Monopoly*; Janice Rae McTavish, *Pain and Profits: The History of the Headache and Its Remedies in America* (New Brunswick, N.J.: Rutgers University Press, 2004) See especially Chapter 3, "Doctors and the Drug Trade."

patent model of intellectual property protection rather than to eschew it, as they had done in the early and mid-nineteenth century.[24] That is to say, ethical pharmaceutical companies and their drugs were becoming increasingly integrated in clinical medicine starting at the turn of the century, and certainly by the interwar period.[25] Other scholarship pushes the argument further, demonstrating that pharmaceutical companies were also producers of scientific and medical knowledge.[26]

We also have an old but still-growing literature showing that doctors were gaining in prominence and confidence at the turn of the century and were capable of doing more than just receiving or resisting scientific knowledge from laboratories. Paul Starr has famously argued that American physicians were developing their "sovereignty" in this period,[27] and as other scholars have shown, this sometimes amounted to resistance to scientific knowledge and scientific instruments,[28] and scientific processes for treating disease.[29] In some cases, and as this dissertation demonstrates specifically, doctors found themselves in the role of primary knowledge producers, especially when there was an absence of guidance from physiologists and chemists. [30] This led them to turn to each other, to drug companies, and to their own experimental programs for new answers.

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[24] Gabriel, *Medical Monopoly*.
[25] John Patrick Swann, *Academic Scientists and the Pharmaceutical Industry: Cooperative Research in Twentieth-Century America* (Baltimore: Johns Hopkins University Press, 1988); John Parascandola, *The Development of American Pharmacology: John J. Abel and the Shaping of a Discipline* (Baltimore and London: Johns Hopkins University Press, 1992); Liebenau, *Medical Science and Medical Industry*.
[26] See Jeremy A. Greene, *Prescribing by Numbers: Drugs and the Definition of Disease* (Baltimore: Johns Hopkins University Press, 2007).
[27] Paul Starr, *The Social Transformation of American Medicine* (New York: Basic Books, 1982).
[28] Maulitz, "The Therapeutic Revolution"; Geison, "The Therapeutic Revolution"; Hammonds, *Childhood's Deadly Scourge*.
[29] See John Harley Warner, *The Therapeutic Perspective: Medical Practice, Knowledge, and Identity in America, 1820-1885* (Cambridge: Harvard University Press, 1986); John Harley Warner, "Ideals of Science and Their Discontents in Late Nineteenth-Century American Medicine," *Isis* 82, no. 3 (September 1991): 454–78, https://doi.org/10.1086/355837; Eli Osterweil Anders, "'A Plea for the Lancet': Bloodletting, Therapeutic Epistemology, and Professional Identity in Late Nineteenth-Century American Medicine," *Social History of Medicine* 29, no. 4 (November 1, 2016): 781–801, https://doi.org/10.1093/shm/hkw026.
[30] Ilana Löwy, "Biotherapies of Chronic Diseases in the Inter-War Period: From Witte's Peptone to Penicillium Extract," *Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences*, Drug Trajectories, 36, no. 4 (December 1, 2005): 675–95, https://doi.org/10.1016/j.shpsc.2005.09.002; Ilana Löwy, *Between Bench and Bedside: Science, Healing, and*

If we know so much about the rising prominence and significance of both doctors and drug companies at the turn of the century, why do they continue to be left out of accounts of progress in scientific medicine in this period? It can be partly explained by the disciplinary divides of historians, who are liable to treat differently the subject matters of the sciences, clinical medicine and pharmacy and pharmaceuticals. For example, a historian of science, who is interested in scientists, might not be very interested in what doctors did in clinics, and so they do not appear in their history. But it can also be explained by long held and antiquated assumptions in the history of science and medicine about who was responsible for making science, and where it got made. Scientists, usually based in academic institutions and universities, have been given the most credit for scientific development at the turn of the century. I am referring here to historical literature, young and old, that underscores the influence of individual scientists, individual physiological research schools and high-powered institutions in transforming the state of medicine at the turn of the century.[31]

Yet, doctors and pharmaceutical actors did scientific work too, and should be given credit for their role in new fields of clinical medicine.[32] In the case of endocrinology, and as I show throughout this dissertation, doctors who worked with glandular drugs kept abreast of physiological and chemical literature and tested newly elaborated principles in clinical trials. Ethical pharmaceutical houses employed physiologists and chemists, recruited directly from universities, and produced their own portfolios of scientific research. What's more, both

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Interleukin-2 in a Cancer Ward (Cambridge, Mass.: Harvard University Press, 1996); Christiane Sinding, "Making the Unit of Insulin: Standards, Clinical Work, and Industry, 1920-1925," *Bulletin of the History of Medicine* 76, no. 2 (2002): 231–70.

[31] See Gerald L. Geison, *Michael Foster and the Cambridge School of Physiology: The Scientific Enterprise in Late Victorian Society* (Princeton, N.J.: Princeton University Press, 1978); Geison, *Private Science*; Daniel Philip Todes, *Pavlov's Physiology Factory: Experiment, Interpretation, Laboratory Enterprise* (Baltimore: Johns Hopkins University Press, 2002); Laura Otis, *Müller's Lab* (Oxford; New York: Oxford University Press, 2007); Aro Velmet, *Pasteur's Empire: Bacteriology and Politics in France, Its Colonies, and the World* (New York, NY: Oxford University Press, 2020); Bruno Latour, *The Pasteurization of France* (Cambridge, Mass.: Harvard University Press, 1988); Christoph Gradmann, *Laboratory Disease: Robert Koch's Medical Bacteriology* (Baltimore: Johns Hopkins University Press, 2009).

[32] In this stance I join the likes of Christiane Sinding, who has foregrounded the role of manufacturers and clinicians in making insulin. See Sinding, "Making the Unit of Insulin."

doctors and drug companies performed considerable experimental labor in getting new drugs made and into patient bodies. This is argument is pursued in particular in the second half of the dissertation, starting with Chapter 3.

By exploring this experimental work done by clinicians and drug companies at the turn of the century, I am contributing to the conversations already initiated by Alison Li and Christiane Sinding, who have spotlighted the stories of doctors who were deeply involved in the drug production process in the late 1910s and early 1920s.[33] I am also building on work by historians of American medicine, who have focused on the daily labor of physicians, their perspectives, and the pragmatics of doing clinical work.[34] Histories of American medicine are starting to seriously consider the role of the marketplace in shaping twentieth-century medicine, and "Glands on the Market" aims to contribute to this conversation.[35] Historian of medicine Nancy Tomes is at the vanguard of this literature, showing recently that American patients became "medical consumers" at the turn of the century and "remade" the experience of being a patient.[36] Similarly, "Glands on the Market" shows that doctors, too, bought into a

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[33] Li, "J. B. Collip, A. M. Hanson and the Isolation of the Parathyroid Hormone, or Endocrines and Enterprise"; Sinding, "Making the Unit of Insulin"; Löwy, "Biotherapies of Chronic Diseases in the Inter-War Period"; Ilana Löwy, "The Strength of Loose Concepts — Boundary Concepts, Federative Experimental Strategies and Disciplinary Growth: The Case of Immunology," *History of Science* 30, no. 4 (December 1992): 371–96, https://doi.org/10.1177/007327539203000402.

[34] This body of scholarship was pioneered by John Harley Warner, who wrote about the agency of American doctors who were trained in the ways of the new scientific medicine in Europe, but who came back to deal with different realities in America. See Warner, *The Therapeutic Perspective*; John Harley Warner, *Against the Spirit of System: The French Impulse in Nineteenth-Century American Medicine* (Baltimore and London: Johns Hopkins University Press, 1998). Histories Christopher Crenner and Steve Stowe have built on this work, revealing that some doctors who were well-schooled in medical doctrine had to adapt their methods to the needs of their patients and the exigencies of the clinic. Christopher Crenner, *Private Practice in the Early Twentieth-Century Medical Office of Dr. Richard Cabot* (Baltimore: The Johns Hopkins University Press, 2005); Steven M. Stowe, *Doctoring the South: Southern Physicians and Everyday Medicine in the Mid-Nineteenth Century* (Chapel Hill, London: The University of North Carolina Press, 2004).

[35] Tamara Venit Shelton, *Herbs and Roots: A History of Chinese Doctors in the American Medical Marketplace* (New Haven, London: Yale University Press, 2019); Greene, *Prescribing by Numbers*; Nancy Tomes, *Remaking the American Patient: How Madison Avenue and Modern Medicine Turned Patients into Consumers* (Chapel Hill: University of North Carolina Press, 2016).

[36] Tomes, *Remaking the American Patient*; I am also inspired by new histories of science and capitalism, such as Lukas Rieppel, Eugenia Lean, and William Deringer, "Introduction: The Entangled Histories of Science and Capitalism," *Osiris* 33, no. 1 (2018): 4, https://doi.org/10.1086/699170; Victoria Lee, "The Microbial Production of Expertise in Meiji Japan," *Osiris* 33, no. 1 (2018): 171–90; Robert Bud, "Introduction (Focus: Applied Science)," *Isis* 103, no. 3 (2012): 515–17, https://doi.org/10.1086/667971; Paul Lucier, "The Origins of Pure and Applied Science in Gilded Age America (Focus: Applied Science)," *Isis* 103, no. 3 (2012): 527–36.

new model of commercial medicine around 1900, and even invited it into their clinics, at least in early endocrinology. While the doctors in my story were hyper-aware of the importance of maintaining professional boundaries between profit and medical practice, they also knew instinctually that these lines had to be blurred if they were to access and improve the newest line of medicine. Simply, evidence shows that developing a new drug was not possible without the assistance of a reliable drug company.

Historians of pharmacy have made note of the partnerships that started to form between American doctors and ethical firms at the turn of the century,[37] and there is a body of literature that describes this process in the interwar and postwar years.[38] The discovery of insulin in 1921 is heralded by these historians as the moment when university researchers and pharmaceutical houses came into dynamic collaboration, evidenced by the pioneering partnership brokered between the University of Toronto and Indiana-based pharmaceutical company Eli Lilly in their development of Illetin (insulin). The history of early endocrinology that I am excavating suggests that this infrastructure—the network between university medical departments, physicians, and ethical drug companies—was established well before the discovery of insulin. It was built in America at least as early as the 1890s, evidenced by collaborations between physicians and drug companies including Parke, Davis & Co. in the production of drugs such as thyroid extract, Adrenalin and Pituitrin (pituitary extract).

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[37] For example, see Liebenau, *Medical Science and Medical Industry*. Joseph Gabriel has also written on this topic. See Joseph M. Gabriel and Bennett Holman, "Clinical Trials and the Origins of Pharmaceutical Fraud: Parke, Davis & Company, Virtue Epistemology, and the History of the Fundamental Antagonism," *History of Science* 58, no. 4 (December 1, 2020): 535, https://doi.org/10.1177/0073275320942435; Gabriel, *Medical Monopoly*.

[38] Swann, *Academic Scientists and the Pharmaceutical Industry*; Parascandola, *The Development of American Pharmacology*; John Parascandola, "Industrial Research Comes of Age: The American Pharmaceutical Industry, 1920-1940," *Pharmacy in History* 27, no. 1 (1985): 12–21; Nicolas Rasmussen, "The Drug Industry and Clinical Research in Interwar America: Three Types of Physician Collaborator," *Bulletin of the History of Medicine* 79, no. 1 (2005): 50–80; Nicolas Rasmussen, "The Moral Economy of the Drug Company–Medical Scientist Collaboration in Interwar America," *Social Studies of Science* 34, no. 2 (2004): 161–85, https://doi.org/10.1177/0306312704042623.

Historians of American medicine have been slower to realize these connections, however. The field has been preoccupied with the antagonism that existed between medical elites and manufacturing houses in the period before World War I, leaving little room for exploration of moments and sites of collaboration. Much of this literature is concerned with the medical community's efforts to regulate the medical marketplace to prevent fraudulent and dangerous drugs from entering the clinic. Well documented are the efforts of American Medical Association (AMA) elites who successfully lobbied for sweeping drug legislations that arrived in 1902 and 1906,[39] curtailed drug company advertisements in medical periodicals, and set up the Council of Pharmacy and Chemistry, established in 1905, to chemically and pharmacologically test commercial drugs for their safety and "ethical" status.[40] Well documented, too, is the unruly state of the American medical marketplace at the turn of the century, which included both "toadstool millionaires"—James Harvey Young's endearing term for profit-seeking patent manufacturers—and a plethora of unlicensed alternative healers who posed a threat to orthodox medicine in myriad ways.[41] The medical establishment was in the mood for reform at the turn of the century, historians of medicine have long-argued, and this took the form of aggressive professional gatekeeping.

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[39] Morris Fishbein, *A History of the American Medical Association, 1847 to 1947* (Philadelphia: Saunders, 1947); Starr, *The Social Transformation of American Medicine*; Simon and Gradmann, *Evaluating and Standardizing*; Daniel P. Carpenter, *Reputation and Power: Organizational Image and Pharmaceutical Regulation at the FDA* (Princeton: Princeton University Press, 2010); Eric W. Boyle, *Quack Medicine: A History of Combating Health Fraud in Twentieth-Century America* (Santa Barbara, Calif.: Praeger, 2013); Terry S. Coleman, "Early Developments in the Regulation of Biologics," *Food and Drug Law Journal* 71, no. 4 (2016): 544–607.

[40] Starr, *The Social Transformation of American Medicine*. Starr explains that the Council on Pharmacy and Chemistry was established in 1905 to test drugs within the AMA laboratory for the purposes of communicating to physicians the nature of the "ethical" drug on the market. These drugs were listed in the "New and Nonofficial Remedies" section of *JAMA*, which served as the AMA's recommendation on whether a drug was worthy of clinical application. Officially, the CPC stated that they did not make recommendations about drugs, or test for therapeutic efficacy. In practice, however, if a drug was deemed "ethical" and safe by the CPC, then it did serve as a ringing endorsement for AMA members. See especially pp. 112-144 of Paul Starr.

[41] James Harvey Young, *The Toadstool Millionaires: A Social History of Patent Medicines in America Before Federal Regulation* (Princeton, N. J.: Princeton University Press, 1961); Norman Gevitz, ed., *Other Healers: Unorthodox Medicine in America* (Baltimore, London: Johns Hopkins University Press, 1988).

What the history of endocrinology shows us is that doctors could also regulate the production of commercial medicine at the turn of the century by working *with* the company. As this dissertation demonstrates, American physicians accepted Parke, Davis & Co.'s advances, and established relationships with the company, not as subordinates but as empowered and discerning stakeholders. Doctors had their own agenda, which was specifically concerned with getting good quality glandular drugs into the clinic and preventing bad quality products from reaching the marketplace.

Working with the company, and not against it, was especially important in American endocrinology, where the major producers of glandular products were corporate actors, and where the state declined to formally regulate drug production and distribution, as Chapter 2 will detail. Doctors had nothing to gain by ostracizing Parke, Davis & Co. or getting them offside. This is because by 1910, it was very clear to both doctors and the company that the ethical manufacturer was physicians' best pathway for improving and further developing the pharmaceutical and clinical field.

Sources

"Glands on the Market" begins with Brown-Séquard's story, which has been, at times, challenging to unearth. This is because Brown-Séquard was shunned by some of his elite scientific and medical colleagues in Paris in the immediate wake of his address, which makes his story sometimes difficult to track in the archive. The Académie des Sciences and the Académie de Médecine, two of academic societies that Brown-Séquard frequented, collectively disapproved of his testicular injections, and remained remarkably silent on the subject in their official organs, the *Comptes rendus de l'Académie des Sciences* and the *Bulletin de l'Académie nationale de Médecine,* especially in the first few years.[42] Their

[42] Brown-Séquard's name was not mentioned in either the Académie de Médecine or the Académie des Sciences in association with his testicular liquid in 1889, 1890, or even 1891. The *Bulletin de l'Académie nationale de*

resolve did crack a little in 1892 and 1893, when Brown-Séquard's unusual therapy picked up more momentum with elite savants, some of whom, including the likes of Carl Vogt and Louis Pasteur himself,[43] professed personal benefits from being injected with Brown-Séquard's elixir. And yet, of the fifty-odd publications authored by Brown-Séquard about testicular injections or injections of other organic extracts between 1889 and his death in 1894, only five of them were published in the *Comptes rendus de l'Academie des Sciences* and none were published in the *Bulletin*.[44]

Brown-Séquard was left to place his articles about his testicular injections in two scientific venues in which he had ultimate editorial control. They were the *Comptes rendus de la Société de Biologie*, the organ of the Société de Biologie, of which he was president, and the *Archives de physiologie*, a journal that Brown-Séquard himself founded and continued to edit through the testicular years. Almost all his academic publications, commentaries, and joint papers with his assistant Jacques-Arsène d'Arsonval about his new therapy appear in these two journals, and I rely on them heavily for the rich descriptions they

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médecine mentions Brown-Séquard's testicular injections for the first time in September of 1891, but only in passing and as a way of signaling to his more respectable work on the physiology of glands. See M. Lancereaux, "Ablation presque complète du pancréas ; diabète," *Bulletin de l'Académie nationale de médecine*, séance du 29 Septembre, 1891, p. 369. He writes : "L'histoire de M. Brown-Séquard n'est pas à dédaigner à cet égard ; il a fait quelque chose de bizarre avec son suc testiculaire qu'on a tourné en ridicule. Mais dans ces derniers temps, M. Brown-Séquard et M. d'Arsonval ont étudié les organes qui paraissent ne servir à rien : les capsules surrénales, la rate, la thyroïde."

[43] *Le Figaro* documents the treatment of Karl Vogt with Brown-Séquard's injections. The article is entitled "The Road to Damascus," and explains Vogt's initial skepticism of testicular injections and then his change of heart when his doctor-son convinced him to try the method "séquardienne" to treat his neurasthenia. It seemed to do the trick—after seven injections, Vogt perked up, felt a return of his masculine vigor, and resumed his normal university duties. He then continued the injections, even though he felt well again, out of "simple curiosity." His son, William Vogt, was so impressed with his father's recovery that he decided to go to Paris to study and collaborate with Brown-Séquard and d'Arsonval in their production of the "precious potion." See Émile Gautier, "Un Chemin de Damas," *Le Figaro*, May 6, 1893, p. 1. For details on Pasteur's foray with Brown-Séquard's injections, see Louis-Cyril Celestin, *Charles-Edouard Brown-Séquard: The Biography of a Tormented Genius* (Springer International Publishing, 2014), 205. There is evidence that Pasteur also recommended that others be treated with Brown-Séquard's injections. See "The Deathbed of M. Taine," *The New York Times*, March 7, 1893, p. 9, which reports the death of Mr. Hippolyte Adolphe Tain of the French Academy, who had been receiving Brown-Séquard's fluid before his death "on the advice of M. Pasteur."

[44] To make these estimates, I am using the complete bibliography of Brown-Séquard's works collated by Michael J. Aminoff, *Brown-Séquard: An Improbable Genius Who Transformed Medicine* (New York, NY: Oxford University Press, 2011). See Aminoff's appendix.

provide about Brown-Séquard's method and publishing strategy. They also introduce us to some of the doctors who participated in his movement. Eager commentators wrote in to the Société de Biologie or the *Archives* with clinical reports that detailed their successes and failures with the liquid, sometimes citing hundreds (and in some cases, thousands) of experiments they had performed on patients.

To get a sense for the public reception of Brown-Séquard's therapy in France, I have consulted six widely circulated national newspapers, taking my cue from the papers that Brown-Séquard himself read and in which he sometimes published commentaries. They are: *Le Figaro, Le Matin, Le Petit Parisien, Le Journal, Le Petit Journal* and *La Presse.*[45] Together, they give voice to the ridicule that Brown-Séquard faced in 1889, as well as his steady rise to popularity in the medical community. I also draw much insight about how testicular injections fared in France—and abroad—through a close reading of Brown-Séquard's personal communications with d'Arsonval.[46] Their writings to each other during this period, from 1889 to Brown-Séquard's death in 1894, were prolific, rich, and revealing of both their nuanced thoughts about the injections and the wider political and cultural context in which their therapeutic movement was born.

In telling the American story, I engage the voices of physicians as they were expressed in medical reports, commentaries, and testimonials that appeared in the medical press and lay press from 1889 to 1919. My survey of the lay press has been deliberately broad

[45] Brown-Séquard's laboratory predominantly supplied Parisian doctors, which is why I have decided to focus on these Paris-based papers to track his movement. At one point, Brown-Séquard does complain that he was stuck supplying doctors from "every corner of France," which indicates that there was a regional market for his therapy. Brown-Séquard also mentions that doctors in "all the Hospitals" and especially a "very large number" of doctors in Lyon were using his liquid. See Brown-Séquard to d'Arsonval, December 30, 1892, in Léon Delhoume, *De Claude Bernard à d'Arsonval* (Paris: J.-B. Baillière, 1939), 494–95. A future study could further investigate this regional reception, and especially methods that might have been employed to preserve the liquid as it travelled from the metropole to regional and rural centers in France, as well as overseas to London and America (Chapter 3 of this dissertation includes evidence that some American doctors had Brown-Séquard's liquid shipped directly from his laboratory, and Delhoume's work includes correspondence between Brown-Séquard and d'Arsonval about getting shipments of the liquid to London).

[46] Their correspondence can be found in Delhoume, *De Claude Bernard à d'Arsonval*.

and wide-ranging, to get a sense for how deeply Brown-Séquard's method penetrated the American states, and how commonly it was used. Online newspaper databases, especially those with regional representation, have been most helpful in this regard.[47] My survey of medical literature has been more targeted and intended to capture the depth of medical thought concerning early endocrinology. In total, I have made a comprehensive survey of five general medical journals and two specialist journals. [48] The general medicine journals are the *Journal of the American Medical Association* (*JAMA*),[49] the *Philadelphia Polyclinic,*[50] *The Boston Medical and Surgical Journal,*[51] *The Medical Age, and The Medical Record*. These journals were selected for their wide circulation and national reach,[52] and for featuring robust exchanges between a wide cross-section of the medical community—ordinary GPs, elite GPs, and medical professors working in universities.[53] Additionally, I have surveyed two specialist medical journals: *The American Journal of Obstetrics and Diseases in Women and Children* and the *Alienist and Neurologist*. These journals were selected because they deal with diseases that were often treated by Brown-Séquardian extracts, namely myxedema in women, cretinism in children, and "hysteria" and neurasthenia in both men and women.

On the surface, the consultation of medical periodicals might seem like an uncomplicated means for sampling American physicians' opinions and work habits in the 1890s, just like a medical journal today could serve as a useful barometer for key issues in the

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[47] Most of the American newspaper sources that I rely on in this dissertation come from "Gale Primary Sources: Nineteenth Century U.S. Newspapers" and individual newspaper databases managed by Proquest Historical.
[48] By "general" medical periodicals, I mean those that were pitched to the whole orthodox medical community at large, as opposed to specialist journals that targeted a specific subfield of medicine. For a discussion of the difference between "general" and "specialist" periodicals, see W. F. Bynum and Janice C. Wilson, "Medical Journals in Nineteenth-Century Britain," in *Medical Journals and Medical Knowledge,* ed. W. F. Bynum, Stephen Lock, and Roy Porter (London and New York: Routledge, 1992), 32.
[49] *JAMA* was, and still is, the official organ of the American Medical Association.
[50] The organ of the Philadelphia Polyclinic and College for Graduates in Medicine.
[51] *The Boston Medical and Surgical Journal* was later termed the *New England Journal of Medicine.*
[52] Despite all being produced in the Northeast, these journals attracted contributions from doctors all around the country.
[53] Contributions from physicians range from clinical reports, article-length op-eds, editorials, brief quips, book reviews, and conference proceedings.

field. But what was the nineteenth-century American medical journal? Historians of medicine W. F. Bynum, Stephen Lock and Roy Porter remind us that the medical journal was a new emerging medium of medical communication in the nineteenth century. [54] Studying the rise of the British medical periodical, Porter claims that while medical periodicals did exist in the seventeenth and eighteenth centuries, their lifespans were short: they were launched and then collapsed after a short period in circulation, then replaced by new journals that would enjoy a similarly short lifespan. By 1800 a "quite extensive medical press was operating" in Britain,[55] with more durable journals, but serious questions concerning their production and circulation still plagued the medical community. What ought to be published? Who owned this information? Should it be made freely available?

Despite these unresolved questions, the number of new medical journals launched skyrocketed throughout the nineteenth-century, with especial growth between 1880 and 1900.[56] The journals launched in this period were more likely to last than their predecessors, and some of these journals are still extant today, including *The Lancet*, the *British Medical Journal* (*BMJ*) and the American Medical Association's official organ, the *Journal of the American Medical Association* (*JAMA*), which was launched in 1883, and a journal I rely on heavily in this dissertation. According to Elizabeth Knoll, one of the few historians to write on the rise of American medical publishing, *JAMA* was launched only after much internal discussion at the AMA about their desire to establish a culture of medical publishing that was independent from England, [57] and resolved to create a journal that was modelled on the *BMJ*,

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[54] W. F. Bynum, Stephen Lock, and Roy Porter, eds., *Medical Journals and Medical Knowledge: Historical Essays* (London and New York: Routledge, 1992). There is a paucity of literature on the history of the medical periodical, and Bynum, Lock and Porter's edited collection still stands as an authoritative work, according to Sally Frampton and Jennifer Wallis, eds., *Reading the Nineteenth-Century Medical Journal* (London and New York: Routledge, 2021). Frampton and Wallis' edited collection concerns medical publishing in Europe.
[55] Britain is the locus of Bynum's study. In Bynum, Lock and Porter's edited collection only three chapters address medical journalism in the United States.
[56] Bynum and Wilson, "Medical Journals in Nineteenth-Century Britain," 30.
[57] As Elizabeth Knoll suggests, American physicians read British medical literature because they lacked a home-grown culture of medical publishing. The publication of *JAMA* in 1883 heralded a new era in American medical

its "English brother."[58] By the 1890s, *JAMA* was characterized by its "extreme self-consciousness" about publishing only high quality scientific and clinical material,[59] which calls to mind Porter's claim (albeit for a century earlier) that the British medical press was "rapidly becoming a vehicle for anti-quack professional consciousness-raising." [60]

More scholarship is needed on the rise of the American medical journal, but we might take this existing analysis as a reasonably good indication that the culture of the medical periodical, in both Britain and America, was stabilizing by the late nineteenth century, and that some journals deliberately courted an orthodox audience—an appropriate source base for my project, which seeks the opinions of this community. Yet, as Harry M. Marks reminds us, not all periodicals were as they seemed. Drug companies, too, had their hands in medical publishing, and it was sometimes difficult to disaggregate the opinions of physicians from drug company employees. For example, George S. Davis, a partner in Parke, Davis & Co., also worked as renowned medical publisher, and was responsible for publishing *The Medical Age* and *The Therapeutic Gazette*. These journals adopted the form of the orthodox medical periodical and purported to gather and make available the collective experiences of American physicians for the common good. Marks is critical of these efforts by Parke, Davis & Co., claiming that some reports by physicians in these journals were legitimate, but "most resembled the testimonials common to the era's 'ethical' drug industry. With few exceptions,

publishing. See Elizabeth Knoll, "The American Medical Association and Its Journal," in *Medical Journals and Medical Knowledge*, ed. W. F. Bynum, Stephen Lock, and Roy Porter (London and New York: Routledge, 1992), 151–52. More historical research is needed on the history of the American medical periodical, and the reading preferences of nineteenth-century American physicians, in light of America's late arrival to medical publishing relative to Britain.

[58] Knoll, 154, 155.

[59] Koll writes that it was in a position by the 1890s to reject articles that were not up to standard. See Knoll, 157.

[60] Roy Porter, "Medical Journalism in Britain to 1800," in *Medical Journals and Medical Knowledge*, ed. W. F. Bynum, Stephen Lock, and Roy Porter (London and New York: Routledge, 1992), 18. Note that Porter describes the situation in British publishing in the seventeenth and eighteenth centuries, not the nineteenth century.

the studies were neither collective nor investigations, but endorsements gathered to promote the company's products."[61]

Following Marks' counsel, I think it wise to be aware of the market influences that shaped the content of medical periodicals in the late nineteenth century, and to consider whose opinions were included and not included in this published medium.[62] Yet, contra Marks, I suggest that even those sources most curated by drug companies, such as George S. Davis' *Medical Age* and Parke, Davis & Co.'s *Therapeutic Notes*, which I also rely on in this dissertation, still offer valuable insights into the history of drug production and prescription.[63] They reveal the strategies of drug companies, their relationships with physicians, and a culture of "collective investigation" that, however flawed and unrepresentative of the community of general practitioners, does give evidence of the drugs that were being used, how they were being used, and by whom. Medical periodicals have proved to be the most direct window into this world of drug production and drug prescription, and a means for capturing diverse opinions from both medical and pharmaceutical stakeholders. Archival research indeed reveals that sometimes these stakeholders—the medical and the pharmaceutical—were hard to disaggregate, as Marks forewarns, but these entanglements are precisely the story that I hope to describe.

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[61] Harry M. Marks, "'Until the Sun of Science … the True Apollo of Medicine Has Risen': Collective Investigation in Britain and America, 1880–1910," *Medical History* 50, no. 02 (April 2006): 161–62.

[62] Marks argues that ordinary doctors were not as willing to participate in data drives led by medical journals, perhaps because they regarded their own clinical experiences as personal property. Marks, 162.

[63] It bears mentioning that nineteenth-century medical periodicals that were purportedly "untouched" by market forces were still modelled in their image. Tom Mahoney explains that George S. Davis of Parke, Davis & Co., established a new pattern of medical publishing in America before the launch of JAMA in 1883. Mahoney suggests that Davis' influence as a successful medical publisher was by blurring the lines between company periodicals and physician literature. See Tom Mahoney, *The Merchants of Life; an Account of the American Pharmaceutical Industry* (New York: Harper & Brothers Publishers, 1959), 71. Historian of science Alex Csiszar, who has recently studied French and British scientific publishing in the nineteenth century, tracks a related development in the world of nineteenth-century scientific publishing, whereby early nineteenth century scientific academies and societies, who had long "disdained" the press for reporting their findings, resolved to "[reshape] themselves in its image, creating journals of their own, often modeled directly on their market-oriented competitors." See Alex Csiszar, *The Scientific Journal: Authorship and the Politics of Knowledge in the Nineteenth Century* (Chicago and London: The University of Chicago Press, 2018), 17.

What of accessing pharmaceutical company records and the voices of their employees? This has proved more challenging. Records of pharmaceutical companies are notoriously difficult to access for they are often held under lock and key in corporate archives. [64] Fortunately, the Parke, Davis & Co. records are held in the public domain at the Smithsonian. These collections are full of memoranda between company employees, correspondence between employees and doctors, and records of how the company organized its laboratories and clinical trials. Together, these sources offer invaluable insights into how endocrinology was developed by this company. I have also made use of the abundant trade literature that exists in various archives around the country,[65] which faithfully records the advertising strategies of Parke, Davis & Co. as well as numerous other pharmaceutical companies that sold glandular products in this period.

Scope

My story begins in France, where Brown-Séquard was based at the time of his announcement of his new therapeutic method, and where he set up a manufacturing operation from his laboratory, in which he attempted to distribute thousands of free samples of testicular extracts to French doctors. It then shifts focus to America, where doctors took up his method with gusto, and where drug companies, especially Michigan-based Parke, Davis & Co., were active in formulating high-quality glandular drugs in the early twentieth century.

After a long, successful and itinerant career, Brown-Séquard was well-known internationally, and his new therapy was taken up by scientists and doctors from all over the world. As historian Merriley Borell noted, the method of Brown-Séquard "came to be the

[64] Academic historians are often prevented from accessing corporate archives that hold pharmaceutical records, especially if these records pertain to the activities of a company that still exists today. For example, I have tried but failed to gain access to the Eli Lilly archives, even after securing the contact details of the archivist (a difficult task), corresponding with them, and having insiders to the company vouching for me.

[65] In addition to the Smithsonian, which holds some of this trade literature, I have visited the American Institute for the History of Pharmacy at UW-Madison, the College of Physicians of Philadelphia, the Science History Institute, the Library Company of Philadelphia, and Ebling Library at the University of Wisconsin-Madison.

therapeutic hope of physicians from Cleveland [Ohio] to Bucharest,"[66] emphasizing its quick and sensational spread across the globe. The early history of endocrinology could therefore be told with an international perspective, or from the perspective of any one of these geographies.[67] My interests in offering a predominantly American story are partly due to my own physical location in the U.S.,[68] but also to the size and significance of the American pharmaceutical industry and their early success in developing effective glandular drugs.[69]

It is important to note, too, that Brown-Séquard had real roots in the U.S., which facilitated the reception of his method across the Atlantic. As his biographers have shown, Brown-Séquard himself was an American citizen, having been born to a French woman, Charlotte Séquard, from Mauritius and a sea captain from Philadelphia, Charles Edward Brown, who died at sea before his son's birth.[70] Brown-Séquard was culturally French, and felt at home in Paris, but parts of his career were spent on the eastern seaboard of the U.S. He took up professorships at Medical College of Virginia at Richmond (1854-1855)[71] and Harvard University (1864-1867),[72] and returned repeatedly to the U.S. from Europe to lecture in Boston and New York mostly, but in other locations including Philadelphia, Baltimore and Charleston. He had two American wives, which gives context to his frequent visits to the New World. The first was Ellen Fletcher, of New England, whom he married in 1853 and who died of typhoid fever in 1860.[73] The second was Maria Rebecca Carlisle of Cincinnati,

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[66] Borell, "Brown-Séquard's Organotherapy," 310.
[67] Note that an early history of endocrinology has been given for the French context. See Marchand, "Opothérapie: émergence et développement d'une technique thérapeutique (France, 1889-1940)."
[68] It is not conventional in the academy to admit how our personal circumstances have shaped our own research projects. I hope, however, that this culture will change in the age COVID, where we are getting better at having conversations about privilege, language barriers, financial constraints, and mental health.
[69] I am referring here to Parke, Davis & Co., who developed the widely successful Adrenalin in 1901. But we should also remember that the world's first blockbuster endocrine drug, insulin, was also manufactured in Indiana at Eli Lilly & Company.
[70] Aminoff, *Brown-Séquard: An Improbable Genius Who Transformed Medicine*, 17–19; See also Celestin, *Charles-Edouard Brown-Séquard*.
[71] Aminoff, *Brown-Séquard: An Improbable Genius Who Transformed Medicine*, 82, 84.
[72] Aminoff, 127, 131.
[73] Aminoff, 58.

who died just two years after marrying Brown-Séquard in 1872.[74] His third wife, Emma Dakin, who he married in 1877, was English, but even so the couple still returned to Boston for periods so that Brown-Séquard could lecture.[75] When his therapy was taken up in America, some newspapers claimed him as their own,[76] describing him as "Franco-American" physiologist with ties to Massachusetts and Ohio through his two wives.[77] The story of early endocrinology is thus as much an American story as it is a French story, although of course national and regional differences are sure to apply.[78]

The early history of endocrinology could also be told as a physiological rather than a clinical story. As Medvei and others note, there were key physiological and chemical developments that occurred in this period, which contributed to the emerging sense of the endocrine glands as a bodily system, and endocrinology as a new body of scientific knowledge.[79] I have chosen to focus on the clinical and pharmaceutical story, rather than continuing to flesh out the physiological and chemical landscape, for two key reasons. The first is to raise the profile of the contribution of clinicians and drug companies in the history of scientific medicine at the turn of the century, as this introduction has already detailed. The second is to investigate how physicians and drug company workers built their own culture of

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[74] Aminoff, 142, 147.
[75] Aminoff, 150. Emma died in January 1894, just months before her husband. According to Michael Aminoff, "it was a loss from which Brown-Séquard never recovered." See Aminoff, 223, 225.
[76] For example, see how Brown-Séquard is introduced "Famous Elixir of Life: Dr. Brown-Séquard Tells What His Tonic Can Do. How the Fluid Is Made. Practical Proof. Dangerous Trifling," *Chicago Daily Tribune*, November 20, 1889. One article from the *St. Paul Daily News* simply described Brown-Séquard as "an American." See "An American," *St. Paul Daily News*, August 20, 1889. See also "Brown-Séquard Dead: The Discoverer of the Elixir of Life Passes Away: One of the Foremost of the World's Physicians," *Milwaukee Daily Sentinel*, April 3, 1894; "Brown-Séquard Dead," *News and Observer*, April 7, 1894.
[77] See "Dr. Brown-Séquard's Romance: How the Famous French Specialist Got an American Wife," *Galveston Daily News*, August 23, 1889. Originally printed in *Cincinnati Enquirer*. This article stated that news of Brown-Séquard's elixir had greatly interested Cincinnati, but that "this feeling has been greatly heightened by the rather important fact that the doctor married a well-known society lady of this city, and at one time visited Cincinnati, remaining here for some time." For reference to his Boston wife, see "An American."He had three wives in total. See Aminoff, *Brown-Séquard: An Improbable Genius Who Transformed Medicine*, ix.
[78] Apart from the period of 1889-1894, between Brown-Séquard's initial announcement to the Société de Biologie and his death, I have not made a study of how endocrinology developed in France.
[79] Medvei, *A History of Endocrinology*; Welbourn, "The Emergence of Endocrinology."

clinical experimentation, and created new empirical therapies, in a period when physiological and chemical concepts—such as the new entity of "hormone"—were still being elaborated and were of little use to the clinic. How was a clinical movement and pharmaceutical industry nurtured under these circumstances? What this dissertation does not address, and what future historians might consider investigating, is the relationship of the drug company and the clinic to the university laboratory between 1889 and 1919. This could be especially interesting and important to investigate in the 1910s when momentum in endocrinology was building in academic spaces.

Chapter Outline

While this dissertation seeks to make a general case for the utility of studying doctors and drug companies in histories of scientific medicine, it also builds an argument about why these two collective actors were of particular importance to the development of endocrinology. As Chapters 1 and 2 demonstrate, it came down to the conditions of endocrinology's emergence in France, under the stewardship of Brown-Séquard. Unlike bacteriological medicine, which was imagined and promoted by its forefathers as highly technical and unable to be formulated outside a laboratory setting, the first generation of glandular products were deemed very easy to make. Brown-Séquard said so himself and encouraged doctors to make their own drugs by following the recipe that he had published for their benefit. In these chapters, I emphasize the importance of Brown-Séquard's very public method, his regular communication with doctors, and his refusal to corporatize and monopolize the early drug trade between 1889 and 1894. This, I argue, goes a long way toward explaining why so many doctors in France and then America bought into his idea, and involved themselves in both drug production and experimentation.

Chapter 3 shifts to the American context and shows how doctors there followed Brown-Séquard's advice and public recipe and began to experiment with glands between

1889 and 1900. It was hard and grisly work, but they took it upon themselves to refine the drug production process, test new therapies in the clinic, and slowly develop guidelines for the field. Chapter 4 shows that when the labor of the producing glandular products became too much, doctors turned to a natural ally to help produce new glandular drugs: the "ethical" pharmaceutical company, who by 1900 had advanced and ever-improving drug production capabilities. Doctors started buying commercial preparations from 1895, and by 1910 they had all but given up their own DIY preparations in favor of company-produced medicaments. By the first decade of the century, the ethical manufacturing company had become a mainstay in glandular product manufacturing. Chapter 5 shows, however, that as Parke, Davis & Co. became more involved with glandular drug production, doctors became more involved with the company.

By 1919, where this project ends, American doctors and Parke, Davis & Co. had developed systems for collaboration and were jointly invested in further developing the still burgeoning field. Through their efforts, the clinical field was poised for the 1920s, in which blockbuster drugs were isolated and universities in Europe and America began to invest in what had come to be termed "endocrinology."

In a short concluding chapter, I consider how the origins of clinical endocrinology have been remembered by interwar endocrinologists who felt embarrassed by Brown-Séquard's claims and the therapeutic work that ensued. I suggest that it is time for historians of science and medicine—and endocrinologists—to embrace the clinical and pharmaceutical experience between 1889-1919, for it enriches our understanding of how a major field of twentieth-century medical science came to be.

Chapter 1: Brown-Séquard and His Disciples: Doctors, Supply and Demand, and the Origins of Endocrinology in Paris, 1889-1893

Brown-Séquard's new testicular therapy took some of his scientific and medical colleagues by surprise, but it found a warm reception with doctors in clinics. In the weeks after his first address in June of 1889, reports began trickling in to Brown-Séquard from clinicians, both in France and abroad, who reported successful attempts at using testicular injections. Snickering lingered in the columns of medical periodicals, as it did in scientific venues, but practicing doctors were warming up to the idea of injecting their patients—and themselves— with Brown-Séquard's elixir. They had the means to produce the new therapy with their own two hands, for Brown-Séquard had published explicit instructions for how it could be formulated with nothing but a filter, some glycerine, and some fresh animal testicles.[80] Yet, many doctors approached Brown-Séquard's laboratory directly for free samples rather than producing the liquid themselves. At first a handful of doctors approached Brown-Séquard for free samples, then scores, and then hundreds. By the end of 1892, Brown-Séquard was regularly supplying testicular liquid to 1,200 doctors from Paris.[81] Thousands more came knocking, demanding access to the coveted drug.[82]

At first, Brown-Séquard and his principal collaborator and close friend, Jacques-Arsène d'Arsonval, were only too happy to supply the doctors of France. It meant getting their new therapy into the hands of practitioners and obtaining more data on its efficacy. They also had the capacity to produce it at their laboratory at the Collège de France, which was

[80] In Brown-Séquard's first address in 1889, and in many subsequent publications, he included his recipe for making the testicular injections, as well as any amendments he had made through experimentation and revision. This is a point that will be addressed at length in this chapter.
[81] See Brown-Séquard and d'Arsonval's notice in Louis Chavois, *D'Arsonval: Soixante-cinq ans à travers la Science* (Paris: Éditions J. Oliven, 1937), 215; "Brown-Séquard Again: French Doctors Claim Great Results from His Invention," *New York Times*, June 10, 1893.
[82] Notice in "Les académies," *Le Matin*, September 6, 1892, 3. The volume of interest in the testicular injections caused Brown-Séquard considerable stress, for he estimated that his laboratory only had the capacity to supply about 1000 doctors.

helped by d'Arsonval's ingenious invention of a mechanized filtration machine that, by the middle of 1892, could formulate as many as five hundred bottles of testicular liquid in less than a month.[83] But when demand for their injections continued to grow, and Brown-Séquard received nearly 3,000 letters from doctors with requests for liquid in a 5-week period at the end of 1892, [84] he started to have serious doubts. Could he and d'Arsonval continue down the path of drug manufacturing? How much liquid could they feasibly produce and distribute? And if their laboratory at the Collège de France did not supply the liquid to the doctors who demanded it, who—or what—would take their place?

At the end of 1892, and after producing and distributing more than 10,000 bottles of testicular liquid,[85] free of charge, Brown-Séquard had had enough. He announced to the French medical community that his laboratory was ceasing production of testicular injections altogether, effective immediately. [86] In private correspondence, Brown-Séquard expressed deep concerns for the future of the industry, and for the new line of therapeutics that he had single-handedly launched over the past three years,[87] for there was no clear successor to take his and d'Arsonval's place in formulating the injections. And yet he saw no other way forward: his laboratory was inundated, and overstretched, and poor d'Arsonval—the real muscle behind the operation—was thoroughly spent. Thus, when Brown-Séquard closed the doors of his laboratory-turned-factory, he did so without a plan, and without a resolution about who would produce testicular injections in his absence. His best suggestion was that the doctors themselves should make their own personal supply—something he had

[83] Charles Brown-Séquard, "Boite aux lettres : A. Monsieur Maurice de Fleury, rédacteur au Figaro," *Le Figaro*, July 9, 1892, 3.
[84] Notice in "Les académies," September 6, 1892, 3.
[85] Jacques-Arsène d'Arsonval, "Remarques à propos de la communication de M. Guinard," *Comptes rendus des séances de la société de biologie et de ses filiales*, March 11, 1893, 272.
[86] Brown-Séquard and d'Arsonval's notice in Chavois, *D'Arsonval: Soixante-cinq ans à travers la Science*, 215.
[87] Charles Brown-Séquard to Emmanuel-Charles Poupinel, March 2, 1893, in Revue Historique et Litteraire de l'ile Maurice: Archives coloniales, no. 13 (1894): 204-5. Dr. Emmanuel-Charles Poupinel de Valencé was a Mauritius-based savant and friend to Brown-Séquard, who also hailed from Mauritius. The next chapter will explore some of their correspondence from 1893.

encouraged them to do from the very beginning. Some doctors accepted the challenge, but others were left grappling with questions about how, and by whose hands, the new testicular therapy should be produced.[88]

In this chapter, I return to the beginning of Brown-Séquard's medical movement, and specifically to his manufacturing crisis, to investigate a simple question: how did Brown-Séquard shape the emergence of endocrinology? We are accustomed to thinking about Brown-Séquard in quite broad strokes as the eccentric physiologist who had a quirky idea and generated some excitement among doctors, but we know very little about what he actually did between 1889, when he first went live with his therapeutic method, and 1894, when he died. Merriley Borell is one of the few historians to have given him concerted attention, dedicating several articles and her doctoral dissertation to studying his physiological ideas.[89] In this chapter and the next, I give Brown-Séquard the respect afforded to him by Borell, but I focus less on his intellectual contributions and more on the logistical and cultural work he did to get his campaign off the ground. I ask: how did he create a medical movement? How did he encourage others to take up his method?

I approach these questions by focusing on Brown-Séquard's heavy involvement in drug production, and I have done this for two reasons. The first is historical and arises directly from archival material. In his published scholarly work, public commentaries, and private correspondence—all sources that I rely on—Brown-Séquard made it abundantly clear that he was concerned with, and at times positively frazzled by, the task of supplying

[88] French doctors took to the papers in the wake of Brown-Séquard's announcement, writing impassioned commentaries about how drug production should proceed in the realm of glandular therapeutics. Some of these commentaries will be unpacked in the next chapter.

[89] Borell, "Origins of the Hormone Concept"; Borell, "Brown-Séquard's Organotherapy"; Borell, "Organotherapy, British Physiology, and Discovery of the Internal Secretions." Brown-Séquard's biographers have also given attention to his manufacturing enterprise. See especially J. M. D. Olmsted, *Charles-Edouard Brown-Séquard, a Nineteenth Century Neurologist and Endocrinologist* (Baltimore: Johns Hopkins Press, 1946); Aminoff, *Brown-Séquard: An Improbable Genius Who Transformed Medicine*; Celestin, *Charles-Edouard Brown-Séquard*.

testicular liquid to "the doctors who requested it." Indeed, from 1889 to his death in 1894, Brown-Séquard was arguably just as preoccupied with the business of producing the testicular injections for doctors as he was the science behind his theory—a fact that has received very little attention from historians.[90]

The second reason I focus on Brown-Séquard's role as testicular-extract manufacturer is for the insights it yields about how endocrinology developed as a nascent field. I show that by distributing his recipe to doctors, encouraging them to produce extracts in their clinics, and then engaging with them as both dedicated interlocuter and drug supplier, Brown-Séquard placed clinicians at the very center of his movement. For him, they were not mere recipients of his therapy. They were rather co-producers of new knowledge about the therapeutic potential of testicular extract and other extracts of the body. As I show in this chapter and others, physicians responded by experimenting with Brown-Séquard's method and taking ownership over his therapy in the clinics.

The close involvement of doctors in the emergence of endocrinology, and Brown-Séquard's earnest engagement with them, ought to give us pause. This was an era when the laboratory was ascendent and making steady inroads into the clinic. It was also the era of Louis Pasteur whose vaccines, produced in a laboratory, were changing the face of medical practice. If we think about doctors in this period, then is often as antagonists or resistors to the new scientific medicine, or as passive observers of the wave of "scientific progress." If we follow Bruno Latour's characterization of a "pasteurizing France," then doctors were on the periphery of the laboratory, looking in from the outside, and only adopting bacteriological technology when they were trained in microscopy.[91] The early history of endocrinology casts

[90] Most historical commentary on this episode on Brown-Séquard's career is focused on the sensationalism of the movement and the ridicule he endured in advocating for his therapy. However, see Merriley Borell's work on Brown-Séquard, which does touch on his and d'Arsonval's mission to supply doctors with the fluid. Borell, "Brown-Séquard's Organotherapy," 313.
[91] Latour, *The Pasteurization of France*.

doctors in a very different light, for it shows that they could also be contributors to the development of new medicine in this period. In contrast to bacteriology, the laboratory was not a central component of Brown-Séquard's vision. Instead of becoming "Medicine at Last"—Latour's phrase for the delayed arrival of bacteriology to the clinic—early endocrinology was medicine from the very beginning.[92]

My story of Brown-Séquard, doctors, and the origins of endocrinology, is told in two separate but chronologically contiguous chapters. This chapter focuses on the first three years of Brown-Séquard's campaign, from his initial announcement in 1889 to the closure of his laboratory, for production purposes, in 1892. It begins by looking at Brown-Séquard's original publications in 1889, and physicians' responses to his announcement, with a focus on how Brown-Séquard established a culture of transparency concerning the "preparation of the liquid" with medical practitioners who wanted to use it. I show that Brown-Séquard encountered problems from the beginning after making his recipe publicly available to doctors—a choice he did not regret, but something he had to manage.

The second section of this chapter tracks the rising popularity of Brown-Séquard's new therapy with both physicians and druggists, and his and d'Arsonval's frustrated attempts at supplying physician demand for the liquid, which led to the closure of their laboratory, for production purposes, at the end of 1892. I close out the chapter by offering a comparative analysis between Brown-Séquard and Louis Pasteur, who was also trying to make scientific medicine in the fin-de-siècle but struck up a very different relationship to the medical community. This comparison helps us situate the emergence of endocrinology in the early 1890s as a physician-centered enterprise.

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[92] "Medicine at Last" is a chapter title in Latour, *Pasteurization of France*. Judith Swazey and Karen Reed have launched a similar argument about the precedence of medicine vis-à-vis science. See Judith P. Swazey and Karen Reeds, *Today's Medicine, Tomorrow's Science: Essays on Paths of Discovery in the Biomedical Sciences* (U.S. Department of Health, Education, and Welfare, Public Health Service, National Institutes of Health, 1978).

The next chapter, “Looking for an Ethical Manufacturer,” deals with the fallout of Brown-Séquard and d’Arsonval’s decision to stop producing testicular extracts, with a focus on the conversations these two men had in their private correspondence in 1892 and 1893. This second chapter is especially concerned with the proposals that were submitted to Brown-Séquard and d’Arsonval by hopeful manufacturers and benefactors, and Brown-Séquard’s complicated and evolving views on how scientific medicine should be produced vis-à-vis the medical marketplace. It also considers the regulatory apparatuses that emerged in France and then the United States after Brown-Séquard’s death. The first country officially sanctioned some commercial manufacturers to produce Brown-Séquardian therapies; the second maintained the trade of organic extracts as an unregulated and unruly market.

When Brown-Séquard died in 1894, he left the trade of organic extracts with a very uncertain future. Yet, his decisions about drug production practices, and especially his insistence that physicians be involved in the process of establishing a new field, fundamentally shaped the emergence of endocrinology in both France and America, as these chapters argue, and the rest of the dissertation will show. It is an overstretch to declare that “endocrinology” had been launched by Brown-Séquard in this period, for there was not yet a clearly defined concept of a “system” of hormone-secreting glands, or even a sense for what a “hormone” was, let alone a professional body of scientists and doctors who were dedicated to its study and practice. This would all emerge in the early twentieth century, long after Brown-Séquard’s name had disappeared from scientific and medical literature as well as the lay press. But what Brown-Séquard did do in his highly productive final years of life was to nominate doctors as producers of new knowledge and producers of new drugs, and this was a culture that survived in endocrinology well beyond his death.

The Use and Abuse of the *Méthode de Brown-Séq*uard

When Brown-Séquard unveiled his new therapy in 1889 at the Société de Biologie, he did not just tell his colleagues that he had injected himself with a testicular concoction and that he felt fantastic. He also told them exactly how he made it. Under the subtitle, "Presentation of the Experimental Procedure Used," he shared with his audience, and any readers of the *Comptes rendus de Société de Biologie* in which this presentation was published, the secrets to his success:

> This method consists of injections under the skin of a liquid obtained by crushing the testicles from dogs or from guinea pigs, with the addition of a little water (of 2 to 3 cubic centimeters per testicle). This liquid is a product of 3 sources: the blood from the testicular veins, tied before the extirpation of the gland, of clean tissue of the testicles, and of sperm contained in the organs and in their excretory canals…The resulting liquid was employed only after filtration sometimes through a paper filter, sometimes through the Pasteur filter.[93]

He went on to explain his injection schedule—8 injections given daily at the end of May—the quantity of liquid in each injection—"a cubic centimeter"—the type of dogs and guinea pigs he had used—young and "extremely vigorous"—the pain he felt after injecting—persistent, sharp and sometimes excruciating—and the very good physical and mental effects he felt from his treatment regime, despite the considerable discomfort it caused him. He concluded his first paper on the subject with a hopeful line to his fellow physiologists at the Société de Biologie: "I hope that other physiologists, of an advanced age, repeat these experiments and show if the effects I have obtained on myself depend or not on my personal idiosyncrasy."[94]

The first report that came in was not from a physiologist but a doctor. His name was Dr. G. Variot, from Paris, and in the weeks after Brown-Séquard's address he had performed

[93] Brown-Séquard, "Des effets produits chez l'homme par des injections sous-cutanées d'un liquide retiré des testicules frais de cobaye et de chien."
[94] Brown-Séquard.

a series of "experiments" on three ageing men with various health complaints using testicular liquid that he had prepared himself.[95] Writing in to the Société de Biologie, he explain how he had followed Brown-Séquard's instructions that were published earlier that month, but he made some alterations, such as crushing up the testicles of rabbits and guinea pigs instead of guinea pigs and dogs. He also neglected to filter the liquid before injecting it into his patients, even though it was "colored rose by the blood…and contains in suspension some little particles of pulp."[96] Despite this, his patients did well under the treatment, and even seemed to improve in condition. Variot concluded that the injections, while still very much in the experimental stage, seemed to be a "fortifying liqueur," a conclusion that was helped by his own patients who "insisted that injections be continued."

Brown-Séquard was chuffed to have his first formal respondent in the Société de Biologie, and very pleased with the "numerous letters" he had received from doctors since his last publication, but he was admittedly a little concerned about how Variot had altered his method. He wrote in to the Société de Biologie to commend Variot for his good work, and then to gently scold him for his potentially dangerous practices. "It is important that I restate that the liquid …must be employed only after filtration and that the Pasteur filter must be preferred to paper filters," Brown-Séquard wrote. "Even though Mr Variot has made, without accident, some injections of an unfiltered liquid, it is not unlikely that we run the risk of septicemia in acting thus."[97] He also had an opinion on Variot's use of rabbit testicles, which he thought were at higher risk of conveying disease (such as rabies) than guinea pigs.

If Brown-Séquard was a little troubled by Variot's use of unfiltered extract, he was seriously bothered by the next respondent in the Société de Biologie. It was Dr. Conan, a

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[95] G. Variot, "Trois expérimentes sur l'action physiologique du suc testiculaire injecté sous la peau, suivant la méthode de M. Brown-Séquard," *Comptes rendus des séances de la Société de biologie et de ses filiales*, June 29, 1889, 451–54. One had anemia, one had a heart condition, and the other had bronchitis.
[96] Variot.
[97] Charles Brown-Séquard, "Remarques à l'occasion du travail de M. Variot, sur les injections de liquide testiculaire chez l'homme," *C R Soc Biol*, June 29, 1889, 455.

homeopath, who not only had the gall to suggest that he had been using Brown-Séquard's method for his entire career, and that priority should go to him, but also that the same method could be applied to morsels of kidneys, bladders and penises as well as testicles, the latter of which could be used to treat genito-urinary infections.[98] Brown-Séquard, who was annoyed on multiple levels, not least his association with a homeopath, issued a response in the Société de Biologie that bordered on outrage: "I do not believe that I need to give many reasons to demonstrate that I have not at all tried to make what Mr. Conan believes he has made…" he said, explaining that Conan's treatise was completely lacking in scientific reasoning. What enraged Brown-Séquard most about Conan was how he had fundamentally misunderstood his method. Where Brown-Séquard was careful to preserve the active principles that resided in the testicular tissue by maintaining stable temperatures, Conan threw his glandular tissues into a high-temperature oven for multiple days before giving it to patients. On this, Brown-Séquard remarked, emphatically: "He destroys all the organic properties of these [tissues]…Indeed, *for six days he submits it to desiccation in an autoclave at 70 degrees*!! After this, no one will find that what I have made resembles what is made by this homeopathic doctor …"[99]

More serious medical practitioners came forward in the Société de Biologie with experiments on the testicular injections but, like Variot, they too slightly altered Brown-Séquard's original recipe to suit their own particular needs. The next two respondents were a L. H. Goizet, a Parisian doctor from the Faculté de Médecine of Paris, who was so convinced of the merits of Brown-Séquard's therapy that he would later write books about it and found

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[98] Dr. Conan, "Correspondance Imprimée," *Comptes rendus des séances de la Société de biologie et de ses filiales*, June 22, 1889, 429. "Homeopaths" practiced medicine in the homeopathic tradition, which is remembered by historians as a "pseudo-scientific" tradition established by Samuel Hahnemann in the late eighteenth century. Homeopaths abided by the principle that "like" cures "like," which is demonstrated by Conan's suggestion that genito-urinary infections could be treated with testicular extract. For more context on nineteenth-century homeopathy, see: Gevitz, *Other Healers*.

[99] Charles Brown-Séquard, "Remarques de M. Brown-Séquard à l'égard de la Réclamation de M. Conan," *Comptes rendus des séances de la Société de biologie et de ses filiales*, June 22, 1889, 429. Original emphasis.

an institute in his name.[100] Then there was a veterinarian Émile Thierry, who was the director of l'Ecole pratique d'agriculture de la Brosse at Yonne. They both prepared the mixture themselves, following Brown-Séquard's instructions, but both took liberties with injection schedules, the amount of water they used to dilute the testicular tissue and, in Thierry's case, the species of patient on whom the experiments were made. Goizet was thoroughly impressed with Brown-Séquard's new therapy, giving one of his patients no less than 116 injections over twenty-two sessions,[101] but Thierry was less enamored. The prize ram that he had injected had not improved its poorly condition and now had one more complaint to boot: a very stiff leg where Thierry had administered the shots, which gave the long-suffering creature a staggered walk.[102]

Brown-Séquard did not respond directly to Goizet and Thierry's studies possibly because, already by 1890, there were too many doctors using the testicular liquid for him to comment publicly on every single study. There were now clinical reports trickling in from all corners of France, but also from America, Russia,[103] Poland, Romania, Austria, Hungary,

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[100] See Louis-Henri Goizet, *La vie prolongée au moyen de la méthode Brown-Séquard* (Paris: Librairie Marpon & Flammarion, 1891); Louis-Henri Goizet, *The Transfusion of Life: Twenty Years Later: A Continuation of Life Polonged by Means of the Method of Brown-Séquard* (C. Richter & Co., 1909). In 1891, Goizet founded an institute at rue de Berri that produced and sold organic extracts, à la Brown-Séquard. He later referred to it as the "Sequardian Institute." (See front matter to *The Transfusion of Life*)

[101] Dr. Goizet, "Mémoire: Dr Goizet, plusieurs cas d'emploi du suc testiculaire contre diverses maladies," *Comptes rendus des séances de la Société de biologie et de ses filiales*, 1890.

[102] Émile Thierry, "Note sur l'action du liquide testiculaire: resultat négatif sur un bélier," *C R Soc Biol*, October 11, 1890.

[103] How many doctors were using Brown-Séquard's liquid in these locations? The next chapter will detail the reception in America. As for the other geographies, which I do not address in this dissertation, it is difficult to get a clear sense of the volume. We do know, however, that in Russia, "several hundred" doctors were using it daily by the end of 1890. This is noted by Brown-Séquard in a letter to d'Arsonval, penned in December of 1890. See Brown-Séquard to d'Arsonval, December 29, 1890, in Delhoume, *De Claude Bernard à d'Arsonval*, 350. Curiously, mentions of the English and German reception are few and far between in Brown-Séquard's reporting on the matter, although there is evidence that he was in conversation with British physiologist Victor Horsley in February, 1891. See d'Arsonval to Brown-Séquard, February 25, 1891, in Delhoume, 366. Brown-Séquard and d'Arsonval's correspondence (in Delhoume) also details attempts to ship testicular liquid to London for testing in Brown-Séquard's old hospital in Queen's Square. Brown-Séquard remarked that this would help the "slow" reception of his therapies in English if the trials went well.

Italy,[104] and even from locations as far as Melbourne, Australia.[105] Brown-Séquard approved of some of these clinical reports, like the work done by fellow countryman Dr. R. Suzor, from Mauritius, who had used the testicular injections to treat leprosy and malaria. Brown-Séquard, who considered Suzor to be a "conscientious and exact" observer, endorsed these experiments because they were measured, based on clinical fact, and suggested "the great power of the testicular liqueur on the nervous system." He then recounted them in abridged form in *Archives*, for fear that they would never be known in Europe if they did not reach a wider audience than Port-Louis, where they were initially shared.[106]

Brown-Séquard was also interested, but surprised, by experimental work coming from America, such as a French doctor "of merit" living in San Francisco who had been successfully using testicular injections to treat people with ataxia.[107] There was also a Dr. H. C. Brainerd from Cleveland, Ohio, who used ram testicles to make up enough liquid to inject more than 200 individuals, 19 of whom were women.[108] Brainerd's patients suffered from diverse illnesses, such as rheumatism, debility, paralysis and sexual impotence. Many of them

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[104] Charles Brown-Séquard, "Exposé de faits nouveaux montrant la puissance du liquide testiculaire contre l'affaiblissement dû à certains maladies et en particulier la tuberculose pulmonaire," *Arch Physiol Norm Pathol*, 1891, 224; Charles Brown-Séquard, "Nouveaux faits relatifs à l'influence sur les centres nerveaux de l'homme d'un liquide extrait de testicules d'animaux," *Archives de physiologie normale et pathologique*, 1890, 641.

[105] For Melbourne and Budapest activity, see Brown-Séquard's summary of Dr. Crivelli and Dr. A. Szikszay's work in "Nouveaux faits relatifs à l'influence sur les centres nerveux de l'homme d'un liquide extrait de testicules d'animaux," *Archives de physiologie normale et pathologique*, 1890, p. 641. Note, also, that this is not an exhaustive list of locations in which Brown-Séquard's therapy was taking root. In a 1893 letter to d'Arsonval, Brown-Séquard mentions that he had requests for liquid from numerous individuals in Copenhagen, Hungary, Belgium, Italy and Russia. See Charles Brown-Séquard to Jacques Arsène d'Arsonval, January 2, 1893, Delhoume, 497.

[106] Charles Brown-Séquard, "Nouveaux faits relatifs à l'injection sous-cutanée, chez l'homme, d'un liquide extrait de testicules de mammifères," *Archives de physiologie normale et pathologique*, 1890, 201. They were initially shared at the Société des arts et des sciences de Port-Louis.

[107] Brown-Séquard, "Nouveaux faits relatifs à l'injection sous-cutanée, chez l'homme, d'un liquide extrait de testicules de mammifères," *Archives de physiologie normale et pathologique*, 1890, p. 205 (ft). The name of this doctor was not noted by Brown-Séquard. Ataxia is a disorder of the nervous system which manifests in poor muscle coordination and affected speech.

[108] Brown-Séquard, "Nouveaux faits relatifs à l'injection sous-cutanée, chez l'homme, d'un liquide extrait de testicules de mammifères," 204. For more information on Brainerd, see "The Latest Fad," *San Francisco Chronicle*, August 14, 1889, 1.

did not improve under the treatment, but a sizable class of them did, especially if several injections were made, and not just one or two jabs.

Even more reports came in from doctors who continued to use his therapy in both men and women, some of whom even trialed the use of ovarian extracts in both sexes as an experimental treatment for debility, insomnia, hysteria and uterine problems.[109] Brown-Séquard marveled at the creative applications of his therapy in the clinic. Despite his misgivings about the liberties some doctors were taking with his method—especially those who did not follow proper aseptic protocols—he was being forced to think more broadly about his initial testicular prototype. At the end of 1890, he remarked on its generalization and globalization, stating that "the facts are multiplying" around the world which took his therapeutic vision "much further than I dared hope." He said, "a number of us show that this liquid possesses much greater power and much greater variety than I had supposed."[110] The next year, in 1891, and in response to doctors' reports, he and d'Arsonval significantly broadened the scope of Brown-Séquard's initial theory; instead of arguing that the testicular glands contained an active principle that could be harnessed therapeutically, they put forward that probably all glands and tissues of the body contained some active particle that might be used therapeutically.[111]

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[109] More reports came in from two French doctors, a Dr. Villeneuve, professor at l'Ecole de médecine at Marseille, and Dr. Augusta Brown, of the Faculté de Paris, who had started to experiment, successfully, with the injection of ovarian juice in both men and women who suffered from age-related debility, insomnia, hysteria and uterine problems. Brown-Séquard, who had never worked with ovarian tissues himself, was struck by how similarly ovarian liquid acted to enliven the nervous system, although quite a bit less powerful than testicular injections, he supposed. See Charles Brown-Séquard, "Remarques sur les effets produits sur la femme par des injections sous-cutanées d'un liquide retiré d'ovaires d'animaux," *Archives de physiologie normale et pathologique*, 1890, 456–57. Augusta Brown is not easily tracked through the archives, but evidence indicates that she was an American doctor living and working in Paris in the early 1890s. See a discussion of her work in Goizet, *La vie prolongée au moyen de la méthode Brown-Séquard*, 173–74. See also M-Augusta Brown, "Students to the Fore," *The New York Herald*, July 21, 1889, 2.

[110] Brown-Séquard, "Nouveaux faits relatifs à l'influence sur les centres nerveaux de l'homme d'un liquide extrait de testicules d'animaux," 641; See also Brown-Séquard, "Nouveaux faits relatifs à l'injection sous-cutanée, chez l'homme, d'un liquide extrait de testicules de mammifères," 208.

[111] Charles Brown-Séquard and Jacques-Arsène d'Arsonval, "De l'injection des extraits liquides provenant des glandes et des tissus de l'organisme comme méthode thérapeutique," *Comptes rendus des séances de la société de biologie et de ses filiales*, April 18, 1891, 248–50. See also a letter d'Arsonval penned to Brown-Séquard in late March of 1891, where he describes the many doctors who want to try Brown-Séquard's method in all the

Their confidence was no doubt strengthened by the growing number of well-known physicians from France who were jumping on the band wagon. These included Professor Albert Jean Jules Mairet of the Faculté de Médecine of Montpellier and Dr. Jean-Martin Charcot, Brown-Séquard's esteemed friend from the Académie de Médecine and the Académie des Sciences, and co-founder of *Archives*.[112] There was also Dr. Depoux at Val-de-Grâce who used Brown-Séquard's injections to treat soldiers with ataxia,[113] Professor Cornil who treated patients at Hospital Laénnec,[114] and a Dr. Frémy from Nice who, with Brown-Séquard's help and feedback, made new experiments by administering testicular injections by the rectum instead of the normal subcutaneous route.[115] Yet another new iteration of his original method, Brown-Séquard mused, and possibly a mode of administration that was a trifle less painful than subcutaneous injections.

Yet, despite the gusto with which doctors were taking up his call to experiment, not everything was going well for Brown-Séquard and his movement. His open encouragement to doctors to work with his liquid had yielded quite startling results about its value as a broad-spectrum drug, but it also incited a number of studies and claims of which he was far less appreciative. These came from heavy-handed doctors from regional places who mussed with

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tissues of the body, and how it had prompted Brown-Séquard to experiment. This letter shows that Brown-Séquard was responding to the experimental direction of the medical community. See Jacques Arsène d'Arsonval to Charles Brown-Séquard, March 24, 1891, Delhoume, 377-379.

[112] Brown-Séquard, "Nouveaux faits relatifs à l'influence sur les centres nerveaux de l'homme d'un liquide extrait de testicules d'animaux," 454.

[113] Dr. Depoux, "Observation d'un cas d'ataxie locomotrice guérie par les injections sous-cutanées suc retire testicules de cobayes venant de mourir," *Comptes rendus ses séances de la société de biologie et de ses filiales*, May 30, 1891, 399–402.

[114] Jules Hénocque, "Comparaison des résultats obtenus par les injections de tuberculine et les injections de liquide testiculaire, chez les tuberculeux au point de vue hématoscopique," *Comptes rendus des séances de la société de biologie et de ses filiales*, October 24, 1891, 715–16.

[115] Charles Brown-Séquard, "Exposé de faits nouveaux à l'égard de l'influence sur les centres nerveux d'un liquide extrait de testicules d'animaux," *Archives de physiologie normale et pathologique*, 1890, 443–55; Brown-Séquard, "Nouveaux faits relatifs à l'influence sur les centres nerveaux de l'homme d'un liquide extrait de testicules d'animaux," 647. Physiologists, too, were inspired by Brown-Séquard's work, such as Dr. Gley, physiologist and agrégé of the Faculté de Médecine of Paris who had begun injecting pancreas juice and thyroid juice into lab animals who had had these organs recently removed. See Eugène Gley, "Note préliminaire sur les effets physiologiques du suc de diverses glandes et en particulier du suc extrait de la glande thyroid," *Comptes rendus ses séances de la société de biologie et de ses filiales*, April 18, 1891.

his method, caused death to their patients, and then publicly condemned the "elixir de vie" in either the lay press or scientific literature.[116] For example, in August of 1889, a Dr. Henry Reseding of Paris, Kentucky, who had prepared his own mixture, had caused the death of one of his "decrepit" patients. This was reported in the *Daily Arkansas Gazette* under the title "A Fatal Experiment." The article concluded that there must be "something wrong with the 'life elixir,'" as the patient died in "terrible agony."[117]

Brown-Séquard also took issue with well-meaning doctors, with good reputations, who went too far with their claims, such as Dr. Uspensky from St. Petersburg who suggested that testicular injections could cure pulmonary tuberculosis.[118] Brown-Séquard liked Uspensky and admired his scientific work, but he disagreed with his conclusions about the curative power of testicular extracts. While Uspenksy's phthisic patients did seem to improve after treatment with the injections, it seemed to Brown-Séquard that it was far from a "cure." The liquid probably acted on tuberculosis in the way it acted on other diseases: as a general tonic and not a specific treatment against any one disease in particular, let alone infectious disease.[119]

Brown-Séquard's slight correction of Uspensky's work might seem pedantic, but he was in fact taking a stand against a wider problem that was rearing its head in the bourgeoning trade of organic extracts. Doctors and druggists were latching on to the notion that testicular injections and other organic extracts were a panacea treatment for myriad

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[116] *La France Médicale*, September 10, 1889, 1252. Miscellaneous reports detail how the "Elixir of Life" had resulted in "deplorable" outcomes in its subjects, including the death of two reporters in Philadelphia who tried the therapy. So much for it being an "elixir of life!", remarked the report.

[117] "The Fluid's Virtue: A Fatal Experiment," *Daily Arkansas Gazette*, August 16, 1889, 2. This patient was of African descent. The article reports that "the negros in the village became so incensed at the doctor that he was compelled to leave the country immediately after the disastrous experiment. He cannot be found, and it is supposed the friends of the deceased have killed him." My dissertation is not focused on patient experiences but another project could make rich analysis about the types of patients who were subjected to Brown-Séquard's experimental therapy.

[118] Brown-Séquard, "Exposé de faits nouveaux montrant la puissance du liquide testiculaire contre l'affaiblissement dû à certains maladies et en particulier la tuberculose pulmonaire," 224.

[119] Brown-Séquard also entertained reports from doctors who suggested his therapy was useful in treating cholera and cancer. See notice in "Les académies," September 6, 1892, 3.

diseases. This greatly alarmed Brown-Séquard. He had never claimed his injections could cure anything beyond a want of vigor, not even in his most excited and optimistic commentaries on the subject, and he started to worry that medical practitioners were not approaching their use of the injections with a critical and experimental gaze.

In May 1891, Brown-Séquard issued a statement in the Société de Biologie that made an example of one unnamed doctor who was dealing in the myth of the "radical cure." Brown-Séquard explained that this doctor had contacted him directly, hoping that his work might be published in the *Comptes rendus* of the Société de Biologie. Brown-Séquard was on the point of obliging, for he seemed to occupy an "honorable position" in French society, but something did not seem quite right. This doctor had claimed to have "radically cured" a lady with tuberculosis, which put Brown-Séquard on high alert. By chance, Brown-Séquard then stumbled across the same doctor's name in the press where, shockingly, he appeared to be advertising his medical services and Brown-Séquard's injections for profit. Brown-Séquard was disgusted. "We know that the testicular liquid cannot cure tuberculosis directly," he wrote in the *Comptes rendus*, "and that if this affliction brought itself to the point of appearing to be cured under the influence of sub-cutaneous injections of this liquid, this favorable effect is obtained only after several months of treatment and demonstrated itself only thanks to the modifications of the nervous system and an amelioration of nutrition." As for this doctor's profit-seeking ways, Brown-Séquard only offered him the dignity of one withering line of condemnation: "One does not need a useful method of treatment suspended because some men greedy for money serve themselves with this method and abuse it."[120]

[120] Charles Brown-Séquard, "Remarques à propos de l'emploi du liquide testiculaire," *Comptes rendus des séances de la Société de biologie et de ses filiales,* May 9, 1891, 318. It is possible that this unnamed doctor is in fact Dr. Goizet, about whom D'Arsonval and Brown-Séquard were complaining bitterly in their personal correspondence in late March and April of 1891. See especially Charles Brown-Séquard to Jacques Arsène d'Arsonval, March 31, 1891, in Delhoume, 388-390.

But "greedy" men abounded in fin-de-siècle France. Doctors and druggists were on the prowl for profit and had been making Brown-Séquard's testicular liquid ever since he had openly published his method in the Société de Biologie in 1889. There was a Dr. de Ligniéres from Nice who placed an advertisement in the newspaper, claiming that he had perfected the "Method of Brown-Séquard" and supplied pills made from unnamed tissues and organs of bulls.[121] Mr. Oscar Fanyau from Lille was also quick off the mark, producing and selling testicular injections at the price of 4 fr 50 for a flask, and 3 francs for a half-flask.[122] There was the laboratory of "Chaix & Remy," rue de l'Orne, in Paris, who had been making "organic liquid" with Brown-Séquard's method since at least the Fall of 1891.[123] According to Brown-Séquard, there were 200 pharmacists and doctors producing the liquid by 1893.[124]

A key advertising strategy adopted by druggists was to boast that they had prepared their liquid "according to the method of Brown-Séquard," which was a difficult claim to refute, for the method of Brown-Séquard was public property and, in Brown-Séquard's own estimation, still under development. Some even suggested that they had the endorsement of Brown-Séquard themselves, including Mr. Égasse and Mr. Bouyé, a doctor and pharmacist duo based in Paris.[125] They claimed they had learned the method from studying a series of articles on the subject that were published in the *Bulletin general de thérapeutique* in 1892,[126]

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[121] Advertisement in *Le Figaro*, October 20, 1889.
[122] Advertisement in "Comment prolonger l'existence," *Le Petit Parisien*, November 12, 1891. Another advertisement from 1889 confirms that Fanyau had been producing the liquid since 1889. See advertisement in *Le Petit Journal*, November 4, 1889.
[123] Advertisement in *Le Petit Journal*, September 30, 1892, 2.
[124] Brown-Séquard to Poupinel, March 2, 1893.
[125] In his advertisement, Mr. Égasse described himself as "Ancien professeur agrégé aux Écoles de médecine navale," and Bouyé as "pharmacien de première classe." See Égasse and Bouyé, "Extraits Organiques," *L'Union pharmaceutique: journal de la Pharmacie centrale de France*, 1894, 651. In truth, Brown-Séquard and d'Arsonval did like these manufacturers very much, but they did not publicly endorse them. See Jacques Arsène d'Arsonval to Charles Brown-Séquard, January 2, 1893, in Delhoume, 495-96.
[126] They were referring to articles that appeared in October 30, and November 15 and 30, 1892 of *Bulletin general de thérapeutique*.

and then perfected it "under the direction" and "thanks to the kindness" of Mr. d'Arsonval at the laboratory at the Collège de France itself.[127]

Brown-Séquard had been troubled by the moderate modifications that were being made to his method by experimenting doctors, for it possibly put patients at risk, and implicated his own name and therapy in experiments that he did not necessarily condone. But these problems were small fry compared to the commercial activity of druggists who so brazenly exploited his liquid. Not only were these medications almost certainly ineffective, Brown-Séquard contended, but they also dragged his name, and the reputation of his testicular injections, through the mud. He laid out his position to the Société de Biologie in December 1890, by which time he was starting to panic:

> Some charlatans sell under the name "elixir" and also "tonic syrup of the nervous system" a liquid that they pretend contains the principle that I have signaled as endowed of a considerable dynamogenic power and which is found in a liquid that one extracts from the glands and the spermatic canals. It is important that an energetic protestation be made against these exploiters of the credulous public.[128]

One of Brown-Séquard's biggest gripes with commercial actors who prepared testicular extracts "according to the method of Brown-Séquard" was that they often recommended the drug be administered by the mouth. But as Brown-Séquard pointed out, if any active principles did exist in the little pill or tablet—a scenario he found very unlikely, given who had made it—then they would certainly be degraded by the gastric juices in the stomach once swallowed, thus rendering the therapy completely ineffective. Taking testicular tissue by the mouth might be the easy way, Brown-Séquard preached in *Comptes rendus*, but it was most certainly not the right way of administering treatment.

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[127] Égasse and Bouyé, "Extraits Organiques," 651. It is very possible that d'Arsonval did help Égasse and Bouyé prepare the liquid, as he and Brown-Séquard were in the habit of helping people improve their manufacturing skills, but I wager that they would not have approved of the druggists selling their liquid for between 7 and 20 francs—prices that were listed in their advertisement.

[128] Charles Brown-Séquard, "Nouvelles remarques sur le liquide testiculaire, par M. Brown-Séquard," *Comptes rendus des séances de la Société de biologie et de ses filiales*, séance du 20 décembre, 1890, 717–18.

Brown-Séquard's harshest rebukes were reserved for the "charlatans" who abused his method, but he also took aim at doctors who were being led astray. He wrote: "Several doctors, who since last year, make frequent use on themselves of hypodermic or intrarectal injections of testicular liquid, and who obtain great benefits, have thought that it would be easier on them to swallow in bread or in a pill some morsels of spermatic organs." It was not only a problem in terms of the drug's efficacy, argued Brown-Séquard, but also a problem of reputation, because "after three, four or five weeks of tests," these doctors would "renounce" the therapy and claim it had no benefit. [129] This was only unfair to him, Brown-Séquard lamented, and it was unfair to the drug.

The abuse of the "méthode de Brown-Séquard" was not just a problem in France. Doctors and druggists all over the world were tinkering and tampering with Brown-Séquard's recipe. Consequently, they got it wrong, dissatisfied patients, and kicked up unnecessary storms of controversy for poor Brown-Séquard, who was beginning to unravel. For example, there had been "enormous scandal" in Russia at the end of 1890, gleefully covered by the French press, which involved the eminent professor Dr. Alexander Poehl and his Brown-Séquardian-inspired drug "spermine." As *La Presse* cheerfully reported, "spermine" turned out to be nothing but diluted water. This might not have been too big a problem for Brown-Séquard if Poehl was a nameless huckster, but he was unfortunately a very well-known scientific figure who had been, horrifyingly, supplying testicular liquid to the imperial family and "all the aristocracy" of Russia, making "millions" of francs in the process.[130] The natural implication of Poehl's gambit was that if one very eminent Russia physician could be found

[129] Brown-Séquard.
[130] "Choses et Autres: La Liqueur Brown-Séquard," *La Presse*, November 1, 1890, 3. Note that "millions" of francs might have been an exaggeration on the part of this unnamed editorialist, as this would have been quite a fortune to amass in the short time between Brown-Séquard's announcement in June of 1889 and the publication of this article.

foisting fraudulent products on unsuspecting patients, then so could one very eminent French physician.

Despite this unfortunate report out of St. Petersburg, Brown-Séquard still thought the biggest culprits for abusing his method were Americans. He outlined the problem as he saw it in *Archives de physiologie*, a journal which was quickly becoming for Brown-Séquard an outlet to air his many grievances with the trade in organic extracts. It was also a venue to set the record straight, for whoever cared to listen:

> Since the experiments that I made on myself and have published, the political press of both worlds speak about it without knowing about it, and it has unfortunately given rise in thousands of individuals weakened by age, sexual excess or sickness, absurd hopes that must have been promptly dashed. In the United States especially, and often without knowledge of what I have done, nor the most elementary rules with regard to the subcutaneous injections of animal materials, several doctors, or rather incompetent doctors and charlatans, have exploited the ardent desires of a great number of individuals and have made them run the greatest risks…"[131]

The risk of scandal, commercial activity, and misapplications of his method only heightened as his testicular injections grew in popularity, and as more and more practitioners and druggists tried their hand at the méthode de Brown-Séquard. If one were only reading the *Comptes rendus* and *Archives*—the two scientific venues in France which remained the most popular places to publish about Brown-Séquard's injections—then one might estimate that by 1891 there were dozens, and probably some hundreds, of doctors testing his liquid around the world. This number is indicated by the clinical reports that were submitted to these journals, and by the very many doctors that Brown-Séquard called out in text in his own commentaries and articles. But the French lay press puts the size of Brown-Séquard supporters at a much higher number. In 1891 and 1892, multiple newspapers were reporting

[131] Charles Brown-Séquard, "Du rôle physiologique et thérapeutique d'un suc extrait de testicules d'animaux d'après nombre de faits observés chez l'homme," *Archives de physiologie normale et pathologique,* 1889, 739.

that there were several thousands of doctors in France alone who were experimenting with Brown-Séquard's liquid.[132]

Emile Gautier, a science reporter in *Le Figaro* who frequently commented on Brown-Séquard's movement, said it best: "If I had told you that, far from evaporating under the withering breath of ridicule, the famous elixir of long life and long love, to which Mr. Brown Séquard had no fear of attaching his venerable name, is, to the contrary, on the point of entering the domain of medical practice by the front door, I would have run the risk of you laughing in my face."[133] Yet, just two years after Brown-Séquard's legendary address, Gautier continued, "nothing, however, is more exact." According to Gautier, the Brown-Séquard method had been put to trial "pretty much everywhere" and the results were such that it was impossible to rally forcefully against it.[134] Another commentary in *Le Figaro* from the same year, entitled "The Triumph of Progress," admitted that the once laughable Brown-Séquardian therapy had made a comeback, as evidenced by its growing support within the Faculté de Médecine de Paris.[135]

Brown-Séquard did not let such positive publicity get to his head, for he knew that the increasing popularity of this method was just as harmful to him as it was helpful. Both good and bad doctors were using his method in good and bad ways, and it was impossible to know who would ultimately triumph. For Brown-Séquard, it was a battle for the medical integrity his movement, and he was left with a few options before him. The first was to dissociate himself, simply but sternly, and as convincingly as possible, from all and any commercial activity that attached itself to his name. He sent d'Arsonval off to the Académie of Médecine in July of 1892 to make this very argument. *Le Petit Journal*, witness to the proceedings,

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[132] Notice in "Les académies," September 6, 1892, 3.
[133] Émile Gautier, "La revanche de Brown-Séquard," *Le Figaro*, March 26, 1891, 1.
[134] Gautier, 1.
[135] Paul Bernier, "Le triomphe du progrès," *Le Figaro*, July 11, 1891, 2.

documented Mr. D'Arsonval's address. He insisted that there were many manufacturers who were "eager to profit" from Brown-Séquard's drug, but that he and his master had nothing to do with it. "These preparations engage only their authors," he is reported as saying, and that "he and Brown-Séquard intend to remain strangers to all deliveries which do not leave their laboratory…"[136]

Brown-Séquard himself gave an interview to a reporter from New York that expressed very similar sentiments, albeit with a much stronger bite.[137] It was in early November 1889, just months after he went public with his method. The reporter was allowed the privilege of meeting Brown-Séquard in his own home, an elegant third-floor apartment on Rue Francois-Premier, just blocks from the Champs-Elysées. Settling down in the drawing room, which was decorated in classic French-style, and where the chairs and sofa were "carefully concealed under linen covers," the reporter asked Brown-Séquard about the elixir. Brown-Séquard was not feeling his best, having just returned from a period of rest in Brighton, where he was recovering from persistent rheumatism, renal pains, and insomnia. This might have accounted for his snappy and irritable response:

> As regards the tonic which your American friends call an elixir of life, and regard as a rejuvenating potion, I may here once and for all state that it is nothing of the sort. I am a man of science, not an alchemist. If quacks in the United States try to raise money by misrepresenting my discoveries or giving a false color to the results hitherto obtained by me, of course I cannot prevent them; but I am not to be held responsible for their quackery."[138]

Brown-Séquard knew that what the medical marketplace did or did not do with his method was completely out of his control. His recipe was out there in the public domain, and there was no going back. This left Brown-Séquard and d'Arsonval to double down on another

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[136] Thomas Grimm, "La méthode du professeur Brown-Séquard," *Le Petit Journal*, July 9, 1892, 1.
[137] "Famous Elixir of Life," 9. This reporter was likely James Gordon Bennett Jr. of the *New York Herald*. See "For Women Also. Dr. Brown-Séquard's New Elixir," *San Francisco Chronicle*, September 8, 1889, 9.
[138] "Famous Elixir of Life," 9.

very practical step to protect themselves and their movement: encouraging the good doctors, whoever they may be, to continue working with the liquid. Despite everything that had happened, both Brown-Séquard and d'Arsonval still put a remarkable amount of trust in medical practitioners to do the right thing, to produce liquid in the right way, and to produce quality data about the testicular injections. They needed the clinical data, but they also needed doctors to take up their movement, and to rescue it through high-quality clinical practice. In another presentation to the Académie de Médecine, this time in 1892, d'Arsonval stated: "Laboratory experiments have shown that there is a (veritable) line of enquiry, and now it is up to the clinic to do the rest—it's why, my dear colleagues, that we call on your experience, we who are not (currently) practicing medicine."[139]

To assist the good doctors, Brown-Séquard and d'Arsonval continually updated their method and made it available to the medical community via publication. In fact, they used almost every publishing opportunity to make amendments, in real time, to Brown-Séquard's initial set of instructions for how testicular injections should be prepared. This included adding bullet point notes at the end of publications on how extracts should be filtered, which tissues should be used, and how many injections should be made, and when. They also included commentary on publications about their therapy authored by high-profile doctors, such as those made by members of the Académie de Médecine, with feedback on how their experiments might be improved.[140] This kind of advisory approach also manifested in helpful

[139] Jacques Arsène d'Arsonval, "Historique de la méthode thérapeutique basée sur l'injection des extraits organiques," *Bulletin de l'Académie nationale de médecine*, June 21, 1892, 858. While Brown-Séquard and d'Arsonval were both trained as physicians, they were not, to my knowledge, actively treating patients during the testicular years. They rather saw themselves first and foremost as scientists and experimenters and, increasingly, producers of the liquid. This is why they relied so heavily on the clinical experience of doctors; without doctors' data, Brown-Séquard and d'Arsonval would have little sense for the efficacy of their therapy in human patients. To gain an insight into d'Arsonval's experimenter/drug producer identity, see his letter to Mrs. Brown-Séquard, January 1, 1891, in Delhoume, *De Claude Bernard à d'Arsonval*, 353.

[140] For example, writing in the *Bulletin de l'Académie Nationale de Médecine* in February of 1892, d'Arsonval commented on work done by Paul Constantin, a new convert to the method of Brown-Séquard, who had started to experiment with injections of brain tissue, sourced from sheep, as a treatment for neurasthenia. D'Arsonval, excited by Paul's novel work, had some suggestions on how he could improve his method. See Jacques Arsène D'Arsonval, "De l'injection des extraits liquides provenant des différents tissus de l'organisme, comme méthode

tips to medical practitioners on how to avoid injury and pain when administering the injections. [141] For example, in an American newspaper article, which appeared under the title "Dangerous Trifling," Brown-Séquard is quoted as saying: "Great care should…be taken to avoid septic trouble incident on putrefied meat, as butchers have an elastic conscience regarding the number of hours or even days since their animals were brought to the shambles." He went on to advise doctors that "the strictest attention should be paid to the cleanliness of the tools and cases employed, and as often as possible a Pasteur filter should be used for filtering the fluid. Doctors who have recourse to the process should bestow on the operation, simple as it is, as much care and they would in the case of any more serious surgical operation."[142] Brown-Séquard also made himself available for consultation to doctors who felt uneasy about producing the elixir. He recounted a story about one doctor who caused blood poisoning in a patient, and then contacted Brown-Séquard for advice. Brown-Séquard replied: "The mischief is done now, Why didn't you ask me about it before the operation?"[143]

But as much as he wanted to, and as generous as he was with his time, Brown-Séquard simply could not help or advise all the doctors who experimented with his liquid. This left him and d'Arsonval to implement another practical measure for controlling the

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thérapeutique; technique de la préparation de ces extraits," *Bulletin de l'Académie nationale de médecine*, February 23, 1892, 253.

[141] From the beginning, Brown-Séquard intended his experiments to be replicated by doctors and scientists, and he had their comfort and safety at the top of his mind. One idea he had was to employ some cocaine along with the injections. He said: "It cannot be denied that the physiologists and physicians who may desire to repeat upon themselves my experiments might escape the pain by employing, simultaneously with the testicular fluid, cocaine." See Newell Dunbar, ed., *The "Elixir of Life."* (Boston: J.G. Cupples Company, 1889), 40. Brown-Séquard was insistent about the value of using filters to make his injections safer. In another publication, he said: "When I employed liquids having passed through Pasteur's filter, the pains and other bad effects were somewhat less than when a paper filter was used." See Dunbar, 26.

[142] "Famous Elixir of Life," 9.

[143] "Famous Elixir of Life," 9. This source also reveals some of Brown-Séquard's thoughts about the life-prolonging benefits of his therapy. He said that "to say that it will conquer death… is a preposterous exaggeration. I do not pretend to rob death of its sting or the grave of its victory. So far experimentation has not yet shown even that it will restore certain functions that depart with the advance of age. But I do hold that, by imparting strength to an otherwise weakened constitution, it will prolong the life of the patient and render one less subject to the attacks of disease…"

narrative about testicular injections, and ensuring the right product got into the right hands: to produce the liquid themselves, at the Collège de France, and to distribute it freely to the doctors who requested it.

Starting and Stopping Production

Brown-Séquard had been supplying free samples of testicular liquid to doctors who asked for it since his initial announcement in 1889, but it was not until early 1891 that he and d'Arsonval got very serious about upscaling production. By this time, the popularity of the drug with the doctors of France was apparent, but so were the dangers of its exploitation by commercial actors and negligent doctors. Moreover, Brown-Séquard was being approached directly by an increasing number of physicians who wanted to source the testicular liquid directly from him at the Collège de France, rather than make it themselves or buy it from a commercial supplier. The calculation for Brown-Séquard was simple: if the doctors of France wanted testicular liquid, and the market was awash with bad product, then it was up to him and d'Arsonval to give it to them.

D'Arsonval was the key to Brown-Séquard's ability to make testicular liquid in bulk and to transform his laboratory at the Collège de France into a mini-factory. While Brown-Séquard had been waging a war of words against charlatans and quacks, d'Arsonval had been designing a complex machine that could filter huge amounts of organic liquid in record time. Filtration was the slowest step in producing the testicular liquid, for one had to wait for the mixture of testicular tissue and diluted water to drip-drip through the Pasteur filter or paper filter. But, as Brown-Séquard so often outlined, it was an essential step and could not be skipped, for unfiltered liquid could lead to blood poisoning and death.

D'Arsonval laid out the problem in a presentation to the Société de Biologie in January 1891. "Filtration is long and fastidious," he said, and using "a pressure of five or six atmospheres (as in the model of the pump of Mr. Chamberland) is absolutely insufficient

when we have to filter certain liquids, such as for example the testicular liquid prepared following the method of M. Brown-Séquard." "The pump of M. Chamberland" is a reference to the Pasteur-Chamberland filter, which was known both as the "Pasteur filter" and the "Chamberland" filter. D'Arsonval continued: "It is the difficulty that I have encountered in making this preparation requested from the laboratory by a certain number of doctors, which has brought me to work out this very simple device that I have the honour of submitting to you." [144]

D'Arsonval then showed the Société de Biologie the results of his engineering efforts: an impressive, industrial-looking filtration machine, purpose-built for mass production. It made use of high pressures of carbonic acid [$CO_2 + H_2O$] to push organic liquid quickly through the pores of porcelain, which meant that d'Arsonval could filter large volumes of organic liquid in just minutes, rather than the ten to twelve hours it would normally take. Just as Brown-Séquard had given explicit instructions on how to prepare and employ his testicular injections, d'Arsonval explained to his audience exactly how the machine worked and even offered blueprints for its construction, so that others might try their hand at building it and benefitting from high-powered filtration.[145] His paper in the *Comptes rendus* ended with a directive from his master, Brown-Séquard.[146]

> Thanks to this method, it is easy to rapidly prepare large quantities of testicular liquid. Mr. Brown-Séquard, to whom I have given word of this result, has asked me to announce to our medical colleagues or surgeons from the hospitals that for all those among them who would like to experiment with the injections of testicular liquid in their service will now find them henceforth in our laboratory, 12, rue Claude-Bernard, free of charge, of course.[147]

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[144] Jacques-Arsène d'Arsonval, "Filtration et stérilisation rapides des liquides organiques par l'emploi de l'acide carbonique liquéfié (Présentée le 17 janvier)," *Comptes rendus des séances de la société de biologie et de ses filiales*, February 7, 1891, 90–92.
[145] D'Arsonval, 92. He also included information on the cost of certain parts (eg. carbonic acid), clearly factoring in the budgets of practicing clinicians who might have less resources than their laboratory at the Collège de France.
[146] D'Arsonval, 92.
[147] D'Arsonval, "Filtration et stérilisation."

The physicians and surgeons of Paris took Brown-Séquard and d'Arsonval at their word, for a few months later, they had dispensed over four hundred bottles of testicular liquid prepared by d'Arsonval's machine, which was enough to make twelve thousand injections.[148] By the middle of 1892, the French press reported that more than twenty thousand people had been injected with Brown-Séquard's liquid, a statistic they surmised from Brown-Séquard's own reporting at the Académie de sciences.[149] By 1893, d'Arsonval reported that ten thousand bottles had been distributed from their laboratory, enough to make 300, 000 injections.[150] Included in these counts were not just general practitioners in France, but also esteemed doctors who worked in France's hospital system, to whom they supplied not only testicular injections, but also an array of liquid extracts from other glands of the body. D'Arsonval explained:

> As the laboratory cannot lend itself completely to clinical experience, we have supplied a number of doctors with some liquid extracts of all kinds, prepared by myself at the laboratory with the aid of the carbonic acid sterilizer. Among the hospital doctors who have received and experimented with these liquid extracts, I can cite, at random, MM. Cornil, Variot, Dumontpallier, Merklen, Dejerine, Ballet, etc…[151]

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[148] Charles Brown-Séquard and Jacques-Arsène d'Arsonval, "Additions à une note sur l'injection des extraits liquides de divers organes, comme méthode thérapeutique," *Comptes rendus des séances de la société de biologie et de ses filiales*, April 25, 1891, 268. See also "Note par MM. Brown-Séquard et d'Arsonval," *Comptes rendus Société de biologie*, April 25, 1891, 265–68.

[149] Notice in Échos et Nouvelles in *Le Petit Parisien*, May 25, 1892. According to this article, none of these people had experienced any serious side effects from Brown-Séquard's injections.

[150] Jacques-Arsène d'Arsonval, "Remarques à propos de la communication de M. Guinard," *Comptes rendus des séances de la société de biologie et de ses filiales*, March 11, 1893, 272.

[151] d'Arsonval, "De l'injection des extraits liquides provenant des différents tissus de l'organisme, comme méthode thérapeutique; technique de la préparation de ces extraits," 252. D'Arsonval continued to state that the laboratory supplied "M. Constantin Paul himself, because the first nervous extract of rabbit that he injected was prepared by me at the laboratory of the College de France…" See also notice in "Les Académies," *Le Matin*, February 24, 1892, 2. I should note here that Brown-Séquard and d'Arsonval's main business was to produce testicular extracts but, as we can see here, they also supplied some doctors with other organic extracts.

Deciding to produce the testicular liquid in bulk, and distributing it free of charge,[152] was a multi-pronged strategy from the Brown-Séquard laboratory. It was a strike against those pesky charlatans who were dispensing oral medications, for it set an example to the medical community of how testicular therapy should be produced and administered. Next, it established a network of medical colleagues-turned-experimenters, who received liquid directly from Brown-Séquard's laboratory and then (hopefully) reported back with experimental data. A third key benefit to producing liquid at the College de France was the effect it had on salvaging the reputation of their laboratory and their therapy, for it demonstrated to the medical community that they were serious and highly ethical operators.[153]

Indeed, it was on the strength and virtues of this new filtration machine, and its ability to produce huge amounts of filtered liquid, that D'Arsonval found himself making a presentation about it to the Académie de Médecine in 1892, which was one of the first occasions in which Brown-Séquard's new controversial therapy was put on the table for conversation at the Académie—in an official capacity, at least. After explaining how the machine worked, and sharing blueprints with the doctors, like he had to the Société de Biologie, d'Arsonval was engaged in a robust discussion by leading Pasteurian Edmond Nocard, as well as several other members of the Académie de Médecine,[154] about microbes and infectious disease. Greatly impressed by the powers of the machine, these doctors marveled at, among many things, the filter's ability to separate out all microbial material

[152] I have found no evidence that Brown-Séquard charged anyone for this liquid, other than suggesting that doctors, in submitting their requests to the laboratory, include 3 stamps valued at 15 centimes, to abet the cost of return postage. See Dr. Poverio, "Incurie," *Le Figaro*, December 2, 1892, 1–2.
[153] What did it mean to be "highly ethical operators"? The next chapter will dive into this idea in depth, using letters of correspondence between Brown-Séquard and d'Arsonval that addresses the question of "ethical" and "non-ethical" business practices in fin-de-siècle France.
[154] For more details on Nocard, see Simon, *Diphtheria Serum as a Technological Object*, 25.

from the filtrate below. The machine, and d'Arsonval as its creator, made a strong argument that Brown-Séquard's laboratory took safety—and science—seriously.

Yet, despite the success of d'Arsonval's filtration machine in upscaling his and Brown-Séquard's production capacity, it was still not enough to meet physician demand. Some of the first signs of trouble at the Collège de France came in the middle of June of 1892, when d'Arsonval, again presenting to the Académie de Médecine, explained that despite his willingness to continue supplying doctors, he was happy to see that some of his colleagues in hospitals were taking on the burden of production by producing liquid themselves in their own labs.[155] D'Arsonval said this measure relieved him of the "worry and loss of time caused by preparations."[156] Then, that same month, Brown-Séquard and d'Arsonval decided to take a short break from manufacturing and issued a simple notice in *Le Petit Journal* announcing that they were going on summer vacation, that supply would be disrupted, and that they would not be taking any new orders until further notice, except for doctors who wanted to use organic extracts "for their personal use."[157] They came back from vacation to an "avalanche" of letters, according to d'Arsonval, so much so that he could only satisfy between a quarter to a third of the requests received.[158]

More stress signals were issued by Brown-Séquard a few months later, in September of 1892, when he reported that he and d'Arsonval were becoming worn out by the demands placed on them by doctors. In the last five weeks alone, he bemoaned, they had received

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[155] According to the Brown-Séquard and d'Arsonval's private correspondence, they were struggling to supply doctor demand from early 1891 and turned down many requests for liquid. See especially letters from late March and early April, 1891, in Delhoume, *De Claude Bernard à d'Arsonval*, 385–95. There is evidence, too, that d'Arsonval was being "encumbered" by physicians' demands for the liquid as early as January, 1891. See Jacques Arsène d'Arsonval to Mrs. Brown-Séquard, January 1, 1891, in Delhoume, 353.

[156] d'Arsonval, "Historique de la méthode thérapeutique basée sur l'injection des extraits organiques," 861. But at the same meeting, he announced that the laboratory did have liquid available for distribution, indicating to doctors that, despite the strain it was placing on his schedule, he and Brown-Séquard were still prepared to supply liquid to doctors who asked for it. See notice in "Les académies," *Le Matin*, June 22, 1892, 3.

[157] "La méthode Brown-Séquard," *Le Petit Journal*, July 28, 1892, 2. It is not clear from the notice what Brown-Séquard meant by the phrase "personal use."

[158] Jacques Arsène d'Arsonval to Charles Brown-Séquard, July 12, 1892, in Delhoume, 445-46.

2,800 letters from doctors from every corner of France demanding samples of his liquid, which was far more than he and d'Arsonval could handle.[159] In the same month, Brown-Séquard and d'Arsonval issued a circular to the medical community, indicating that their laboratory-turned-factory had reached its limits.[160] The announcement, written with emphasis by the always-expressive Brown-Séquard, declared:

> The Laboratory of Medicine cannot satisfy the immense number of new demands to supply testicular liquid. It will continue, *despite the enormous amount of time that must be sacrificed to it*, to supply the organic liquid to the twelve hundred doctors to whom we had promised the liquid or who has already received it. It is absolutely impossible for the laboratory to do any more."[161]

The notice concluded by urging doctors to make their own preparations: "It is so easy to prepare these liquids that any doctor who wants to can have them. A pamphlet from one of us (M. d'Arsonval), giving the technique of this preparation, will appear soon with M. Masson."[162]

Despite Brown-Séquard and d'Arsonval's strong suggestions that doctors should be stepping up and making their own liquid, there is evidence that the Collège de France. continued to supply doctors through September.[163] But their operation finally collapsed just a few months later, at the beginning of December, 1892, when Brown-Séquard issued a short but regretful notice announcing that due to the very high demand placed on them by doctors who wanted testicular liquid, and their struggle to meet this demand, they had decided to

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[159] Notice in "Les académies," September 6, 1892, 3. The volume of interest in his injections caused him considerable stress, as his laboratory only had the capacity to supply about 1000 doctors, according to Brown-Séquard.

[160] Brown-Séquard and d'Arsonval's notice in Chavois, *D'Arsonval: Soixante-cinq ans à travers la Science*, 215.

[161] Brown-Séquard and d'Arsonval's notice in Chavois, 215. This also appears in Thomas Grimm, "Pour prendre patience!," *Le Petit Journal*, September 26, 1892, 1. Original emphasis.

[162] Brown-Séquard and d'Arsonval's notice in Chavois, *D'Arsonval: Soixante-cinq ans à travers la Science*, 215. Mr. Masson was a French publisher of medical and scientific texts.

[163] On September 17, 1892, Brown-Séquard wrote to a Dr. Poverio, promising him the goods. Poverio shared this letter with *Le Figaro*, which appeared in a longer editorial he had written on the subject. It read: "Monsieur, we are finally in the position to regularly send you the liquid. We would have started supplying you today if we had been sure of your address. Please accept the expression of my best sentiments, C.-E Brown-Séquard." See Poverio, "Incurie."

cease production altogether. This communication, which was printed in *Le Figaro*, was framed, with officiality and finality, by the letterhead of the Laboratoire de Médecine du Collège de France:[164]

> The number of demands for Organic Extract has become really so great that, as we can no longer satisfy them, we are forced to stop supplying it. Nonetheless, continuing the scientific investigation that we have begun, we will make an exception in favor of doctors who will ask us for it for the treatment of superficial cancer…"[165]

Committed to ongoing scientific investigation, but bowing out from high-volume production, Brown-Séquard and d'Arsonval signed this circular and issued no more.[166] It officially marked the end of their high intensity but short-lived foray into formulating and suppling testicular extracts, and other organic extracts, to the medical community.[167]

Brown-Séquard & Doctors in the Bacteriological Revolution

Before diving into the next chapter, which continues the story about how Brown-Séquard and d'Arsonval managed their manufacturing crisis, first a key question. Why did Brown-Séquard go to such extraordinary lengths to supply doctors with free testicular extracts? He had very practical reasons, as this chapter has demonstrated. He did not want doctors to source bad products from the medical marketplace, and he wanted to collect good data from clinics about how his new therapy was faring; giving doctors free liquid, and asking them to report back, seemed to hit two birds with one stone. But to zoom out a little further, we might question, more broadly, why Brown-Séquard cared so deeply about physicians' experiences in the

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[164] Poverio.
[165] Poverio. For more context on Brown-Séquard's interest in the effect of organic extracts on cancer, see Charles Brown-Séquard to Jacques Arsène d'Arsonval, January 12, 1893, in Delhoume, 500-501.
[166] Appearing in Brown-Séquard and d'Arsonval's letters of correspondence is a copy of another circular, dated June 23, 1893, clarifying to the medical community they would not recommend any commercial manufacturer. I have not been able to find this circular printed in the press, but it appears in Delhoume, *De Claude Bernard à d'Arsonval*, 528.
[167] This was the "official" end of Brown-Séquard and d'Arsonval's venture, but their correspondence reveals that they continued to supply some doctors well into 1893. See also d'Arsonval's comments in his interview with Francisque Sarcey. See Sarcey, "Nous sommes trop chevaleresque," *Le Petit Journal*, January 12, 1893, 1.

clinic, and why he engaged with them so consistently, to the point of encouraging them to produce their own organic extracts, and helping them to do so through advice and feedback.

To put Brown-Séquard's close relationship to doctors in context, let us consider briefly the machinations of another French savant who was making scientific medicine in Paris in the 1880s and early 1890s: Louis Pasteur.[168] Very few historians have compared the development of Brown-Séquard's medical movement to Pasteurism,[169] despite the fact that they were colleagues almost of the same age, working in the same city and both launching therapeutic ventures that had national and international reach. And yet considering Brown-Séquard and Pasteur's careers side-by-side reveals a striking contrast between their approaches to doctors.

As we know, Brown-Séquard thought doctors were central to the process of knowledge-making and medicine-making, which manifested in his sharing knowledge and technical-know how for producing testicular liquid. Pasteur, by contrast, favored the laboratory over the clinic and treated doctors as the merely the recipients of bacteriological knowledge and bacteriological medicine, as scholars have noted.[170] As Bruno Latour has argued, for Pasteur it was the laboratory and not the clinic that was the central site of control

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[168] My investigation of Brown-Séquard's approach to drug production has been inspired by scholarship that considers the nuts and bolts of vaccine production in the fin-de-siècle. See: Jonathan Simon, "Monitoring the Stable at the Pasteur Institute," *Science in Context* 21, no. 2 (2008): 181–200, https://doi.org/10.1017/S0269889708001683; Ilana Löwy, "On Hybridizations, Networks and New Disciplines: The Pasteur Institute and the Development of Microbiology in France," *Studies in History and Philosophy of Science Part A* 25, no. 5 (October 1, 1994): 655–88, https://doi.org/10.1016/0039-3681(94)90035-3.

[169] Bert Hansen, who works on the history of Pasteur's vaccines, is one of the few historians to place Brown-Séquard in the wider context of developments in scientific medicine in the late nineteenth century. See: Hansen, "America's First Medical Breakthrough"; Bert Hansen, *Picturing Medical Progress from Pasteur to Polio: A History of Mass Media Images and Popular Attitudes in America* (New Brunswick, N.J.: Rutgers University Press, 2009). See also Borell, "Brown-Séquard's Organotherapy." There is more work to be done on comparisons between Pasteurism and Brown-Séquard's movement, especially because historical actors made these comparisons themselves. See, for example, "The Week: Brown-Séquard's Testicular Fountain of Youth," *The Cincinnati Lancet and Clinic* 23 (July 20, 1889): 79.

[170] See Bruno Latour's classic characterization of Pasteur in Latour, *The Pasteurization of France*. See also Gerald L. Geison, "Pasteur, Roux, and Rabies: Scientific versus Clinical Mentalities," *Journal of the History of Medicine and Allied Sciences* 45, no. 3 (1990): 341–65, https://doi.org/10.1093/jhmas/45.3.341.

for his production of vaccines.[171] French doctors, who had neither the capacity nor the technical know-how to produce vaccines and serotherapies, or even the skills in microscopy or equipment to diagnose infectious disease, were forced to rely on scientists at the Pasteur Institute for their clinical needs in bacteriology.[172]

How can we account for these important differences? Professional biographies can be of service. [173] Brown-Séquard was a doctor by trade and training and spent long periods of his life working in hospitals and clinics in France, England and America.[174] He was also a lab-based experimental physiologist, Claude Bernard's successor at the Collège de France, and was working in the Bernardian tradition of "experimental medicine," which regarded the laboratory and the clinic, experimentalists and physicians, as necessarily bound together in the joint mission of elaborating pathology and curing disease.[175] Thus, when Brown-Séquard made drugs in his laboratory at the Collège de France, his priority was to get them out into the clinic for testing by practicing doctors, and to listen seriously to doctors' experience, especially as he was not maintaining a clinic himself during the testicular years.

Pasteur was also a lab-based experimentalist, but he was a chemist by training and not well-versed in the ways of the clinic. He was also secretive and possessive with the knowledge he produced in his laboratory, as historian Gerald Geison has argued.[176] He expended considerable effort to conceal his drug-making process to outside observers so that he could retain a competitive edge, and remained deliberately opaque about how his drugs

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[171] Latour, *The Pasteurization of France* See especially chapter 2, "You Will Be Pasteurs of Microbes" and chapter 3, "Medicine at Last."
[172] Latour See especially chapter 3, "Medicine at Last."
[173] On this point, I owe thanks to historian of medicine Bert Hansen who drew my attention, in personal correspondence, to the professional and educational differences between Brown-Séquard and Pasteur and how this might have influenced their approaches to drug production.
[174] See Aminoff, *Brown-Séquard: An Improbable Genius Who Transformed Medicine*.
[175] For Claude Bernard's own take on the role of the practicing physician in "experimental medicine," see Claude Bernard, *An Introduction to the Study of Experimental Medicine,* trans. Henry Copley Greene (New York, NY: Dover Publications, 1957) See especially chapter 4, "Philosophical Obstacles Encountered by Experimental Medicine."
[176] Geison, *Private Science*.

worked, even to the point of committing acts of fraud.[177] Pasteur refused to build capacity in other laboratories to produce his vaccines, according to Maurice Cassier, which effectively placed the Pasteur Institute at the center of the vaccine business in France and beyond.[178] His creation of a medical monopoly was not necessarily an attempt at personally profiting from his scientific inventions. Like Brown-Séquard, and as a nineteenth-century savant, Pasteur eschewed commercialism and upheld the value of disinterestedness, at least in public spaces.[179] Indeed, as Aro Velmet has recently shown, the Pasteur Institute was regaled in France and the world in the 1890s as a beacon of scientific charity and ascetism.[180] Monopoly for Pasteur was rather a means to "control" and "stabilize" his products while they were still in development. [181]

As the next chapter will fully detail, Brown-Séquard vehemently rejected proposals that his laboratory seize control of the trade and create a monopoly.[182] He associated monopoly with "commercialism," and this also formed the basis of his personal criticisms of Pasteur and the Pasteur Institute, which will also be detailed in the next chapter. Brown-Séquard thus relinquished control of his ideas and equipment to doctors: he regarded them as

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[177] Geison.

[178] Maurice Cassier, "Producing, Controlling, and Stabilizing Pasteur's Anthrax Vaccine: Creating a New Industry and a Health Market," *Science in Context* 21, no. 2 (June 2008): 253–78, https://doi.org/10.1017/S0269889708001713; Maurice Cassier, "Appropriation and Commercialization of the Pasteur Anthrax Vaccine," *Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences* 36, no. 4 (December 2005): 722–42, https://doi.org/10.1016/j.shpsc.2005.09.004.

[179] See Velmet, *Pasteur's Empire* See especially chapter 3, "Monks and Warriors, Bureaucrats and Businessmen."

[180] Velmet See especially chapter 3, "Monks and Warriors, Bureaucreats and Businessmen." The next chapter deals more closely with the finances of the Pasteur Institute, and especially Brown-Séquard and d'Arsonval's thoughts on Pasteur's business-making venture.

[181] Cassier, "Producing, Controlling, and Stabilizing Pasteur's Anthrax Vaccine"; Cassier, "Appropriation and Commercialization of the Pasteur Anthrax Vaccine"; Geison, *Private Science*. For more literature on the production of Pasteur's vaccines, and bacteriological medicine in general, see: Simon, "Monitoring the Stable at the Pasteur Institute"; Löwy, "On Hybridizations."

[182] Brown-Séquard's story provides an interesting case study for thinking about the relationship of science and commercialism in the late nineteenth century. See special issue in *History and Technology* (33, no. 1, 2017) which nicely summarizes the last thirty years of history of science scholarship in this space.

critical stakeholders in his bid to create a new experimental medicine, and he also feared losing their favor should he make moves toward monopolizing the drug trade.

The Brown-Séquard-Pasteur comparison is productive insofar as it helps reveal an important and particular condition that shaped the emergence of endocrinology, and one which has not yet been fully elaborated by historians of science and medicine. It was launched *by* a doctor *for* doctors, and it emerged as a discipline in the clinic. The laboratory was certainly present in this story; indeed, Brown-Séquard worked *from* a laboratory, and this is where he and d'Arsonval produced testicular liquid. But the laboratory was not a central or even an essential component to making Brown-Séquardian products and using Brown-Séquard's method. As he repeatedly insisted, his injections could be easily made in the clinic by any doctor who took a bit of care and could read his recipe.

Brown-Séquard thus facilitated a model of drug production, and a relationship to doctors, that appears to sit at odds with what we know about the revolution in scientific medicine in the fin-de-siècle. Brown-Séquard's story shows us that it was the clinic, and the doctors who were willing to experiment with his method, that drove the early years of Brown-Séquard's movement, and not the laboratory as we have become accustomed to expect of this period.

Brown-Séquard's story has also revealed that there was a cost to so earnestly engaging doctors as stakeholders and putting drug recipes in their hands. Organic extracts became everyone and anyone's drug, and this both enabled and crippled the bourgeoning drug industry, as this chapter has begun to detail. On the one hand, well-intentioned and careful doctors could easily and cheaply make testicular injections if they could not find (or afford) a supplier, and their patients could reap quick and lasting benefits from these drugs if they were successfully prepared. On the other hand, there was no stopping careless and commercially motived actors from making bad or fraudulent products, claiming they had

made it according to the "méthode de Brown-Séquard." It was a problem that Brown-Séquard had unwittingly created in the very act of making his method so accessible, and one that might make one think about the value of Pasteur's decision to conceal his drug-making processes. Was this a serious alternative for Brown-Séquard? The next chapter steps through his explicit thoughts on the matter and, in doing so, confronts pressing questions about how medicine ought to be produced in the fin-de-siècle, and who should produce it.

Conclusion

If Brown-Séquard and d'Arsonval were no longer producing drugs, then who or what would take their place? In the next chapter, I sift through Brown-Séquard and d'Arsonval's personal correspondence to show that this troubling question was at the forefront of their minds both before and after they closed down production in December of 1892. They considered various proposals for how to get testicular injections, and organic extracts more broadly, produced by an "ethical" manufacturer, and yet almost all of them fell short of Brown-Séquard's expectations for how scientific medicine should be produced. This next chapter deals with the thoughts and views of Brown-Séquard and d'Arsonval, doctors who wrote into the French press, and potential business partners who approached them directly with proposals to invest in their business, including one wealthy American pharmaceutical company. But therein lay the crux of the problem for Brown-Séquard: in his mind, his testicular venture was absolutely *not* a business, and he refused to be part of any proposals that hinted at commercial activity. But how else would his injections get produced? The next chapter is situated between the boundaries of Brown-Séquard's laboratory and the medical marketplace, and it complicates the notion that scientific therapies, if produced on a large scale, could be anything but commercial.

Chapter 2: The Ethics of Manufacturing: Brown-Séquard, d'Arsonval, and the Business of Not Doing Business, 1892-1895

When Brown-Séquard and d'Arsonval announced on December 1,1892 that they were no longer able to produce and distribute organic extracts from their laboratory at the Collège de France, they left thousands of French physicians in the lurch and a void in the drug market.[183] Demand for their liquid had grown so rapidly in France, especially toward the middle and end of 1892, that Brown-Séquard was receiving thousands of letters a week from doctors with requests for free samples. As the last chapter detailed, he and d'Arsonval were run ragged trying to keep their venture afloat, and their solution was to close the laboratory at the Collège de France for production purposes, effective immediately.

Brown-Séquard and d'Arsonval wanted a clean break from the business of drug production, but this was easier said than done. First, they continued to receive numerous letters from "desperate" patients and doctors who demanded the liquid, which was a constant reminder to them that their laboratory had been providing an important service to the medical community since 1889, when Brown-Séquard first started distributing free samples of testicular extracts. Second, they worried constantly about the future of the industry, and fretted about how French doctors would obtain organic extracts now that their laboratory at the Collège de France was no longer acting as a supplier.

Doctors could, of course, continue working with Brown-Séquardian extracts after December 1, 1892, by simply making the concoction themselves using the recipe that Brown-Séquard had made public. Indeed, this is exactly what Brown-Séquard encouraged doctors to do when he closed down his laboratory, as the last chapter detailed.[184] But what concerned Brown-Séquard and d'Arsonval was that doctors would instead procure organic extracts on the medical marketplace, where commercial manufacturers were selling all manner of

[183] Poverio, "Incurie."

[184] The next chapter will show that, indeed, many doctors opted for this approach.

medications that were inspired by "the method of Brown-Séquard." According to counts by Brown-Séquard and d'Arsonval, who monitored the "leaflets" and advertisements that were sent to their laboratory, there were approximately 150 to 200 druggists who were already selling such wares by the end of 1892, and even more were emerging in 1893.[185]

Brown-Séquard and d'Arsonval had a very low opinion of these commercial manufacturers and the drugs they produced. They were convinced that their method and therapy would become completely debased if left only in the hands of these commercial actors. Thus, the two friends and collaborators set themselves the task after December 1, 1892, of searching for an ethical manufacturer who could carry on with production of the organic extracts in their absence, providing doctors with a high-quality product.[186] In short, Brown-Séquard and d'Arsonval were on the hunt for their own replacement.

Finding this manufacturer, however, proved to be an impossible task, and it was not through a dearth of promising leads or good ideas. Investors and benefactors approached the laboratory with proposals about how Brown-Séquard's venture could be transformed into a sustainable business. There were also public calls for the French government to step in to subsidize their laboratory, or to create a kind of institute, similar to the Pasteur Institute, in Brown-Séquard's name. Brown-Séquard and d'Arsonval waged their own private campaigns to source government funding for drug production, and to set up production in existing institutions, such as hospitals and even the Pasteur Institute. Yet, each and every one of these plans fell through, and Brown-Séquard and d'Arsonval were left dejected and defeated. When

[185] This number seems to have increased in 1893, as indicated by the increasing number of druggist advertisements in French newspapers.

[186] My use of the term "ethical manufacturer" is inspired by histories of pharmacy and pharmaceuticals in the U.S., which note the divide between "patent" manufacturers and "ethical" manufacturers in the late nineteenth century. See, for example, Liebenau's *Medical Science and Medical Industry* (1987) and Gabriel's *Medical Monopoly* (2014). Note, however, that "ethical manufacturer" was not a phrase used by Brown-Séquard and d'Arsonval. They did not even use the term "éthique" or "moral" in French in their correspondence about the issue, as far as I am aware. But an "ethical manufacturer" is exactly what they were searching for. What constituted "ethical" in their minds? As this chapter fully details, it was a rejection of profit-seeking in medical manufacturing as well as a repudiation of shoddy scientific work. There were nuances to their views, of course, and these will be fully unpacked in this chapter.

Brown-Séquard died in April, 1894, his method remained exploited on the medical marketplace, no ethical manufacturer had been found to replace him, and doctors were still at a loss for how to procure a high-quality product.

In this chapter, I continue to flesh out Brown-Séquard's influence on the development of early endocrinology by examining the fallout of his manufacturing enterprise. I ask: what conditions prevented Brown-Séquard and d'Arsonval from securing an ethical manufacturer to take over drug production? By sifting through their personal correspondence about this issue, which was penned mostly between December 1892 and March 1893, two key themes emerge. The first is Brown-Séquard's ongoing commitment to doctors, and his consistent consideration of their place within his therapeutic movement. This manifested in his refusal to consider manufacturing proposals that were exploitative of them. The second theme that was wrestled with by both Brown-Séquard and d'Arsonval, and that I investigate at length in this chapter, is commercialism.

Commercialism posed both an opportunity and a threat to endocrinology, in the eyes of these two men, but they could never agree on exactly how to chart the right path forward. Brown-Séquard, who was much older than d'Arsonval and more traditional in his views, thought that the work of the savant should be strictly separate to all and any form of commercial activity, as commerce was a corrupting force on both the scientist and the products he produced.[187] D'Arsonval, who was over thirty years younger, was more progressive. He gently encouraged his boss to consider the ways in which the commercialization of their laboratory could be both practical and ethical. If they resumed drug production at the Collège de France with a new business model, he suggested, they

[187] Mordechai Feingold and Ann Elizabeth Fowler La Berge, *French Medical Culture in the Nineteenth Century*, Wellcome Institute Series in the History of Medicine (Amsterdam; Atlanta, GA: Rodopi, 1994). My thinking about the generational differences between Brown-Séquard and d'Arsonval has also been influenced by Lynn Nyhart's work on German morphologists. See Lynn K. Nyhart, *Biology Takes Form: Animal Morphology and the German Universities, 1800-1900*, Science and Its Conceptual Foundations (Chicago: University of Chicago Press, 1995). See especially pp. 20- 24.

could continue supplying doctors with subsidized organic extracts and undercut commercial competitors in the process.

Brown-Séquard, however, refused to commercialize his laboratory, or to recommend any other commercial enterprises to doctors, but I show that neither strategy was helpful to stability of the trade in organic extracts. I do not go so far as to argue that Brown-Séquard was to blame for their inability to find an ethical manufacturer—many things were out of their control, as this chapter will demonstrate. But while there was a cost to commercialization—an argument continually waged by Brown-Séquard—there was also a high cost to not engaging in business of any kind. This is because Brown-Séquard's refusal to commercialize his laboratory, and his lack of decision-making about who should produce organic extracts in his absence, actually served to stimulate the commercial market for organic extracts. This was an irony that was not lost on anyone.

In stepping through Brown-Séquard and d'Arsonval's thoughts, we are forced, through them, to take stock of the relationship between scientific medicine and the medical marketplace in the fin-de-siècle. The two friends waste little time in posing big questions: how should scientific medicine be produced? Are all forms of commercialism bad? What is the government's role in producing and regulating scientific medicine? To get perspective on their own therapeutic movement, Brown-Séquard and d'Arsonval draw comparisons between early endocrinology and Pasteurism. Following their lead, I circle back to thinking about bacteriology, and how very different was endocrinology's development pathway under the stewardship of Brown-Séquard.

The first part of the chapter returns to the moment when Brown-Séquard's laboratory closed, in December of 1891. I show the public's response, as expressed in the lay press. This included calls for the government to establish a Brown-Séquard Institute that would supply doctors with high quality organic extracts, and questions about how the trade could become

regulated, given Brown-Séquard's decision to publish his recipe to all and sundry. The chapter then considers Brown-Séquard and d'Arsonval's response to these proposals, along with their own thoughts about how the French government should intervene. Next, it considers arguments put forward by d'Arsonval about "profit" and "cost," and whether commercializing their own lab might in fact be the best path forward. In the final section, I show that the French and American governments finally did act to regulate biologic drugs after Brown-Séquard's death, in 1895 and 1902 respectively, but perhaps not in a way he would have imagined.

Calls For Government Action

When the laboratory at the Collège de France closed for production purposes on December 1, 1892, the French government immediately came under fire by dismayed doctors and political commentators, who turned to turned to newspapers to air their grievances and express concern for the future of the industry. One editorial published in *Le Matin* on December 9, penned and signed by an unnamed "Group of Admirers," addressed itself directly to the Minister of Public Instruction and called for a provision in the municipal budget that recognized Brown-Séquard's lab. The letter outlined Brown-Séquard's service to humanity in providing therapy for "thousands of sick people," his "disinterestedness" in commercial gain, and how much of his own money he had already shelled out in getting testicular injections to the doctors who needed it.[188]

> Permit us, Mr. Minister, a confidence that would no doubt make these scientists blush if they made it themselves. They have dispensed…a significant sum. …If the budget does not permit the compensation of money so nobly given to science and to the general good, we urgently ask you to enable them to continue their work without further emptying their pockets. A tiny article inscribed in the budget in favor of the laboratory of Brown-Séquard and d'Arsonval will give us satisfaction and you the gratitude of the public."[189]

[188] A Group of Admirers, *Le Matin*, December 9, 1892.
[189] A Group of Admirers.

Another editorialist, physician Dr. Poverio, also took aim at the French government for their inaction.[190] His editorial, published in *Le Figaro* on December 2 and entitled "Negligence," outlined the huge demand for "Sequardian juices" from the medical community, which had by 1892 reached a consensus that these new products provided "unexpected improvements" in most diseases and sometimes "cures." Poverio recounted that he—and others—had expected that public funds would have been already mobilized to create a Brown-Séquardian Institute, for the therapy had become "indispensable" to doctors. But instead, the laboratory had closed, the government had watched it happen, and doctors were left with nothing.[191] He was flummoxed by this series of events and was deeply concerned about what would happen next. In his article, he painted an alarming picture:

> First, doctors will take it upon themselves to prepare and to sell [the organic extracts]. Then, commercial enterprises will be established (they exist already) which will make a fortune in preparing not only organic juices, but also cerebral juices, etc, and in a word all juices imaginable. Finally, nothing will prevent each pharmacist from manufacturing organic extracts as he pleases and to sell them at a reduced price…all these fanciful extracts…being close to simple distilled water won't cure anyone, but they will kill, without fail, the discovery of Mr. Brown-Séquard and d'Arsonval…[192]

Here Poverio was touching on a real and well-justified fear shared by doctors and Brown-Séquard and d'Arsonval themselves: that without Brown-Séquard's laboratory to produce and freely distribute high-quality organic extracts, doctors would be forced to turn to the marketplace for their medicinal needs, and that these products would be of questionable quality.[193] In Poverio's view, Brown-Séquard's laboratory, when it was operational, acted as

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[190] Poverio, "Incurie."

[191] Poverio made a reference to an article that was published some months ago, in an unnamed newspaper and unnamed authors, that called for an institute. I have not been able to locate this article.

[192] See also Émile Gautier, "Les petits cochons de la régie," *Le Figaro*, December 27, 1892, 1–2. Gautier outlines the practical problems of asking *Assistance publique* to supply the liquid. How will this be governed? By what law? How will it be produced? How could the monopoly be protected when the recipe is out in the public?

[193] As the last chapter detailed, Brown-Séquard had made his recipe public and hopeful drug producers were free to do with it what they wished. Indeed, and as Poverio intimated, Brown-Séquard's recipe had been taken up,

a kind of informal regulator of the trade, because the product he produced functioned both as a reliable drug for doctors, and also a kind of gold standard for quality and safety. This was especially important in a burgeoning and experimental field that had not yet developed principles of best practice. If Brown-Séquard was no longer available to act as regulator, then it was time for the government to step in, thought Poverio. He concluded his article with a "cry of alarm" to doctors: "It is still possible to wake up our sleeping administration!"[194]

Emile Gautier, another commentator, also shared Poverio's concerns about Brown-Séquard's departure from the market, and the effects of unfettered commercial exploitation of Brown-Séquard's therapy. But he thought that calls for the French government to attempt to regulate the market through subsidizing a Brown-Séquardian Institute would not have the desired effect of curbing commercial exploitation of the drug.[195] The first problem, as Gautier saw it, was the absence of any existing regulatory framework in place that would allow the French government to bequeath a de facto medical monopoly to such an institute, as his supporters seemed to be suggesting the government should do.[196] The second problem, which was related to first, was the impossibility of preventing other actors from producing and selling Brown-Séquard's drugs due to the very public nature of Brown-Séquard's recipe. Gautier wrote:

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produced, and sold for profit by commercial manufacturers, pharmacists, and doctors ever since his initial announcement in 1889, but especially since the closure of the laboratory at the Collège de France in December of 1892. A survey of advertising pages in French newspapers confirms that there were more commercial actors advertising Brown-Séquardian wares after December 1892 than before, which suggests that the departure of Brown-Séquard's laboratory had indeed created a market opening that was filled by commercial manufacturers.

[194] Poverio, "Incurie"; See also Gautier, "Les petits cochons de la régie."

[195] Gautier, "Les petits cochons de la régie."

[196] For a background context on the French regulatory environment in the 1890s, and important changes that took place in 1895, see Simon, *Diphtheria Serum as a Technological Object*; Simon and Gradmann, *Evaluating and Standardizing*; Christoph Gradmann, "Locating Therapeutic Vaccines in Nineteenth-Century History," *Science in Context* 21, no. 2 (2008): 145–60; Volker Hess, "The Administrative Stabilization of Vaccines: Regulating the Diphtheria Antitoxin in France and Germany, 1894–1900," *Science in Context* 21, no. 2 (2008): 201–27; Alexander von Schwerin, Heiko Stoff, and Bettina Wahrig, *Biologics: A History of Agents Made from Living Organisms in the Twentieth Century* (London: Pickering & Chatto, 2013); Coleman, "Early Developments in the Regulation of Biologics."

> By what right and by which means, in virtue of which law, of which edict, of which police regulation, of which jurisprudence or even of which moral, would prevent a doctor, a pharmacist, a chemist, or even a simple amateur…from taking a guinea pig, opening its stomach, extracting certain easy to recognize organs, then crushing these anatomic parts, still palpitating, in a mortar, then filtering the juice *secundùm artem* under high pressure carbonic acid, and then inoculating the liqueur thus obtained, between hide and flesh, either to himself or to a willing "subject" [un 'sujet' de bonne volonté]

As Gautier went on to elaborate, the barriers to entering organic-extract production were almost non-existent. He claimed the recipe was neither "excessively complicated" nor "excessively delicate" to follow. "In case of hesitation [about producing the liquid]…one would only have to refer to the instructions, so complete and so precise, which were recently deposited, under the inspiration of Brown-Séquard himself…with the thought, apparently, that anyone who wanted to would appropriate them."[197] To prove his point, Gautier included in his editorial a copy of Brown-Séquard's method, taken directly from the *Bulletin de l'Académie de médecine*.[198]

Gautier did not condemn Brown-Séquard for these his actions. Indeed, he much preferred Brown-Séquard's approach of transparency and charity to that of Robert Koch, the German bacteriologist who had recently brought shame on his country through the tuberculin scandal.[199] What Gautier was rather calling attention to, and what Dr. Poverio and the "Group of Admirers" were also hinting at, was an intractable problem that had affected the trade of organic extracts even since its inception in 1889. By virtue of making his recipe public and declaring it simple to make, Brown-Séquard had created a drug market that was difficult and

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[197] Gautier, "Les petits cochons de la régie."

[198] Gautier gives the location of this article in the *Bulletin*: 56^{e} année, 3^{e} série, tome XXVII, no. 8, pp. 253-262. Gautier carried on to say: "As we can see the recipe that we would purport to withdraw from circulation today and put under a bushel, was revealed to the grand public by Brown-Séquard himself, along with the manner in which he used it."

[199] Gautier, "Les petits cochons de la régie." For a historian's account of the tuberculin scandal, see Hansen, *Picturing Medical Progress*. See also Christoph Gradmann, "Money and Microbes: Robert Koch, Tuberculin and the Foundation of the Institute for Infectious Diseases in Berlin in 1891," *History and Philosophy of the Life Sciences* 22, no. 1 (2000): 59–79.

perhaps impossible to regulate. Brown-Séquardian remedies had "fallen into the public domain," to use Gautier's word, "from which they are not able to be removed."[200]

Gautier's assessment of the situation might have been accurate, and Brown-Séquardian drugs would be interminably appropriated in the marketplace, but this did not mean that an ethical producer could not be found, and high-quality organic extracts could not be made available to the doctors who wanted them. This, at least, was Brown-Séquard's take on the matter in December 1892. He tended to side with the argument that the government should take on the responsibility of drug production. However, he was decidedly *not* impressed with the "Group of Admirers" suggestion that the government offer his laboratory a cash injection. In fact, he was startled when he read this in *Le Matin* and fired off a response which appeared in the same paper just two days later.[201]

> I read with surprise and regret, in yesterday's *Le Matin*, a letter which asks the government to give my laboratory funds so that it may continue to freely distribute a well-known therapeutic liquid. Those who make this request are misguided. If we cease to make the liquid, it is not because of the expense: I am ready to continue to do it indefinitely; the only reason that obliges us to no longer furnish the liquid is that the number of doctors who ask for it has really increased and expanded so rapidly that Mr. D'Arsonval can no longer find the time necessary for its preparation.[202]

If we were to take Brown-Séquard's comment at face value, we might imagine him to be a man of unlimited resources whose primary concern was not overworking poor d'Arsonval. But his logic in this comment does not quite add up: if labor was the major problem, not money, then why not employ more staff from his personal funds so that the operation could continue? Or, if he were loath to use his own personal funds for this purpose, why not lend his own support behind the idea of receiving public funds for staffing and laboratory expansion?

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[200] Gautier, "Les petits cochons de la régie."
[201] Charles Brown-Séquard, "Correspondance," *Le Matin*, December 11, 1892.
[202] Brown-Séquard.

There were many things left unsaid in this comment, as revealed by Brown-Séquard's personal correspondence, and it brings us to the heart of the problems that he and d'Arsonval were wrestling with at the end of 1892. First and foremost, we learn from Brown-Séquard's writings that his funds *were* becoming exhausted, and he could not continue to produce the liquid "indefinitely." We get hints of the financial pressure he was under through a private letter he wrote at the start of 1893 to his friend and colleague in Mauritius, Dr. Emmanuel-Charles Poupinel de Valencé.[203] Brown-Séquard reported to him that "things go admirably here with regards the employment of the liquid and the effects that it produces," but admitted that, unfortunately, prospects did not look good for the industry in the "long-term." At issue was the question of how the liquid would be produced now that he and d'Arsonval had stepped away from producing it. He wrote: "it will be impossible for me to supply [the liquid] without selling it and I do not want to tarnish my name by selling anything." He reported that in the last 9 months alone, he had spent north of 20,000 francs on production expenses. Brown-Séquard continued to state that "I am poor, but I would be able to continue to dispense for some more months to obtain some [more] demonstrations of the power of the liquid." But as for producing the liquid in bulk, "I am obliged to stop," he wrote "especially because of d'Arsonval who no longer has the time to give to preparing the liquid."[204] Clearly, the pressure that their production venture was putting on d'Arsonval's was a real weight on Brown-Séquard's mind, but so too were his personal finances.

Why did Brown-Séquard not admit his financial woes in public, or throw his support behind the suggestion that the government should fund his laboratory, as the "Group of

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[203] Brown-Séquard to Poupinel, March 2, 1893. Brown-Séquard's correspondence to Poupinel was published in this periodical the year after it was written, apparently as an attempt by the journal to preserve important the works and conversations of "illustrious savants" of Mauritius. See the brief preface to the letters in the previous issue (no. 12, p. 183). These letters were published in July 1894, just months after Brown-Séquard's death in April. It is not clear how the journal got their hands on these letters, but one could imagine how Poupinel himself might have wanted to commemorate his friend by publishing the letters and preserving them for posterity.

[204] Brown-Séquard continued to state that "I am poor, but I would be able to continue to dispense for some more months to obtain some [more] demonstrations of the power of the liquid."

Admirers" had suggested? In a letter to d'Arsonval, we learn exactly what was on Brown-Séquard's mind:

> It was extremely unpleasant for me to see that people search for money for us so that our laboratory would have the charge and the responsibility for the preparation of the testicular liquid. You have read yesterday's *Le Matin* where there is an article that we will be accused of having written and published by paying for the insertion. You will have also seen the dispatch that I have sent to the *Matin* (149 words) and which, I hope, will appear tomorrow Sunday. It is obvious that we will be accused, *despite my dispatch*, of having tried to obtain money from the government. If you know the authors of this article in the *Matin* from yesterday Friday, stop their effusions.[205]

What Brown-Séquard took issue with, therefore, was being accused of soliciting funds from the government to create a business out of his production venture: he did not want to be seen to be benefiting from the public purse. D'Arsonval, who was a more patient and less reactive correspondent than Brown-Séquard, wrote back with a sympathetic frame of mind. "We can't prevent patients and all the people who want the liquid from protesting and demanding from the public powers some measures for assuring the supply of the precious liquid," he said.[206] He explained to Brown-Séquard that he had been receiving, every day, "heartbreaking" letters from patients and doctors who were at a loss for how to get their hands on the liquid, and so it made sense that they wanted to take their demands to the press. As an aside, and perhaps to indulge Brown-Séquard's bad mood, he added: "people who call for [government action] do so with good intentions, but clumsily."[207]

What was a less clumsy solution to the production of organic extracts, in Brown-Séquard and d'Arsonval's estimation? In letters from Brown-Séquard to d'Arsonval, and indeed in Brown-Séquard's response to the "Group of Admirers," it is clear that he shared the

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[205] Charles Brown-Séquard to Jacques Arsène d'Arsonval, December 10, 1892, in Delhoume, 477-478. It appears that Dr Delhoume was given correspondence by d'Arsonval himself, who was a friend and colleague. The preface to *De Claude Bernard à d'Arsonval* states that Delhoume had given himself the task of telling the story of d'Arsonval's relationship to Claude Bernard and Brown-Séquard. It seems that the original correspondence now lies in the d'Arsonval collection at the Académie de sciences in Paris. See: https://rhpst.huma-num.fr/items/show/86.

[206] Jacques Arsène d'Arsonval to Charles Brown-Séquard, December 11, 1892, in Delhoume, 480.

[207] d'Arsonval to Brown-Séquard.

public's sentiment that the government *should* take on the burden of drug production, although not via payments to his laboratory. "The only solution to the problem is that the administration of the hospitals be given the responsibility of preparing the liquid for all the doctors of France who ask for it," he stated publicly in his article in *Le Matin*.[208] To d'Arsonval, he wrote: "What the government should do (this is what I say in my telegram) would be to prepare the liquid for all the French doctors who would ask for it. They could charge the cost price per vial."[209] Brown-Séquard was serious about this idea, for the next day, Sunday December 11, he wrote d'Arsonval urging him to the go to the next meeting of the Academy of Medicine on Tuesday where, allegedly, there was a plan afoot to have the doctors of Paris and the provinces lobby the government to produce and sell the liquid at cost to any doctor who wanted it. "It is necessary to push for the execution of this plan," wrote Brown-Séquard to d'Arsonval.[210]

Surviving letters do not confirm that d'Arsonval went to the Tuesday meeting, or what happened there, but he had written back to Brown-Séquard on the Sunday before, expressing his hope and expectation that government-led production could be arranged in some form. He had friends within government who were lobbying on their behalf, he told Brown-Séquard, including two (unnamed) members of the Conseil de surveillance de l'Assistance publique who promised him they would take up his and Brown-Séquard's ideas with the Council. Dr. Dumontpallier of the Paris Hospital and member of the Academy of Medicine, who had supported Brown-Séquard's work in the past, had also promised

[208] Brown-Séquard, "Correspondance," 2. By "administration of the hospitals," it is likely that Brown-Séquard was referring to the *Assistance publique.*
[209] Brown-Séquard to d'Arsonval, December 10, 1892. Indeed, he and d'Arsonval had been trying to offload responsibility to the hospitals for a long time, even pointedly publishing their method in *Gazette des Hôpitaux* with a "very simple" list of instructions for preparation of the liquid. See d'Arsonval to Brown-Séquard, July 12, 1892.
[210] Charles Brown-Séquard to Jacques Arsène d'Arsonval, December 11, 1892, in Delhoume, 478-79.

d'Arsonval that he would be taking up the question at the next meeting of the Société des hôpitaux.[211]

Brown-Séquard wanted this to work out but urged d'Arsonval to temper his expectations and even appeared cynical about the prospect of government doing anything at all. "Have no illusions," he wrote d'Arsonval on Tuesday—the same day the meeting at the Academy occurred. "We won't get anything from the Government and your two friends from the Conseil d'Assistance publique, if they succeed in doing something, will get nothing but the preparation of the liquid for the Paris Hospital. Dumontpallier won't get anything more."[212] It is not clear from their letters why Brown-Séquard was so skeptical that d'Arsonval's friends would not be successful in getting the government to act, and why he thought a movement from within the Académie de médecine might be a more convincing ploy. Possibly the campaign that he spoke of at the Académie had not gone well that day and he was feeling bitter. Possibly, he was just feeling snappy with d'Arsonval—in the same letter, he scolded him for continuing to send liquid out to doctors who asked for it. "I regret that you allow yourself to be touched [by letters] and that you continue to give almost as much liquid as before."[213] Or perhaps this was more an expression of Brown-Séquard's general sense of defeatism about the trade in organic extracts; when writing to d'Arsonval, he

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[211] d'Arsonval to Brown-Séquard, December 11, 1892.

[212] Charles Brown-Séquard and Jacques Arsène d'Arsonval, December 13, 1892, in Delhoume, 481-2. What Brown-Séquard meant here is that the hospital of Paris, and not provincial hospitals, would become a site of production. This displeased Brown-Séquard, for he thought the entire nation's network of public hospitals ought to produce and distribute the liquid to doctors.

[213] Brown-Séquard and d'Arsonval continued to supply to some doctors after the closure of their laboratory for production purposes in December, 1892, but they tried to limit this practice as much as possible. As this letter shows, d'Arsonval found difficult to refuse people. Brown-Séquard, on the other hand, had fewer qualms in saying "no." This even applied to his close friends and correspondents. For example, at the end of July, 1893, he told Poupinel, who had evidently requested the liquid, that he could no longer supply it. "I regret that it is impossible for me to send you the liquid; but you can prepare it," said Brown-Séquard, who had always been a champion of capacity building in medical practitioners. Brown-Séquard even sent Poupinel a d'Arsonval filter, shipped directly from Paris. "I think you can get by easily with this little machine of d'Arsonval's" and "I hope that you will soon have powerful liquid prepared by yourself," reminding him that he could use roosters, rams, bulls, or monkeys—he need not get his hands on guinea pigs. Charles Brown-Séquard to Emmanuel-Charles Poupinel, July 30, 1893, in Revue Historique et Litteraire de l'ile Maurice: Archives coloniales, no. 13 (1894): 206; See also Brown-Séquard to Poupinel, March 2, 1893.

often deployed pessimism to counter his friend's optimism, and was generally less hopeful that things would work in their favor. He reiterated this message again in another letter that followed a few days later, telling d'Arsonval that some of his contacts agreed with him that no "favorable intervention" would come from the government or a minister.[214]

D'Arsonval was not discouraged and went on his own reconnaissance mission. The following week he presented Brown-Séquard with two exciting proposals that had been put for to him by his friends at the *Assistance publique*. The first was that the government give their lab an annual grant—"subvention"—that would allow them to hire more people to continue producing and distributing the liquid. The second option was another grant from the government similar in format to the one received by Pasteur's Institute, whereby the government subsidized the cost of the liquid, but the consumer (doctor) would still make a financial contribution by paying a small price for the product. In both proposals, the laboratory at the Collège de France would resume production of the liquid.

D'Arsonval apparently expected Brown-Séquard to resist this idea, for in the same letter, he added this comment:

> Everyone (patients and doctors) tells me that we very wrong not to retain the laboratory's monopoly on the manufacture and shipment of the liquid. In giving over this manufacture either to industry, or even to the *Assistance publique*, we assume (whether we like it or not) the responsibility of all the accidents and all of the miscalculations that will occur by following a bad technique. I am sending you a letter summarizing the general opinion: danger for patients, danger for the method, and responsibility for us for what we have not done.[215]

He continued to explain that if they left over production to industry, or to the government, and refused to produce the liquid themselves, they would still be suspected of having connections with the many commercial manufacturers who were producing the liquid.[216]

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[214] Charles Brown-Séquard to Jacques Arsène d'Arsonval, December 14, 1892, in Delhoume, 483.
[215] Jacques Arsène d'Arsonval to Charles Brown-Séquard, December 16, 1892, in Delhoume, 484-85.
[216] d'Arsonval to Brown-Séquard.

Returning to their own production venture, in d'Arsonval's mind, would silence these controversies once and for all. He raised another powerful argument: if Brown-Séquard's laboratory accepted funds from the government, upscaled their laboratory with more staff, and resumed production, they could actually do the very good work of undercutting their commercial competitors. Even if they had to charge cost price for organic extracts—say, 1 franc—then it would still function to draw customers away from businesses that were selling the liquid at higher price points (between 5 and 10 francs).[217] What's more, d'Arsonval continued to argue, no one could accuse their laboratory of personally profiting from the operation when they could see how little the laboratory was charging as compared to the commercial manufacturers. D'Arsonval concluded his argument almost with a plea to Brown-Séquard:

> Reflect and let me know how you see it…. These are, I repeat to you, very serious and very competent men [at the *Assistance publique*] who ask me to transmit these reflections to you. Each manufacturer will modify our method to his liking (simply by not making it as we do) and the liquid will be completely denatured if it is not toxic.[218]

D'Arsonval was not normally so forthright and effusive in his letters to Brown-Séquard, which possibly speaks to his passion for these ideas and perhaps his frustration with the response he anticipated from Brown-Séquard. He thought his arguments made perfect sense, and he thought them persuasive: if they accepted some public money, or charged doctors a small sum for organic extracts, or both, they could continue to supply the medical community with high quality products, curb commercial exploitation of the product, *and* convincingly demonstrate that they were not seeking to profit from their efforts.

Brown-Séquard's reply came the very next day, and it addressed d'Arsonval's ideas point by point. First, he disagreed with the premise that they would retain any responsibility

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[217] This was the going commercial rate for Brown-Séquardiain remedies, as seen by advertisements featured in French newspapers.
[218] d'Arsonval to Brown-Séquard, December 16, 1892.

for the drug if the *Assistance publique* or even industry—"l'Industrie"—were charged with the responsibility of production. "We will be free and *the accidents will no longer concern us*."[219] He also thought that they could combat any suspicions that they were involved with commercial manufacturers by continuing to decline to recommend any single commercial producer of organic extracts, even if they in fact had a high estimation of the products that were produced there.[220] As for the proposals that their laboratory receive an "annual pension" from the government, Brown-Séquard told d'Arsonval that he was not opposed in principle. He accepted that receiving government funds could help them in their project to supply the doctors of France who wanted the liquid, especially now that they were a group about five or six thousand strong, according to Brown-Séquard's estimations.[221] But how would d'Arsonval handle the labor, Brown-Séquard asked? Not only would d'Arsonval be charged with supervision of all the manufacturing, but also the bucketloads of mail that would be sent to their laboratory. And what would happen when d'Arsonval took his vacation? As Brown-Séquard reminded him, he had the habit of being out of Paris three to four months every year.

On the matter of charging doctors cost price for the product, Brown-Séquard was unequivocal. "If you insist [on accepting government money] I will accept, but on the condition that the flasks will not be sold, not even for 1 franc."[222] He reiterated this message again to d'Arsonval in yet another letter he wrote on this topic, which was penned and sent even before d'Arsonval had the time to reply to his boss's first letter. "You are young, a long future is before you. So do what seems best for you," wrote Brown-Séquard, with the air of

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[219] Charles Brown-Séquard and Jacques Arsène d'Arsonval, December 17, 1892, in Delhoume, 487. Original emphasis.
[220] Brown-Séquard cautioned d'Arsonval to not publicly endorse any manufacturer so as to protect themselves from being accused of collaborating--and so profiting--with a commercial "préparateur." See Charles Brown-Séquard to Jacques Arsène d'Arsonval, January 3, 1893, in Delhoume, 499.-This rule even applied to commercial manufacturers they did in fact admire. For example, Brown-Séquard and d'Arsonval had a high opinion of Mr. Bouyé and Mr. Egasse's preparations, but purposefully did not publicly endorse them. See d'Arsonval to Brown-Séquard, January 2, 1893.
[221] Charles Brown-Séquard to Jacques Arsène d'Arsonval, December 17, 1892, in Delhoume, 487.
[222] Brown-Séquard to d'Arsonval.

handing off decisions about production to d'Arsonval. He explained that he was personally satisfied with the work he had done with testicular extracts, and if their operation stopped now, then he would be content. But he did not want to inhibit d'Arsonval drug production aspirations, if this is what d'Arsonval wanted from his career. "So do what you want" Brown-Séquard wrote, "entirely, absolutely [do] what you judge to be the best [course of action], with the exception of one single thing: that neither you nor I can expose ourselves to the accusation of being traders [commerçants]. We would not avoid this accusation even if the bottles were only sold for a franc."[223]

Brown-Séquard need not have worried about d'Arsonval proceeding down the path of charging doctors cost price for their products for, as he had suspected, the promising leads within the municipal council came to nothing. After d'Arsonval's impassioned argument about accepting government funds, Brown-Séquard heard nothing from his friend for over a week. When Brown-Séquard gently followed up with him, d'Arsonval replied dejectedly that he had heard nothing more from his contacts on the inside and surmised that the Council must have turned "a deaf ear" to his campaign to source government funding for their lab.[224]

The French government never did fund Brown-Séquard's laboratory, to my knowledge, or sponsor production through the hospital system, despite the pressure that was put on them by the public and by supporters of Brown-Séquard's laboratory. It is difficult to pinpoint why exactly government support was not forthcoming, but circumstantial evidence suggests that there might have been reluctance in government officials to recognize and sanction Brown-Séquardian remedies. When French legislators did act in 1895 to regulate the market of organic extracts—details of which I will elaborate further in the final section—Brown-Séquard's therapy was introduced in parliamentary discussion as sensational therapy

[223] Charles Brown-Séquard to Jacques Arsène d'Arsonval, December 18, 1892, in Delhoume, 488.
[224] Jacques Arsène d'Arsonval to Charles Brown-Séquard, December 25, 1892, in Delhoume, 490-92.

that was greeted with much skepticism in 1889 and 1890, but one that seemed to be slowly gaining favor with doctors and physiologists.[225] Perhaps when d'Arsonval's friends were lobbying their cause in the municipal council in late 1892, there was not yet sufficient belief in legislators for the value of Brown-Séquard's work.[226] Indeed, it took until 1896—a year after their initial round of discussions in 1895—for the government to officially recognize "the method of Brown-Séquard" as a safe and reliable method for producing organic extracts.[227]

Even though government-sponsored production of Brown-Séquardian remedies were not to be, Brown-Séquard and d'Arsonval's conversations about it lay bare two of the problems with which they were wrestling in 1892 and 1893. The first related to Brown-Séquard's professional identity of the scientist and doctor, which he understood to be incompatible with the exigencies of doing business. The second related to the opportunities and costs of engaging in business endeavors more broadly, and emerged as a question posed by d'Arsonval to Brown-Séquard in their correspondence: might some forms of commercialization be ethical?

D'Arsonval was clearly supportive of the idea of commercializing the Brown-Séquardian laboratory in a way that would undercut competitors, even if it meant charging doctors a price for their products. Brown-Séquard, however, did not want to charge doctors under any circumstances. But where did this conviction come from, and where did Brown-Séquard's refusal to commercialize the laboratory leave the trade in organic extracts? In the

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[225] Rapport de M. Bourrillon "Lois annotées: ou, Lois, décrets, ordonnances, avis du Conseil d'état, etc., avec notes historiques, de concordance et de jurisprudence, Volume 11," 1895, 1102.

[226] Note that many legislators in France during this period were actually doctors themselves. See Jack D. Ellis, *The Physician-Legislators of France: Medicine and Politics in the Early Third Republic, 1870-1914*, Cambridge History of Medicine (Cambridge; New York: Cambridge University Press, 1990).

[227] And yet, importantly, this legislation was introduced for the primary purpose of ensuring consumer safety and in the interests of public health; that Brown-Séquard's name appeared in legislation should not necessarily be read as an official nod to the efficacy or value of Brown-Séquardian remedies, but rather the government's acknowledgement of its widespread use and abuse on the medical marketplace and the subsequent need to implement regulatory measures.

next section, I show that Brown-Séquard's attitudes toward commercialization were informed by watching two of his peers go down this pathway and receive professional rebuke in the process. They were German bacteriologist Robert Koch, the discoverer of "tuberculin," the radical "cure" for tuberculosis, and French chemist Louis Pasteur, the revered founder of the Pasteur Institute and discoverer of anthrax and rabies vaccines.

The Cost of Doing Business

Robert Koch and Louis Pasteur appeared as cautionary tales in Brown-Séquard's correspondence well before he decided to close his laboratory for production purposes at the end of 1892. In fact, they came up in March 1891, when he and d'Arsonval were discussing a proposal that had just been put to them by a commercial manufacturer whom they referred to as "G."[228] G was almost certainly the dreadful Dr. Goizet, who had already attracted Brown-Séquard's ire for advertising Brown-Séquardian products in French newspapers for a high price.[229] This time, G had approached d'Arsonval directly with a proposal that he be allowed to sell Brown-Séquard's testicular liquid, with Brown-Séquard's personal endorsement, at high expense to the physician-consumer. What was in it for Brown-Séquard and d'Arsonval? G had a plan: he would reserve some of his profits for Brown-Séquard and d'Arsonval to do with what they pleased. D'Arsonval must have stared at him blankly, for he wrote to Brown-Séquard: "[G] appeared to regret his frankness when he saw my lack of enthusiasm, and I was certainly lowered in his esteem when I told him that I make known the method that I use in

[228] d'Arsonval to Brown-Séquard, March 24, 1891. In this particular letter, d'Arsonval describes being approached by "G***"—with asterisks obscuring the name. Having not seen the original letters myself, I am unable to discern whether the asterisks are editorial input from Delhoume or taken from the original letters.

[229] Circumstantial evidence suggests that "G" is their personal moniker for Dr. Goizet. For example, in one letter, they complain about G*** who wrote *La vie prolongée*—a book authored by none other than Dr. Goizet. See Brown-Séquard and d'Arsonval, December 13, 1892. There is abundant correspondence between D'Arsonval and Brown-Séquard about Dr. Goizet, featured in Delhoume. See especially letters from late March, 1891 (p. 389). One letter, from d'Arsonval to Brown-Séquard on December 11, 1891, described Goizet as a "decidedly a miserable charlatan" (pp. 414-15). See also Brown-Séquard to d'Arsonval, December 13, 1892 (p. 482) in which Brown-Séquard mouths off again about Goizet who had started to advertise himself as the founder of the "Institut Sequardien."

preparing the liquid to anyone who wants to learn." D'Arsonval added: "I am convinced that he does not find me to be 'fin de siècle' enough…."[230]

G's proposal clearly flew in the face of the virtues of transparency and disinterestedness by which d'Arsonval and Brown-Séquard so rigidly abided, and one wonders why G, if he knew anything about the two men at all, wasted his time in proposing such an idea. But it did get d'Arsonval wondering, and writing to Brown-Séquard, about the benefits of generating profit from sales of medical products. He was specifically thinking about how Louis Pasteur ran his laboratory. As d'Arsonval reminded Brown-Séquard, Pasteur sold his diverse vaccines at a price that allowed him to recover the costs of production, which meant that he was not scooping the bottom of the barrel, as they were.[231] D'Arsonval did not pose the question explicitly to Brown-Séquard in this letter from 1891—possibly he was leery of Brown-Séquard' response—but his meaning was clear: would this sort of cost-covering venture be such a bad idea for their work with the testicular injections?

Brown-Séquard was receptive to D'Arsonval's proposal of recovering costs from doctors in this exchange—much more than he would be in December 1892—but he had one major objection. Louis Pasteur was known to not only recoup his costs from price-paying doctors, but also to re-invest the surplus from sales back into the research budget. "We can't do what's done at Mr. Pasteur's," Brown-Séquard explained to d'Arsonval.[232] "You know that Mr. Pasteur is himself accused of making money [from his vaccines]. I do not want that accusation leveled on us—you and me. Let us not make money—whether it be for science or

[230] d'Arsonval to Brown-Séquard, March 24, 1891. This is a curious phrase—"he does not find me to be 'fin de siècle' enough"—which possibly speaks to a changing professional climate in turn-of-the-century France. For, to act with a "fin de siècle" attitude would be to embrace Goizet's proposal and have little thought to the ethics of profiting from their work. Yet, this was not how Brown-Séquard or d'Arsonval saw the world. Even d'Arsonval, who was more amenable to some forms of commercialization than his boss, found Goizet to be a sly operator.
[231] See d'Arsonval's explanation of Pasteur's funding model in d'Arsonval to Brown-Séquard.
[232] Charles Brown-Séquard to Jacques Arsène d'Arsonval, March 26, 1891, in Delhoume, 380-82.

not—in this way. Let us not imitate the laboratory of Mr. Pasteur any more than that of Mr. Koch."[233]

As historians of science and medicine well know, Robert Koch had become embroiled in controversy in early 1891, just months before Brown-Séquard wrote this note, when it was revealed that tuberculin was not only ineffective but also harmful to some patients.[234] Koch had been initially celebrated for his innovative medicine the year before, but when negative reports started emerging about patients deriving little benefit from the therapy, the press began to accuse him of "inappropriately pursuing publicity and fame," to use Bert Hansen's words, and for being "mercenary."[235] Louis Pasteur's anthrax and rabies vaccines never experienced the fall from grace suffered by Koch and tuberculin, but Pasteur did suffer rumors that he was seeking to profit from his vaccines, as Brown-Séquard alluded to.[236]

Brown-Séquard had already received his fair share of abuse in 1889 and 1890 when he first announced his testicular extract therapy, and so it is understandable why the tuberculin scandal had put him on edge. But his comment to d'Arsonval that they should not "imitate the laboratory of Mr. Pasteur any more than that of Mr. Koch" was also a statement about ethical practice. Both Koch and Pasteur had not been transparent about the recipes they used to create their therapy, and both had publicized the success of their products in the hopes of boosting public confidence in them. Pasteur also charged doctors money for his products, which is a practice that Brown-Séquard strongly opposed.[237]

Brown-Séquard imagined himself to be a more ethical actor than both of them, and his own self-comparison to them deeply informed his approach to his own venture at the

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[233] Brown-Séquard to d'Arsonval. Brown-Séquard also worried that they would not have the time to train three or four assistants to make the liquid, even if all the money necessary were made available for their laboratory to upscale into a Pasteur-like Institute. See Brown-Séquard to d'Arsonval, December 11, 1892.
[234] Hansen, *Picturing Medical Progress*, 90; Gradmann, "Money and Microbes."
[235] Hansen, *Picturing Medical Progress*, 91.
[236] Geison, *Private Science*, 171, 174.
[237] See Geison, *Private Science*.

Collège de France. This was certainly the case from at least 1891, when Brown-Séquard first discussed himself in juxtaposition to his entrepreneurial peers, but it is also possible that Brown-Séquard had Pasteur's example on his mind when he published his method in 1889. By this point, Pasteur had already soared to fame with his anthrax and rabies vaccines, and it is possible that Brown-Séquard regarded these events as moments for self-reflection. I suggest this because Brown-Séquard seemed to conduct himself in ways that were contrary to Pasteur's example: he never kept his method secret; he never concealed his experimental results; he refused to profit from his inventions; and he never promoted his laboratory's products to the exclusion of all others. Indeed, in all my interactions with Brown-Séquard's published and personal writings, I have no reason to believe that he ever acted deceptively, selfishly or fraudulently throughout the testicular years. This is not a conclusion arrived at by historians of Louis Pasteur, by comparison.[238]

The Pasteur Institute came up again in Brown-Séquard and d'Arsonval's correspondence when they revisited their conversation about profit and cost in December 1892. This was around the time that d'Arsonval had relayed to Brown-Séquard that the government was not likely to fund their venture, or anyone else's. But no matter, d'Arsonval relayed in another letter, for an even more promising proposal had come their way in the form of Charles Chamberland of the Pasteur Institute itself. D'Arsonval explained to Brown-Séquard that Chamberland had dropped by the laboratory one day in late December of 1892 for the purpose of picking up some testicular liquid.[239] It was then that Chamberland was apparently inspired to suggest that the Pasteur Institute could step in to shoulder the burden of manufacturing. Chamberland told d'Arsonval that Pasteur remained "delighted by the effects

[238] See especially Geison.

[239] d'Arsonval to Brown-Séquard, December 25, 1892. This was just weeks after Brown-Séquard had announced that he and d'Arsonval were ceasing production of testicular liquid. The rules evidently did not apply to Chamberland. It is unclear from d'Arsonval's letter whether the liquid was to be for Chamberland's own personal use, for Pasteur, or for experimental purposes.

of the liquid," which made Chamberland's suggestion even more promising. D'Arsonval was excited. "Would this not be the right solution?" he scribbled in a note to Brown-Séquard soon after Chamberland had left.[240]

Brown-Séquard agreed that it could indeed be a good way forward, but he was emphatic in his return letter that d'Arsonval not "ask" the Pasteur Institute to take on this burden, or "solicit" anything at all from them. "If they want to do it, I will be delighted and I will pay my compliments to Mr. Pasteur, but I do not want to owe him anything."[241] In keeping with his reluctance to be seen sourcing government funding, Brown-Séquard was also adamant that he and d'Arsonval not be seen to pursue the Pasteur Institute. He told d'Arsonval on more than one occasion that if this opportunity with the Pasteur Institute were to work out, he and d'Arsonval must keep themselves outside of the planning.

By these comments, Brown-Séquard seemed to be suggesting that it was acceptable for Pasteur and his team to charge doctors money for the testicular injections, and to possibly line the Institute's research funds from the profits, in the name of science, but it was not okay for him and d'Arsonval to do the same. Why? Because Brown-Séquard did not want to risk offending the medical community, or to compromise in any way his and d'Arsonval's squeaky clean reputation. Pasteur, on the other hand, had already risked his reputation by commercializing vaccines, and was already in the business of fending off external critique. Brown-Séquard seemed to be saying: if Pasteur would risk professional favor by selling testicular liquid at cost, and he and d'Arsonval were not in any way involved, then who were they to stop him?

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[240] d'Arsonval to Brown-Séquard.

[241] Charles Brown-Séquard to Jacques Arsène d'Arsonval, December 26, 1892, in Delhoume, 493-94. Do these remarks by Brown-Séquard suggest possible animosity between him and Pasteur? I have found no evidence of a personal or professional rift between these two men, so perhaps Brown-Séquard's tone was simply affected by his own pride which prevented him from asking Pasteur for help.

But there was more appeal to the Pasteur Institute as a candidate for manufacturing the organic extracts, other than Pasteur's experience in running a commercial enterprise. His was a scientific institute that was staffed by scientific men and it produced scientific medicine that was proven to work, which is ultimately what Brown-Séquard and d'Arsonval were looking for in a manufacturer. It also had a high standing in French society and the world, despite its commercial funding model, which historian Ilana Löwy claims was not widely advertised by the Institute.[242] It was also supported through government subsidy, private gifts, and public contributions.[243] That is to say, the Pasteur Institute was a robust institution with wide public backing—something that Brown-Séquard's own laboratory could not boast. The Pasteur Institute was also (ostensibly, at least) a not-for-profit institute, and if Brown-Séquard had reservations about how Pasteur sold his vaccines and reinvested surplus back into the institute, he would have taken solace in the fact the Institute's owners were not financially benefitting from sales.[244] To d'Arsonval, Brown-Séquard wrote:

> As I wrote to you, let us stay outside of this move. That the Pasteur Institute takes the load which weighed on you and pays for it, I do not find fault there and I believe that it is the best possible solution of the problem to be solved. But I wouldn't want it to be said that we pushed for it.[245]

And yet, despite the momentum that seemed to be building in Brown-Séquard and d'Arsonval's correspondence, the promising suggestion by Chamberland came to nothing. Chamberland never followed up with d'Arsonval about his ideas to produce the extracts,[246] and Brown-Séquard did not allow d'Arsonval to do any prodding. This was despite the fact that Brown-Séquard genuinely thought the Pasteur Institute was the best pathway forward for

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[242] Löwy, "On Hybridizations," 663.
[243] Löwy, 663. See also J.-M Cavaillon, "Bacterial Poisons to Toxins: The Early Works of Pasteurians," *Toxins* 14, no. 759 (2022): 5.
[244] See Brown-Séquard's remarks in Charles Brown-Séquard to Jacques Arsène d'Arsonval, January 5, 1893, in Delhoume, 499. But see, however, Gerald Geison's comments on Pasteur's and profit in *The Private Science of Louis Pasteur* (Princeton, N.J.: Princeton University Press, 1995), 171, 174.
[245] Charles Brown-Séquard to Jacques Arsène d'Arsonval, December 30, 1892, in Delhoume, 494-95.
[246] Brown-Séquard followed up with d'Arsonval about Pasteur a few days later, but d'Arsonval said that he'd heard nothing from Chamberland. See d'Arsonval to Brown-Séquard, January 2, 1893.

organic extracts, and he pestered d'Arsonval for updates: "Tell me what there is in the affair of the preparation of the liquid by the Pasteur institute. Who had had the idea? Who is pushing it? What is the plan? Is it the city (municipal Council) that would supply the funds? Tell me everything and the rest."[247] D'Arsonval didn't have any answers and explained that Chamberland simply asked him if the organic liquids were difficult to prepare. He then showed him how it was done and that Chamberland had then departed the lab and left him wondering if "he would decide to add this preparation to those of the vaccines."[248]

The Pasteur Institute disappeared from Brown-Séquard and d'Arsonval's correspondence and joined the pile of other manufacturing proposals that were entertained by the two men but never took root. This included a large donation of half a million francs offered to Brown-Séquard by "an association of generous men" which was to be used for "founding an Institute like the Pasteur Institute.[249] It also included yet another promising proposal that d'Arsonval had been developing with the Tuberculosis Children's Hospital at Ormesson, whereby the hospital would produce and sell the liquid and invest their profits back into the hospital.[250] D'Arsonval would help the hospital set up production and would continue to supervise from a distance, without being directly involved. He and Brown-Séquard would recommend the hospital as an official vendor, and it would have the same result of undercutting commercial competition as if they themselves were producing the liquid. This plan also had the benefit of him and Brown-Séquard avoiding accusations of engaging in commerce, for the hospital was a charity and not a commercial enterprise.

Brown-Séquard was supportive of this plan, for he ultimately wanted d'Arsonval "relieved of the burden of preparing so many vials of liquid."[251] D'Arsonval was also excited

[247] Brown-Séquard to d'Arsonval, December 30, 1892.
[248] d'Arsonval to Brown-Séquard, January 2, 1893.
[249] Brown-Séquard to Poupinel, March 2, 1893.
[250] Jacques Arsène d'Arsonval to Charles Brown-Séquard, February 12, 1893, in Delhoume, 516.
[251] Charles Brown-Séquard to Jacques Arsène d'Arsonval, February 14, 1893, in Delhoume, 518.

about working with the hospital at Ormesson, for he saw it as a fine candidate to preserve the method that he and Brown-Séquard had worked so hard to launch. He clarified to Brown-Séquard that his eagerness to find a producer was less about finding replacement labor and more about shoring up the "success" and future of the method. He said "We have an excellent therapeutic method on our hands which will be degraded by commerce. It is absolutely necessary that we find a way of manufacturing of which we can get behind without being suspected of doing business."[252] Yet, this plan, too, disappeared from their correspondence and appears to have come to nothing.[253]

Stepping through the proposals that were considered by Brown-Séquard and d'Arsonval can be a frustrating experience, for it is ultimately an exercise of walking down many paths not travelled. One forms the impression from Brown-Séquard and d'Arsonval's letters that the failure of any proposal to take root was due, in part, to Brown-Séquard's apathy about whether they found an ethical manufacturer or not. He was clearly concerned about how the trade would develop, but it is also clear that d'Arsonval was much more invested in the problem, and far more engaged in developing proposals for ethical production of the organic extracts.[254] Some decisions that Brown-Séquard made were genuinely perplexing, such as his refusal to consider the offer made to him by the "association of generous men" who presented 500, 000 francs for him to build an institute. His reasoning for not going forward with the money, as he outlined in a letter to his friend Poupinel, was that "after having dispensed of 300, 000 francs to enlarge my laboratory or to found a new

[252] Jacques Arsène d'Arsonval to Charles Brown-Séquard, February 20, 1893, in Delhoume, 519.
[253] It is not clear from Brown-Séquard and d'Arsonval's correspondence why this Ormesson plan fell by the wayside.
[254] Private correspondence between him and Brown-Séquard reveals, however, that he was more partial than his boss to a Pasteur-like system of setting a fee that would cover costs. Jacques Arsène d'Arsonval to Charles Brown-Séquard, July 25, 1892, in Delhoume, 451-52. He also thought that the *Assistance publique* should take responsibility of production, with his and Brown-Séquard's supervision. See Jacques Arsène d'Arsonval to Charles Brown-Séquard, August 31, 1892, in Delhoume, 455-57. One gets the impression, in fact, that d'Arsonval was a little frustrated that Brown-Séquard would not take further steps toward stabilizing the industry either through commercializing it (responsibly and ethically) or finding public funding for it.

laboratory, there would remain only 200, 000 francs, leaving only 6 or 7, 000 francs per year which is sufficient only to make liquid for 2 or 300 doctors. There are 40, 000 of them in France and more than half will demand it." [255] In the same note to Poupinel, he wrote: "it would take millions to prepare and give the liquid to everyone. I will not be able to find the money. I am sorry for it."

According to this math, Brown-Séquard was imagining an institute that had a near-30-year life cycle that could distribute liquid for free to half the nation's supply of doctors, which can be described as nothing but a utopian idea. If he was serious about supporting the trade in organic extracts, why not take the money that was offered to him in the moment, and get the liquid produced for the limited number of doctors who wanted it in the short term?[256] We are left wondering, and so too were political commentators who watched the developments at Brown-Séquard's laboratory with unease.

Blaming Brown-Séquard?

Even before Brown-Séquard and d'Arsonval had closed their laboratory for production purposes in December 1891, critiques were published in French newspapers that levelled blame on Brown-Séquard for his decision-making about drug production. On July 16, 1892, for example, an unsigned editorial appeared in *Le Petit Journal* that worried about the exploitation of organic extracts on the commercial marketplace and urged the government to found a "Brown-Séquard Institute… like the Pasteur Institute" to supply the medical community with high-quality products. Instead of using this opportunity to rally behind Brown-Séquard's mission, as other editorials had done, this particular author was critical of him, suggesting that drastic and urgent intervention was necessary "because the honorable

[255] Brown-Séquard to Poupinel, March 2, 1893.
[256] Brown-Séquard does not comment further on this proposal in his letters, and neither does d'Arsonval.

scientists who invented the new therapy do not seem to mind letting it be exploited by private industry."[257]

This critique was picked up again in September of 1892 in *Le Petit Journal* by "Thomas Grimm,"[258] who had conducted a rare interview with d'Arsonval that posed some hard questions about the business of producing the organic extracts. This interview was conducted some months before they had shut down the laboratory, but well after Brown-Séquard and d'Arsonval had made it known to the medical community that they were struggling to keep up with physician demand, and that physicians should perhaps produce their own concoctions in the clinic. By way of easing into the conversation, Grimm first asked d'Arsonval to imagine the circumstances in which their laboratory could continue to provide for the doctors of France. D'Arsonval stated that it would take the creation of a new and "special laboratory." By this he meant some arrangement whereby a laboratory could meet the challenges of the huge demand from doctors without lining the pockets of the manufacturers, or the pockets of anyone else. "[We] do not want to do business at any price, even in pharmaceuticals," d'Arsonval stated very firmly.[259]

In d'Arsonval's comment, Grimm spied an opening. Not doing business at any price was very honorable, Grimm was careful to note, but it did not solve the very practical problem of who, or what, would produce organic extracts for doctors in their absence. The "special laboratory" that d'Arsonval spoke of was nothing more than a shaky hypothetical and did not point to real answers for doctors. Grimm was also none too pleased with Brown-

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[257] Unsigned editorial, "La méthode Brown-Séquard," *Le Petit Journal*, July 16, 1892.
[258] According the Bibliothèque nationale de France, "Thomas Grimm" was a "collective pseudonym" for editorials in *Le Petit Journal*, but most were written by journalist Henri Escoffier. See: https://data.bnf.fr/16213936/thomas_grimm/ **.** However, correspondence between d'Arsonval and Brown-Séquard suggests that in this case, Thomas Grimm was in fact a Dr. Astier, who was evidently known to them both. See d'Arsonval to Brown-Séquard, August 31, 1892.
[259] Grimm, "Pour prendre patience!" Brown-Séquard and d'Arsonval weren't even interested in recouping what they had spent on producing testicular injections, which Grimm estimated to be an amount of 1, 000 francs. Evidently, the true amount was significantly higher than this, according to Brown-Séquard's letter to Poupinel.

Séquard's idea that doctors step up and produce their own supply. His article laid out the impracticalities of this proposal: "[Even] with the best will in the world and despite the instruction of the most meticulous formula, many doctors will mess up the preparation of the extracts, which requires equipment of certain importance. We will be forced to resort to specialism, which rhymes annoyingly with industrialism and mercantilism…"[260]

Grimm could see how it was going to unfold. By refusing to engage in commercial activity, Brown-Séquard was de facto guiding his followers into commercial activity. This irony was not lost on other commentators, such as journalist Francique Sarcey of *Le Petit Journal.* In a column published in late December, 1892, in the immediate wake of the closure of Brown-Séquard's laboratory for production purposes, Sarcey claimed to have received an inside scoop from one of Brown-Séquard's principal collaborators about whether Brown-Séquard had, or had not, made the right decisions for the bourgeoning industry.[261] According to Sarcey, this collaborator, whom he anonymized on account of his "modesty," told him that he and Brown-Séquard could have earned millions of francs from their new therapy had they "establish[ed] a monopoly over this product," but they had declined to do so because "this is not the way of French savants."[262] But where did this leave the testicular trade, and the trade in other organic extracts, wondered Sarcey? In closing out the interview and reflecting on the corporate actors who had flooded the market with Brown-Séquard's method, Brown-Séquard's unnamed collaborator stated simply but sagaciously that "the best is sometimes the enemy of the good." "Were we right to leave it to the charlatans to make coin with our product? That is the question."[263]

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[260] Grimm.
[261] Francisque Sarcey, "Le mieux est l'ennemi du bien," *Le Petit Journal*, December 25, 1892.
[262] Sarcey.
[263] Sarcey.

This exclusive interview, which everyone widely suspected was given by d'Arsonval—even Brown-Séquard himself—was revealed to be a fake.[264] But the contents struck at a nerve for Brown-Séquard and d'Arsonval, who read the article and wondered about their own personal responsibility in steering the testicular trade into safer waters. The very next month, in January 1893, d'Arsonval gave a real interview to Sarcey which was published in *Le Petit Journal* under the title "We Are Too Chivalrous."[265] Sarcey framed the interview by outlining the root of the problem as he saw it: that because Brown-Séquard and d'Arsonval had published their recipe, and all and any pharmacists and druggists could make it, doctors and patients were having a hard time telling which products were high-quality and which were fraudulent and perhaps even dangerous. Sarcey asked d'Arsonval: "Why don't you make authentic products yourself, or why not offer your name to a dispensary where sick people can be sure of finding true and effective organic extracts?"

D'Arsonval responded by saying that Sarcey had touched upon "a question that has been bothering and worrying me for a long time." First, d'Arsonval wanted to clarify, their laboratory at the Collège de France was still supplying some doctors, but only those they knew and could personally vouch for. This was so that clinical experiments with organic extracts could continue, and so that he and Brown-Séquard could avoid being taken advantage of by druggists who pretended to be doctors, requested Brown-Séquard's liquid for clinical use, and then sold it for profit on the open market. But it is true they were refusing liquid even to those doctors whom they knew had the single object of treating sick patients, d'Arsonval admitted. "We refuse it because we don't have it, "he stated, "and we don't have

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[264] Once it was established that d'Arsonval had not given this interview, he and Brown-Séquard spent days wondering who could have done it. On December 30, 1892, Brown-Séquard penned a note to d'Arsonval informing him that he was very happy to know that "Mr. Sarcey invented the story about having lunch with one of my collaborators." It's not clear how Brown-Séquard discovered this information. See Brown-Séquard to d'Arsonval, December 30, 1892.

[265] Sarcey, "Nous sommes trop chevaleresque." "We Are Too Chivalrous" is reproduced in Delhoume, *De Claude Bernard à d'Arsonval,* 503–5.

it because we believe we have to refuse it."[266] It was a question of curbing demand by limiting supply.

To Sarcey's question about why they did not personally vouch for a druggist who produced high-quality products, d'Arsonval offered a story. Recently, he and Brown-Séquard had been approached by the head of a "large American pharmacy" who had offered them a million francs[267] in exchange for a letter, signed by them, which officially endorsed the pharmaceutical house to make Brown-Séquardian products. D'Arsonval was clearly bemused by this proposal: how had their own personal brand become so valuable in this free-for-all economy, when they had done nothing to promote themselves or their products? When he and Brown-Séquard did not respond, a "very distinguished" vassal of the pharmaceutical house arrived at their laboratory in Paris to ask why they had refused (by their silence) such a generous offer. The intermediary explained that they could do what they wished with this money, such as updating their laboratory, creating an institute, or anything else for "the advancement of physiology and medicine."[268] According to d'Arsonval, the American told them that:

> You will make your fortune and you will have the pleasure of seeing science progress by your hands. Everyone will therefore gain; and I beg you to tell us how the strictest morality may seem injured by this arrangement. [269]

"And…[were] you convinced by this reasoning, which seems to me to be peremptory?" interrupted Sarcey, who clearly sided with the American's logic.[270] No, d'Arsonval, responded, he was not. "We refused…believing that it is shameful for a French savant to

[266] "We Are Too Chivalrous" in Delhoume, *De Claude Bernard à d'Arsonval*, 504.
[267] Unclear if francs or dollars
[268] "We Are Too Chivalrous" in Delhoume, *De Claude Bernard à d'Arsonval*, 505.
[269] "We Are Too Chivalrous" in Delhoume, 505.
[270] "We Are Too Chivalrous" in Delhoume, 505.

make money [de batter monnaie] from a scientific discovery." [271] But ever since then, d'Arsonval admitted, he had been wondering if they had made the right decision.

> I wondered if, in rejecting these proposals, we had not given in to I don't know what chivalrous prejudice, the fruit of an old atavism. When it comes down to it, what these Americans were telling us was very sensible and very reasonable. [272]

Sarcey was clearly unimpressed with Brown-Séquard and d'Arsonval's inaction on this issue, especially when d'Arsonval could see the logic of the other side, and even the illogic of his and Brown-Séquard's "chivalry." Sarcey's article went on to remind readers that other famous and well-respected savants, such as Edison and Pasteur, had shored up futures for their scientific innovations by "exploiting their discoveries." This was necessary, Sarcey noted, when "experiments are expensive" and the "state gives little money." How would science progress if the scientist did not draw from his inventions "the profit that will be necessary for him to search for others?" Determined to have the last word, Sarcey concluded his provocative piece with an unequivocal line: "There is in the disinterestedness of French savants a turn of sentiment that seduces me. But it's the Americans who might be right." [273]

If Brown-Séquard had been on the hotseat instead of d'Arsonval, how might he have responded? By the Spring of 1894, he was tired and sick and had only a few months left to live. But, as his many biographers have noted, he was obstinate, principled, and emphatic until his dying day. He knew that he had created a sensational new therapy that was produced and practiced by thousands of doctors in France, and hundreds (perhaps more) from around the world. He also knew that his movement was in trouble, with no clear path forward. As for the future of the drug trade that he had launched, Brown-Séquard left it as a problem that was very much unresolved. He continued to place his trust in doctors, despite all the trouble they

[271] "We Are Too Chivalrous" in Delhoume, 505.
[272] "We Are Too Chivalrous" in Delhoume, 505.
[273] "We Are Too Chivalrous" in Delhoume, 505.

had given him, and it was to them that he passed on his method, his technical know-how, his encouragement, and his hopes for the future.[274]

Coda: Government Reponses to an Unruly Marketplace in France and America

On April 25, 1895, a year after Brown-Séquard's death, the French parliament passed a watershed legislation that did act, in a sense, to bring order to the trade of organic extracts, although perhaps not in the way that Brown-Séquard had imagined. It was a law that, first and foremost, attempted to regulate the trade in vaccines and serotherapies by authorizing a "Serum Commission" to inspect and grant manufacturing licenses to druggists who made bacteriological products. The law read:

> Art. 1. Attenuated viruses, therapeutic sera, modified toxins and analogous products that can serve as prophylaxis against or therapy for contagious diseases, and injectable substances of organic origin not chemically defined, applied to the treatment of acute or chronic affections cannot be debited, free or against payment, unless they have received a government authorization either for their fabrication or for their origin. This authorization will be granted following advice from the French consultative committee for public health and the Academy of Medicine. These products will benefit only from a temporary and revocable authorization. They will be submitted to an inspection carried out by a commission named by the relevant ministry.[275]

Historians have remembered this law as a consumer-protection measure that sought to bring much-needed government surveillance to the production of diphtheria anti-toxin—the new serotherapy, developed from the blood of horses, that had found a wide market in children who suffered from the common (and fatal) diphtheria disease.[276] Yet, the law also applied to Brown-Séquardian products, which fell under the terms "therapeutic sera" and

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[274] As he wrote to an Atlanta-based American colonel who wished to book an appointment with him in France to receive the injections: "I have given the whole secret to the profession, and your doctors can subject you to this treatment as well as I can. My work is for humanity, and I have nothing to conceal from my professional brethren." This quote appeared in a newspaper clipping in the Brown-Séquard Collections at the Royal College of Physicians in London, but there are no publication details or date included in the clipping. Anon, "About Brown-Séquard's Great Tonic," n.d., item 1000/141, Royal College of Physicians, London.

[275] Translation taken from Simon, "Quality Control and the Politics of Serum Production in France," 95–96.

[276] See Hammonds, *Childhood's Deadly Scourge*; Simon and Gradmann, *Evaluating and Standardizing*.

"injectable substances of organic origin not chemically defined."[277] The law's application to the trade of organic extracts was made explicit in an amendment to the law that came on November 14, 1896, which decreed that "the preparation of therapeutic serums and animal extracts is authorized" if "prepared according to the method of Brown-Séquard."[278] Even before this decree, glandular laboratories were being inspected and authorized by the Serum Commission alongside bacteriological laboratories.[279] By the end of 1898, there were at least nine certified producers of glandular therapeutics operating in Paris and the provinces.[280]

Was the law of 1895 one step toward official government recognition of Brown-Séquard's therapeutic method? That organic extract laboratories were being visited and authorized by the Serum Commission might suggest a level of government acceptance of Brown-Séquard's new drug, and even a (belated) concern for how it was being produced. Yet, a close reading of the parliamentary discussion that took place during the drafting process suggests this was likely not the motivation of legislators, whose primary concern in drafting this law was protecting the public from the new "biologic" drugs that used animal tissues and organs in the manufacturing process.[281] Brown-Séquard's method was identified by one parliamentarian, Bourrillon, as the best approach to producing organic extracts not

[277] The French law of April 25, 1895 does not appear in histories of endocrinology, despite its importance in the regulatory history of glandular therapeutics. Instead, the law appears almost exclusively in histories of bacteriology, vaccine production, pharmacy, and biologics. In most of these histories, the law is discussed as it relates to the regulation and production of the diphtheria vaccine. Glandular therapeutics are often mentioned in these histories, but they are never drawn into the foreground of analysis. See, for example, Hess, "The Administrative Stabilization of Vaccines"; Jonathan Simon, "Emil Behring's Medical Culture: From Disinfection to Serotherapy," *Medical History* 51, no. 2 (2007): 201–18.

[278] Surgeon-General of the United States Public Health and Marine-Hospital Service, "Public Health Reports (Formerly Abstract of Sanitary Reports)," Vol. XVII.--Part 1. Nos. 1 to 26 (Washington: Government Printing Office, 1902), 93–94.

[279] See Ministère de l'intérieur, *Bulletin officiel de Ministère de l'intérieur*, 1896, 33.

[280] M. Jacquet (Lyon), M. Catillon (Paris), M. Chevrier (Paris) and M. Vicario (Paris) in Ministère de l'intérieur, *Bulletin officiel de Ministère de l'intérieur*, 1898, 175–76; Société chimique des usines du Rhône (Lyon), and MM. Chaix and Remy (Paris) in Straus, "Sur les demandes de vente de sérum antistreptococcique et d'extraits organiques d'après la méthode de Brown-Séquard," *Bulletin de l'Académie nationale de médecine*, séance du 27 octobre, 1896, 459–61; MM. Egasse and Bouyé (Paris) and M. Sazis (Bordeuax) in Straus, "Sur les demandes en autorisation de délivrer des sérums thérapeutiques et des produits microbiens ou organiques," *Bulletin de l'Académie nationale de médecine*, séance du 24 décembre, 1895, 726–28; M. Bazin (Bordeaux) in Ministère de l'intérieur, 1896, 33.

[281] For an introduction to the history of biologics, see Schwerin, Stoff, and Wahrig, *Biologics*.

because it yielded efficacious products, but because of Brown-Séquard's insistence that organic extracts needed to be ground down and then carefully filtered before use, which would leave a microbe-free filtrate. Indeed, this concern for sterility, and not efficacy, was spelled out explicitly in the first notice that granted the licenses to producers of organic extracts. It read:

> MM. Egasse and Bouyé (de Paris) and M. Sazis (de Bordeaux) asked to be authorized to distribute some organic extracts prepared according to the *méthode de Brown-Séquard*. These extracts, after verifications by MM. Nocard and Thoinot, do not contain bacteria and appear thus prepared in an aseptic way. We propose to the *Académie* to not oppose themselves to this, that MM. Egasse and Bouyé and M. Sazis obtain the authorization that they solicit from the minister."[282]

In the numerous authorization announcements that were made for the rest of the decade, there does not appear to be any variation in criteria for granting a license. Manufacturers were licensed by virtue of their general upkeeping of a sterile laboratory environment, and specifically for their ability to produce injections free of microbes. By virtue of authorizing nine commercial producers to make and sell Brown-Séquardian products by the year 1900, the French government was also signaling that the production of high-quality organic extracts was a job for the commercial marketplace to solve. That is to say, the French government would bear the responsibility of the *inspection* of laboratories that made and hoped to sell organic extracts, but they would not bear responsibility for drug production itself.

In 1902 the United States passed its own version of the French law of 1895 but, curiously, it did not recognize Brown-Séquardian products within the remit of the law. This was despite the fact that it adopted similar wording and intention from the French law, namely that the Public Health Service (PHS) prohibited the sale and distribution of "virus, therapeutic serum, toxin, antitoxin, or analogous product" unless prior authorization was

[282] Straus, "Sur les demandes en autorisation de délivrer des sérums thérapeutiques et des produits microbiens ou organiques," 727.

given by the PHS.[283] Why were organic extracts not recognized as "therapeutic serum" or "analogous products"? Legal scholar Terry S. Coleman argues that there was reluctance on the part of PHS to bestow an official endorsement to "organotherapeutics," which were regarded by government officials as not useful and probably harmless. The exact wording, used by John F. Anderson, Assistant Director of the Hygienic Laboratory, in a note to the Surgeon General in 1909, was this:

> [M]ost of these organo-therapeutic preparations are in the experimental stage; but few of them are really useful and but a few of them are occasionally harmful…to license them would give respectability to a class of drugs some of which are on the borderline of being non-ethical…[284]

Thus, in the U.S., as in France, the government struggled to recognize the value of Brown-Séquard's organic extracts in the 1890s and beyond, let alone mobilize money for their production. Instead, commercial manufacturers were given the nod—officially in France, and unofficially in the U.S.—to continue working with Brown-Séquard's method. This was not so much a solution to the manufacturing problem that Brown-Séquard and d'Arsonval wrestled with in the early 1890s, but more a decision to maintain the status quo. Let druggists continue doing what they wish with Brown-Séquard's method, both French and American governments seemed to say, so long it does not endanger public health.

What did this mean for doctors who wanted to use Brown-Séquardian drugs in the clinic, but continued to be frustrated by the poor-quality products that existed on the medical marketplace? Leaving the French context and turning to the American one, the next chapter gives voice to American doctors who, like their French counterparts, were highly suspicious of commercial organic extracts. I show that, in the absence of government intervention, and

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[283] Coleman, "Early Developments in the Regulation of Biologics," 551.

[284] This source was found by Terry S. Coleman in the National Archives and appears in Coleman, 577. Coleman goes on to explain that Brown-Séquardian remedies and later hormonal products remained excluded from the Biologics Act, even when indisputably efficacious endocrine drugs such as insulin came on the market in the 1920s. Coleman describes this as a "prominent regulatory curiosity." See Coleman, 577.

while they waited for an ethical manufacturer to emerge, American doctors decided to take matters into their own hands. This meant making organic extracts themselves, in the clinic, as Brown-Séquard had advised.

Chapter 3: The Laboring Physician: How Brown-Séquard's Method Emerged in the American Clinic, 1889-1899

In America, news of Brown-Séquard's radical testicular therapy "spread like wildfire."[285] Within weeks of his initial announcement in June 1889, major and minor newspapers from coast to coast were reporting on his testicular injection.[286] Within months, general practitioners and hospital doctors from around the country were making his elixir and testing it out in the clinic.[287] Both supporters and critics of Brown-Séquard's new therapy then turned to the lay press and medical press and commented *ad nauseum* on the merits—or lack thereof—of testicular injections.[288] In America, as in France, Brown-Séquard's method had captured the instant attention, though not the instant admiration, of the medical community.

We know that hundreds and then thousands of French doctors were working with Brown-Séquard's liquid in the early 1890s, but what about in the U.S.?[289] Circumstantial evidence suggests that America's enthusiasm for Brown-Séquard's new therapy mirrored that of France, at least in the beginning.[290] For example, we get hints of the Brown-Séquard "craze" from newspaper clippings, which faithfully report the quick and thorough saturation

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[285] One of Brown-Séquard's earliest biographers, J. M. D. Olmsted, wrote in regard to the testicular extracts that "the cult of injection spread like wildfire," although note that he was referring generally to the "civilized world" and not specifically to America. See Olmsted, *Charles-Edouard Brown-Séquard, a Nineteenth Century Neurologist and Endocrinologist*, 211.Americans doctors learned about Brown-Séquard's announcement either by reading French journals, their own American newspapers, or by word of mouth. See "Is Foundation of Youth. Prof. Brown-Séquard Discovered the Elixir," *Chicago Daily Tribune*, July 14, 1889, 25. Dr. N. S. Davis Jr. said that he had read Brown-Séquard's original communication in French journals. Dr. E Wyilyss Andrews said that he read about it in the (Chicago) *Tribune*.

[286] News of Brown-Séquard appeared in small and large newspapers from all over the country, such as the *New York Times*, the *Chicago Tribune*, *the Los Angeles Times*, the *San Francisco Chronicle*, the *Galveston Daily News* (Houston, TX), the *Weekly Inter Ocean* (Chicago, IL), the *Portland Oregonia*n, the *Cincinnati Enquirer*, the *New York World*, *Atchison Daily Champion* (KS), *St. Paul Daily News* (MN), etc.

[287] Newspaper reports demonstrate that Brown-Séquard's method was taken up by all kinds of doctors in the U.S. and were not limited to any one variety. This chapter will demonstrate the wide appeal of Brown-Séquard's ideas in the medical community.

[288] In America, as in France, Brown-Séquard's new therapy received as much praise as it did criticism. This chapter will show the diverse reaction to his announcement.

[289] The first two chapters of the dissertation detailed the volume of medical practitioners in France who approached Brown-Séquard's laboratory with requests for testicular extract.

[290] Brown-Séquard himself did not have a clear sense for the volume of his following in America, and there are no specific numerical estimations given by commentators. We can, instead, use hints from the archive to estimate the size of the market.

of his method in the American public imaginary.[291] The *Chicago Tribune,* for example, reported that the resident physician's room at the Medico-Chirurgical hospital in Philadelphia was "crowded" with patients in the middle of August 1889, "who had either tried or were prepared to try the Brown-Séquard elixir."[292] The same month, the *San Francisco Chronicle* reported that so many physicians were trying to make Brown-Séquard's elixir in San Francisco that there were shortages of guinea pigs and rabbits throughout the city.[293] The *Weekly Inter Ocean* (Chicago, IL) reported that physicians of Indianapolis were "overrun with patients who wanted to be experimented on."[294] In September 1889, Brown-Séquard himself told American reporter James Gordon Bennett Jr., publisher of the *New York Herald*, that he had been receiving twenty-five letters from Americans every single day, and they were stacked and overflowing on the side tables in his drawing room.[295] This was after Bennett, who had visited Brown-Séquard's home to interview him, handed over a "voluminous package" of newspaper cuttings from U.S. periodicals, detailing the experiments that were being performed by doctors all over the country.[296]

Brown-Séquard did not welcome America's enthusiastic reception of his method, however, for he did not feel good about the kind of reports that were surfacing. If he had read

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[291] Historian of medicine Bert Hansen has shown how news of Brown-Séquard's new therapy also extended beyond the medical community: Brown-Séquard's efforts were widely satirized in popular American magazines, including *Puck, Judge* and *Frank Leslie's Illustrated Newspaper*. Cartoons and caricatures depicted a fictional world where decrepit old men could toss away their walking sticks, and perform a youthful jig, immediately upon injection of the "elixir." See Bert Hansen, "New Images of a New Medicine: Visual Evidence for the Widespread Popularity of Therapeutic Discoveries in America after 1885," *Bulletin of the History of Medicine* 73, no. 4 (1999): 653. As Hansen argues, Brown-Séquard's claims were received as another sensational (and alleged) medical breakthrough, along a similar vein to Robert Koch's tuberculin and Louis Pasteur's rabies and anthrax vaccines. See Hansen, *Picturing Medical Progress*.

[292] "Elixir Found Alive with Bacteria: Danger Threatens Indiscriminate Use of the New Discovery," *Chicago Daily Tribune*, August 15, 1889. It seems that Professor Boenning had prepared the mixture and had been making "experiments" at the College to determine if the elixir had any value. The same story appears in "Brown-Séquard's Method," *Weekly Inter Ocean*, August 20, 1889.

[293] "Rough on Cavies: Elixir Experiments Are Exterminating Them," *San Francisco Chronicle*, August 24, 1889.

[294] See "Indianapolis" subheading in "Brown-Séquard's Method."

[295] "For Women Also."

[296] "For Women Also."

the news clippings that were handed over to him by Bennett, he would have seen reports that ranged from the alarming to the bizarre. Perhaps within their midst was the story of 80-year-old miner Henry Seymour from Nevada City, who received a dose of the elixir from a local "Brown-Séquard disciple," but was left in a critical condition, possibly because the liquid was formulated from pig's blood.[297] Or there could have been a report clipped from the *Reno Gazette* that detailed the efforts of a "kind-hearted" rancher who injected his old and beloved horse, John, with Brown-Séquard's elixir and cured it of "all the ills that equine flesh is heir to."[298] The idea came to the rancher when he was "trimming" his pigs and figured he could make use of their "juice" on "old John."[299] There might also have been a story, covered by *The Los Angeles Times,* about a general practitioner, Dr. L. Lichstein, from Birmingham, Alabama, who injected himself and his patient, L.D. May, with Brown-Séquard's elixir, which left them both "writhing in mortal agony."[300] Or there could have been reports about a physician of Fort Worth, Texas, who had "with much care" tried Brown-Séquard's elixir on "several patients" with results that were "entirely negative."[301] Then there was the most bizarre story of all, which might have been stacked in Bennett's bundle: the patient in Nebraska who, upon being injected by his local physician with a concoction made from rams' testicles, charged out of the clinic, ate some grass, and bleated like a sheep.[302]

In truth, Brown-Séquard did not need to be handed a bundle of newspaper clippings from Bennett to learn of the fate of his therapeutic method in the U.S., for he had been closely following the American story from the beginning. When Bennet questioned him

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[297] "Experiments with the Elixir: Dr. Longfellow of Cincinnati Says He Has Had Good Results," *Chicago Daily Tribune,* August 19, 1889.
[298] Article from the *Reno Gazette* reported as "That Wonderful Elixir," *San Francisco Chronicle,* September 15, 1889.
[299] "Made the Horse Too Lively," *San Francisco Chronicle,* September 11, 1889. "Trimming" referred to castration.
[300] "Testing the Elixir," *Los Angeles Times,* August 15, 1889.
[301] "The Brown-Séquard Elixir: Tried with Negative Effects—The Dynamite Explosion Victims," *Galveston Daily News,* August 29, 1889.
[302] "Brown-Séquard in Nebraska," *Daily Picayune,* September 9, 1889.

about the reception of the "elixir of life" in the U.S., Brown-Séquard "smiled rather sadly" and said: "Why, I thought I knew your countrymen pretty well, but it seems that I was mistaken. It never occurred to me that so many of them would undertake experiments of this kind without first mastering all the preliminary details." Brown-Séquard was referring to the "preliminary details" of his method, which he had carefully laid out in print for the benefit of the medical community, as earlier chapters have detailed. Bennett replied: "Your elixir has certainly caused a great sensation in America," to which Brown-Séquard retorted:

> Please don't make use of that word elixir…I never made use of the word 'elixir' still less of the words 'elixir of life.' These are all expressions or inventions of sensational newspapers. If quacks or ignorant men in America have killed people, as stated by the American papers, they would have avoided committing these murders had they paid the least attention to the most elementary rules as regards the subcutaneous injections of animal substances…[303]

Brown-Séquard was deeply pessimistic about what America was doing to his therapeutic method, and he was right to be. In 1889, there were arguably more negative reports coming in from doctors than positive. This was especially the case with elite physicians and former colleagues. Dr. William H. Pancoast, dean of faculty at Philadelphia's Medico-Chirurgical College, told the *Chicago Daily Tribune* that: "I know Brown-Séquard well, but I would like to have his theory proved before I put any faith in it…"[304] Dr. D. R. Brower from Chicago recalled Brown-Séquard's lectures in America on the nervous system, and his towering reputation in physiology, but stated that "as for this pretended new discovery… I place no faith in it."[305] John Hamilcar Hollister, of the Chicago Medical College, was also familiar with Brown-Séquard's work on the nervous system, but he "feared" that Brown-Séquard's "second sight was not as good as his first."[306] When asked about Brown-Séquard's supposed

[303] "Gossip Sent by Cable: Dr. Brown-Séquard Heard From," *Chicago Daily Tribune*, September 9, 1889.
[304] "Dr Brown-Séquard's Wonderful Discovery: Differing Views of Eminent Physicians upon the Elixir of Life," *Chicago Daily Tribune*, August 4, 1889.
[305] "Is Foundation of Youth. Prof. Brown-Séquard Discovered the Elixir."
[306] "Is Foundation of Youth. Prof. Brown-Séquard Discovered the Elixir."

discovery, Surgeon-General of the United States John Hamilton noted: "I used to know him well up to eight or ten years ago and I know that he had never made any experiments in the direction indicated by this story." But if these reports were true, and not exaggerated, Hamilton noted, then he would put it down to the "wandering fancies of an old man in his dotage."[307]

What Brown-Séquard and his critics failed to realize is that the "method of Brown-Séquard" had found fertile ground in the U.S. Incited by Brown-Séquard's claims, a small but growing community of earnest doctors took up his method in the early 1890s and began to experiment. They toiled with animal tissue, made refinements to their process, and found success in the clinic. By the end of the 1890s and early 1900s, some manufacturing firms began to invest in animal remedies and reached out to doctors who were working with glands. In the first two decades of the twentieth century, American doctors and selected drug manufacturers would work together to produce high-quality endocrine drugs. By the 1920s, America would be the world's leader in endocrine-drug manufacturing and responsible for producing the first generation of endocrine drugs that were regarded by the medical community as clinically efficacious and indispensable in medical practice.[308]

This chapter, and the ones that follow, makes sense of this American story. I show how clinical endocrinology was transformed in America from a sensational and frankly odd medical movement in the early 1890s that generated substantial negative press, to a scientific field that was practiced in every American clinic by 1920. I ask: how did a country full of

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[307] "The Elixir of Life," *Portland Oregonian*, July 21, 1889. Dr. John Harvey Kellogg of the Battle Creek Sanitarium was a little more sympathetic to Brown-Séquard's latest work, having spent an entire afternoon with him at his laboratory in Paris, but he still sided with the view that any good effects that came from the elixir were probably the result of "imagination of the patient." Kellogg concluded: "Brown-Séquard, however, is entirely sincere in his belief, and he is exceedingly enthusiastic as regards the future of his operation." See Eugene Glass, "A Conservative View: Dr. Kellogg's Interview with Dr. Brown-Séquard as to the Elixir," *Daily Inter Ocean*, August 29, 1889.

[308] America's largest drug company, Parke, Davis & Company, was responsible for producing Adrenalin and Pituitrin in the early 1900s, as the next chapter will show. Eli Lilly, a large Indiana-based firm, produced the blockbuster drug "Insulin" in collaboration with researchers from the University of Toronto, in the early 1920s.

"quacks" and "ignorant men" produce scientific medicine that is still used today? How did Brown-Séquard's therapy, which was widely criticized by the scientific and medical elite, move from the margins to the mainstream of medical practice?

It began with hard-working and entrepreneurial doctors, as this chapter argues. Focusing on the period from 1889-1900, this chapter shows that there a small but growing community of orthodox physicians in America who approached Brown-Séquard's claims with seriousness and a critical gaze.[309] Starting in the immediate wake of Brown-Séquard's inaugural address, MDs in GP clinics and hospitals began to experiment with the elixir and confer with each other. Were Brown-Séquard's results valid, they asked, and if so, how could his method be rolled out in the clinic for the benefit of American patients? From the mid-1890s, more doctors, including university-based physicians, came on board the Brown-Séquard bandwagon and began to investigate a whole range of drug candidates made from animal glands and organs. Chapters 4 and 5 will show how American physicians began to confer not just with each other, but also with drug companies, which was critical to producing standardized and effective endocrine pharmaceuticals, especially after 1900.

A key theme that emerges from this source material, which has been collected from the lay press and medical press, is the labor performed by American physicians in making and prescribing glandular products. As this chapter shows, many doctors followed Brown-Séquard's advice and produced organic extracts themselves, in-house, using livestock testicles procured from slaughterhouses or local butchers, and according to the method that

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[309] Historians of American medicine differentiate between "regular" [orthodox] and "irregular" [unorthodox] practitioners of medicine. "Regular" or "orthodox" practitioners were those with MDs from widely recognized and elite medical schools, who practiced a style of medicine endorsed and regulated by the American Medical Association, and which gradually aligned with the principles of the new scientific medicine developed by European physiologists and chemists. In contrast, "irregular" or "unorthodox" practitioners were those who practiced a brand of healing that was pitched as an alternative to the increasingly reductionist, secularized and westernized scientific medicine. Examples of this were homeopathy and Christian science in the nineteenth-century, and later osteopathy and chiropractic which gained prominence from the early twentieth century. See Gevitz, *Other Healers*; James C. Whorton, *Nature Cures: The History of Alternative Medicine in America* (Oxford, New York: Oxford University Press, 2002); Venit Shelton, *Herbs and Roots*.

Brown-Séquard had published in medical periodicals for their use. [310] It also shows that American doctors-turned-experimenters saw it as their responsibility to methodically test Brown-Séquard's drugs in the clinic, to refine them, and to make them efficacious.

I use the terms "laboring" and "experimenting" in this chapter partly to accord with actors' categories—physicians' described themselves as "laboring" and "experimenting" with Brown-Séquardian remedies—and partly to make an empirical and theoretical point. Physicians were active participants in the process of scientific research, drug production, and clinical trials, I argue, and they did the most in the 1890s to test, trial and build knowledge about the new glandular drugs. In making this point, I am complicating pervasive historiographic assumptions, laid out in the introductory chapter, that doctors were merely recipients or resistors of new scientific knowledge at the turn of the century. This chapter offers a different perspective on American physicians. Inspired by key works in the history of American medicine that focus on the realities of doing clinical work (successful or not),[311] I situate doctors as key agents of change in the history of endocrinology.[312]

To build this argument, I examine the initial reception of Brown-Séquard's testicular injections in the medical community between 1889 and 1890. In the section that follows, I explain how new physiological work on thyroid glands incited a much larger community of

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[310] Some American physicians used pre-prepared elixir, sometimes shipped directly from Brown-Séquard's laboratory, but others made their own testicular injections from scratch, and even supplied it to their colleagues for use and experimentation. For details on pre-prepared mixture and physician supply chains, see Solomon Solis-Cohen, "The Therapeutic Properties of Animal Extracts," *The Philadelphia Polyclinic* 2, no. 2 (November 1893): 317. Solis-Cohen, who had experimented with Brown-Séquard's testicular liquid, was supplied by his colleague Thomas K. Morton who had had in his possession injections that were delivered directly from Brown-Séquard's laboratory in a "sealed packet."

[311] Crenner, *Private Practice in the Early Twentieth-Century Medical Office of Dr. Richard Cabot*; Morris J. Vogel and Charles E. Rosenberg, eds., *The Therapeutic Revolution: Essays in the Social History of American Medicine* (Philadelphia: University of Pennsylvania Press, 1979); Warner, *The Therapeutic Perspective*; Warner, "Ideals of Science and Their Discontents in Late Nineteenth-Century American Medicine"; Stowe, *Doctoring the South*.

[312] Merriley Borell, a historian who dedicated much of her scholarly energies to the early history of endocrinology, held similar views. See how she is quoted by her own students in Judith P. Swazey and Karen Reeds, "Disease and the Ductless Glands," in *Today's Medicine, Tomorrow's Science: Essays on Paths of Discovery in the Biomedical Sciences* (Rockville, Md.: Dept. of Health, Education, and Welfare, Public Health Service, National Institutes of Health, 1978), 53–68.

American doctors to experiment with animal glands. The third section shows that, as enthusiasm for animal extract therapies grew, disagreement emerged between doctors about what counted as "rational" experimentation. In the absence of scientific and medical consensus about how glands functioned physiologically, doctors were forced to come up with their own ideas about which glands and tissues were appropriate candidates for drug development.

In all, this chapter underscores the difficulties confronted by American doctors who wanted to use glandular drugs to treat their sick patients but did not yet have clear clinical directives or physiological principles to guide them. To make headway in the clinic, they were forced to stand on their own two feet, to experiment with raw tissue, and to create their own field of clinical medicine, even amidst plaguing doubts about the value of their work. This culture of liberal experimentation with animal extracts, performed by doctors, is how endocrinology emerged in the American clinic and gained its footing in medical practice.

Experimenting with Testicular Extracts in the American Clinic, 1889-1891

In the middle of August 1889, just two months after Brown-Séquard's first announcement at the Société de Biologie, medical professor Alexander B. Shaw from Missouri published an editorial in the *Weekly Medical Review* (St. Louis) to describe some initial experiments he had made with Brown-Séquard's elixir.[313] He prepared the concoction himself from the glands of sheep and used a mortar and pestle and some distilled water to create the inoculant, as per Brown-Séquard's recipe.[314] He injected only four patients with testicular fluid, but each had responded negatively. Following the first jab, his patients complained of a variety of side-effects, including poor sleep, dryness of the mouth, sweating, attacks of vomiting and

[313] Reported in Dunbar, *The "Elixir of Life.,"* 93–98. Shaw was Professor of Diseases of the Mind and Nervous System at Beaumont Medical College, St. Louis, according to the byline listed in this source: Alexander B. Shaw, "The Treatment of Locomotor Ataxia by Suspension, Etc.," *JAMA* 14, no. 5 (1890): 149.
[314] See "Elixir Found Alive with Bacteria: Danger Threatens Indiscriminate Use of the New Discovery." This report does not mention if Shaw used a filter.

diarrhea. Some denied a second jab with the elixir either by verbal refusal or by neglecting to return to Shaw for re-administration. Shaw blamed these serious side-effects on the testicular preparation itself, which he claimed contained harmful microbes. Even though the testicles were fresh, taken from a sheep "not yet dead," and Shaw had meticulously filtered per Brown-Séquard's instructions, he could still see under the microscope harmful bacilli, including tuberculosis germs. His colleagues Drs. S. S. Porter, Waldo Briggs and George C. McCosh, who gathered around Shaw's microscope, confirmed these observations. In summing up his experimental efforts, Shaw was openly reproachful:

> … It might be harsh and unjust to style [the elixir] the dotage dream of a prince in physiology, but milder language of a similar import might convey an idea of the impression I have *ab initio* entertained. And what was then an impression, notwithstanding, following the hypodermic use of the mixture, which daily appear in our newspapers, *ad nauseam*, has after careful experimentation…become a conviction…I have no faith in its revitalizing influence…[315]

Shaw's commentary is typical of early negative accounts on the efficacy of Brown-Séquard's elixir. American doctors read about Brown-Séquard's new method in the press, resolved to try it out even if they had "no confidence" in it, prepared the mixture following Brown-Séquard's instructions, and then administered it to their old and debilitated patients via subcutaneous injection. Bad side-effects, or an absence of beneficial results, would see irate doctors writing article-length rebukes in medical journals, which also took the form of an endless stream of (often unsigned) short-form editorials that made jokes and jibes at Brown-Séquard's expense. One anonymous editorial in *The Medical Record*, entitled "The So-Called Elixir of Youth and Its Absurd Pretensions" claimed that Brown-Séquard's method was "ridiculous" and "preposterous" and that if it were not for his reputation, "no one would

[315] Alexander B. Shaw in Dunbar, *The "Elixir of Life.,"* 94–95.

ever have looked upon it in any other light than as the foolish conceit of an old man, in whose mind the dreams of returning youth had assumed the counterfeit of reality."[316]

Appearing side-by-side this genre of negative reporting, however, were positive responses to Brown-Séquard's injections. For example, Dr. Purman of Indianapolis injected his 50-year-old patient, Noah Clark, with the Brown-Séquard elixir for treatment of debility, rheumatism and "disease." To prepare the injections, Purman had driven to the stockyards to select "the healthiest lamb obtainable."[317] It was killed and "the necessary parts were brought to [Purman's office]" to be "pounded in a mortar," mixed with water and then filtered. "One and a half drachms" of this solution were injected by Purman into Clark's arm. [318] All this was witnessed by Theodore Parker, another doctor. The injection was performed within two hours of the lamb's slaughter—impressive work for Purman, who was likely hard-pressed to travel to the slaughterhouse, prepare the liquid, and inject his patient within this timeframe. Unlike Shaw's patients, Purman reported only positive effects. Four hours after the injection, Clark walked down the street unassisted, stood straight, and climbed stairs with ease, which were feats that had escaped him before the elixir. Clark said: "I have not felt this way for twenty-five years. I have new vitality. I do not drag my feet along, and it is no trouble to hold my head up. I used to go along all bent over."[319]

Dr. John W. Palmer of Detroit also shared Purman's success in treating patients with Brown-Séquard's elixir but cautioned that he had "just begun experimenting" and had not yet reached firm conclusions. He added, though, that "the preparation is in no sense dangerous,

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[316] "The So-Called Elixir of Youth and Its Absurd Pretensions," *The Medical Record* 36, no. 8 (August 24, 1889): 210.
[317] Dunbar, *The "Elixir of Life.,"* 99. Dr. Purman also treated patient W. J. Morden, a general manager at Morden Frog and Crossing Works who was suffering from paralysis. Morden had travelled from Chicago to see Purman because "none of the Chicago physicians were willing to experiment with the elixir." After receiving injections from Purman, Morden felt "considerable improved." See "Indianapolis" subheading in "Brown-Séquard's Method."
[318] According to the Merriam-Webster, this was "a unit of weight in the apothecaries' system equal to one eight of an ounce." See online entry: https://www.merriam-webster.com/dictionary/dram#h1
[319] Clark in Dunbar, *The "Elixir of Life.,"* 100.

for an antiseptic enters all its composition, and its base is from the healthiest of animals."[320] William A. Hammond, the celebrated ex-Surgeon General of the Civil War, who was initially skeptical of the Brown-Séquardian idea, had cause to change his mind.[321] He explained that he was initially "dubious" about the claims and was "inclined to think, as others had hinted, that the report was French joke or that Dr. Brown-Séquard was another good man gone wrong."[322] But then, Hammond explained, "I started to experiment."[323] Hammond claimed that: "The preparation of the medicine and the treatment of the patient are simple. I take the selected portion of a lamb freshly killed and pound it into a pulp in a mortar; with this I mix in a teaspoonful or two of water and the mixture I filter through fine Swiss filtering paper…."[324]

Following Brown-Séquard's lead, Hammond first injected himself with the testicular mixture to ensure it was not dangerous, and then proceeded to inject a 60-year-old male patient suffering from a paralyzed arm, without his knowledge to avoid a placebo effect. After just one injection, the patient "could move [his arm] in any direction and almost as vigorously as he had ever done."[325] It was a promising outcome but by no means was it definitive. Hammond wrote: "The whole matter is yet in its experimental stage, and it will there remain until the subject has been examined into by many physicians under difference circumstances, and a general coincidence of opinion obtained."[326]

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[320] Dr. Palmer in Dunbar, 102. It is not clear from this source what "antiseptic" Palmer was referring to. Possibly, he had added glycerin to the tissue mixture, which was a common antiseptic additive that was used in Brown-Séquard's injections, vaccines and serotherapies in the 1890s.
[321] Dunbar, 105. See also "Believes in the Elixir of Life: Dr. Hammond Thinks Dr. Brown-Séquard Has Made a Great Discovery," *Chicago Tribune*, August 1, 1889.
[322] Possibly Hammond was referring to Koch's tuberculin scandal. American newspapers made connections between Brown-Séquard's discovery and Koch's lymph. See, for example, "Dr. Brown-Séquard Talks," *Chicago Daily Tribune*, December 17, 1890."
[323] "Believes in the Elixir of Life: Dr. Hammond Thinks Dr. Brown-Séquard Has Made a Great Discovery."
[324] "Believes in the Elixir of Life: Dr. Hammond Thinks Dr. Brown-Séquard Has Made a Great Discovery."
[325] In Dunbar, *The "Elixir of Life.,"* 106. These words are from Dunbar not Hammond.
[326] W. A. Hammond, "The Elixir of Life," *The North American Review* 149, no. 394 (September 1889): 257–64. He then levelled a critique: not at Brown-Séquard, but at the press who were responsible for sensationalizing this method. He also thought dismissive physicians were to blame: "those physicians who denounce honest investigation in this or any other direction are unworthy of the profession to which they belong…" For more

General practitioners experimented, too, including Dr. L. E. Niles from Springfield, Ohio who injected nine people, most old men, with concoctions of "pinkish colored fluid extracted from the progenitive organs of three buck lambs…"[327] Dr. Niles chose himself as the first test subject and reported that minutes after he pricked himself in the upper arm with one and a half ounces of fluid, he felt "a warm, grateful glow set in, like the exhilaration of fine old wine."[328] Dr. W. B. Fletcher from Indianapolis, who ran a sanatorium, also found success with Brown-Séquard's method. He tried it on a middle-aged male patient with melancholia who was "ignorant of what was being done."[329] Fletcher detailed what was involved in making and experimenting with the liquid: "About 8 o'clock a lamb was killed, the fluid extracted, and an abdominal injection made." Dr. Fletcher noticed that his patient appeared to be in "better humor" after the treatment, and "stepped lighter." Dr. Fletcher was pleased: "I feel gratified at the experiment," he said, but thought that next time he would use "fluid that is near the ventricle of the lamb's head" instead of the "generative glands" to compare the effects.[330]

What this source material shows, aside from the polarizing nature of Brown-Séquard's ideas, are the careful efforts employed by some American physicians to test the validity of his theories through experiment, even amid bad press. This experimental work first involved producing the drug, which was no easy task. Unlike French doctors who could call on

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work on Hammond and his involvement with Brown-Séquard's elixir, see Bonnie Ellen Blustein, *Preserve Your Love for Science: Life of William A. Hammond, American Neurologist* (Cambridge; New York: Cambridge University Press, 1991).

[327] The report was made from "Springfield, O." I am assuming "O" refers to the state of Ohio. See "Regaining Their Youth: Dr. Brown-Séquard's Elixir Is Tested at Springfield, O.," *Chicago Daily Tribune*, August 11, 1889. Dr. Niles said that he also injected a 12-yr old boy with no effect. Research into Dr. Niles' background suggests that he was a general practitioner in the 1890s.

[328] It was on this confidence that Niles then set about injecting a series of "old citizens" with good effect, including one man who "walked away [from the injection] with an elasticity and spryness that surprised his friends." He finished his report by stating that "nearly all the old citizens here are eagerly waiting for their turns." See "Regaining Their Youth: Dr. Brown-Séquard's Elixir Is Tested at Springfield, O."

[329] Injecting patients with the elixir without their knowledge was a common strategy used by doctors to obviate the placebo effect or, as it was often termed by doctors, healing by "imagination."

[330] "Regaining Their Youth: Dr. Brown-Séquard's Elixir Is Tested at Springfield, O."

Brown-Séquard's laboratory for free samples, American doctors who wanted to trial Brown-Séquard's therapy were forced to produce it themselves.[331] As physician testimonials reveal, this often involved going to a slaughterhouse to procure fresh tissue or slaughtering an animal themselves. Sometimes doctors sought to "obviate the long journey to slaughter pens" by buying rabbits and guinea pigs at the city markets. [332] Other times, doctors would go out to pastures to select and "slay" animals. This was the case for Dr. Buckworth from Sheppardsville, Nebraska, who was reported to travel about three miles out of town to take lambs and "full grown sheep" from fields for the purposes of making up the Brown-Séquardian mixture.[333] In Indiana, Dr. Fletcher's "lamb wagon" was seen making repeated trips "out to the country" to obtain experimental material.[334]

It was generally accepted among physicians who were experimenting with Brown-Séquard's method that it was best to use organs and tissue from freshly killed animals. This was for reasons of sterility, but also "in the hope that [the glands'] strength would be greater," as expressed by Drs. Cutler and Hudson at the City Hospital in Kansas City.[335] But this put time constraints on doctors. Dr. Harper from Cincinnati reported that when he used Brown-Séquard's elixir on five inmates at the "infirmary," he made sure to inject them within forty

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[331] Commercially produced animal extracts would become commonly used by physicians by 1900, as the next chapter will detail. But in the early 1890s, and especially in 1889, American physicians produced their own Brown-Séquardian remedies. There are many reasons for this, as I will detail in a later section of this chapter.
[332] This led to shortages, as the *San Francisco Chronicle* reported in an article entitled "Rough on Cavies: Elixir Experiments Are Exterminating Them." The report stated that "Local physicians who are experimenting with the new 'elixir' for making old men young again are complaining of the scarcity of guinea pigs and rabbits in the local markets. The animal extract utilized by the physicians in pursuing their operations must be taken from such animals as lambs, guinea pigs or rabbits. To procure the required material from the bodies of lambs the doctors are compelled to journey away out to Butchertown, where the slaughterhouse men allow them to operate upon the lambs that await killing there." According to a dealer at the California Market, who was interviewed by the *Chronicle*, there were so many doctors on the hunt for guinea pigs that "he did not think there were over a dozen available ones in the city." This led some doctors to experiment with goat tissue, according to the dealer, but not rats, on account of their being "liable to disease."
[333] "Brown-Séquard in Nebraska."
[334] "Brown-Séquard's Method."
[335]See "Kansas City" subheading in "Brown-Séquard's Method."

minutes of the death of the animal.[336] Dr. H C. Brainerd, who used Brown-Séquard's elixir on thirty-two men and women in Cleveland, Ohio, carefully selected his animals from the stockyards and watched with his own eyes as they were slaughtered in his presence. He then whisked away the desired parts for experimentation back in the city.[337]

Once appropriate animal tissue was procured, physicians' labor continued. They then had to pound in a mortar into a "pulpy mass," to use the words of Dr. Spangler of York, Pennsylvania.[338] Careful doctors would then filter the concoction and test it either on themselves or directly on patients. Finally, some doctors would report their findings in medical journals and the lay press, for the benefit of their colleagues, even if their own questions were unresolved. Even Shaw, who expressed doubt in Brown-Séquard's injections, still spent time following due experimental process, going to the lengths of employing microscopy and enlisting his colleagues for second opinions. Brown-Séquard's injections were ridiculous, he thought, and he begrudged the "labor wasted" in arriving at this conclusion. Yet, it was still up to him, the practicing physician, to settle the question through "careful experimentation."

In the months following Brown-Séquard's announcement, it was mostly general practitioners who experimented with his method and used it in elderly patients.[339] But there is

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[336] "Regaining Their Youth: Dr. Brown-Séquard's Elixir Is Tested at Springfield, O." Note that this doctor found beneficial results in only one of these inmates.
[337] "The Latest Fad," 1.
[338] Dr. Spangler of York, PA, reporting in the *Chicago Tribune*. See "Faith in Elixir of Life: Doctors Determined to Prove the Value of the Discovery," *Chicago Daily Tribune*, August 12, 1889. Dr. Spangler used tissue from a "healthy lamb." He didn't just confine himself to testicular tissue: Spangler made use of the pancreas, liver, spinal cord, and brain of the sheep.
[339] General practitioners and hospital-doctors had access to aged patients, who were the primary market for these injections. For example, Drs. L. A. Berger and C. W. Adamas of Kansas City reported that they conducted a "series of experiments" over the course of three weeks in their line of work at the "Home for the Aged." See "Elixir of Life: Dr. Brown-Séquard's Discovery Tested by Physicians," *Atchinson Daily Champion*, August 10, 1889. See also reports from Newark, NJ, where a "well-known local physician" was using Brown-Séquard's elixir on "Jasper Crouse, a decrepit resident of 82 years of age." See "The Elixir of Life: Strange Effect of Its Trial on an Old Man," *Rocky Mountain News*, August 11, 1889. Note, too, that there were also reports of physician's conducting control experiments to determine if the good effects of Brown-Séquard's injections were real or imagined. See "Elixir of Life: Surprising Effects of Hypodermic Injections of Milk and Water—A San Franciscan's Experiments," *Daily Evening Bulletin*, August 22, 1889.

also evidence that his method had gained a limited reception in university spaces in this period. A handful of early reports exist form university professors, such as Dr. Shaw at the Beaumont Medical College in St. Louis, Dr. Robert Longfellow, a Professor of Dermatology in Cincinnati,[340] and Dr. Henry P. Loomis, a Professor of Pathology at New York University, who had been closely observing Brown-Séquard's claims since June. Loomis resolved to test their validity, culminating in a written report to the *Medical Record* in late August entitled "An Experimental Study of the Brown-Séquard Theory." He made his own liquid, distributed it to other physicians,[341] and tested it on ten patients under his care at Bellevue Hospital. They were all men,[342] with ages that ranged from thirty-five to seventy-seven, and with various health complaints including asthma, diarrhea, debility, nervousness, rheumatism, senility and a "loss of sexual appetite."

Loomis' conclusions were as mixed and uncertain as his results: Brown-Séquard's injections worked for some, had no effect on others, and made some patients worse. "As far as my own experiments are concerned," he stated, "sufficient time has not yet elapsed to justify an affirmation or denial of the correctness of Dr. Brown-Séquard's…conclusion," adding that "there is in the theory sufficient ground for further experimentation."[343] In his report, Loomis also detailed what he saw as a grave threat to the experimental field: "Unfortunately," he stated, Brown-Séquard's theory had received "a public and professional notoriety which is not only to be regretted on general principles, but may possibly long

[340] "Elixir of Life: Dr. Brown-Séquard's Discovery Tested by Physicians." Note that Longfellow was testing the general effects of Brown-Séquard's injections on the overall wellbeing of his patients and was not specifically treating dermatological problems.
[341] For experimental purposes. See Henry P. Loomis, "An Experimental Study of the Brown-Séquard Theory," *The Medical Record* 36, no. 8 (1889): 206.
[342] Brown-Séquard's testicular injections were mostly given to men. There are reports of a "an American lady" who had conducted her own experiments on the effects of ovarian juice and tissues on women. Her efforts were even noticed by Brown-Séquard himself, who encouraged this style of broad experimentation with his theories. See Anon, "Therapeutic Brevities: Therapeutic Application of Ovarian Juice," *The Medical Age* 9, no. 24 (December 26, 1891).
[343] Loomis, "An Experimental Study of the Brown-Séquard Theory," 206. Brown-Séquard was aware of Loomis' experiments, and approved of them, but thought his clinical trials should have been longer. See Anon, "Brown-Séquard's Rejuvenator Once More," *The Medical Record* 37, no. 18 (May 3, 1890): 500.

prejudice us against any merit that it may actually possess..."[344] Like Hammond, Loomis was worried about bad press, and hypothesized that honest experimental inquiry would be stunted by "prejudice."

Loomis' words proved to be prophetic. By the end of 1890, reports on Brown-Séquard's methods by American doctors started to wane in the lay press and medical press. The first round of experiments, which were conducted by, at a minimum, many dozens of practitioners around the country,[345] had not produced results convincing enough to warrant the effort of first producing the drug and then conducting more tests on patients. Apart from Loomis and Hammond, who were perhaps Brown-Séquard's two most high-profile proponents in America (but proponents with reservations), no more elite medical figures stepped forward to champion the testicular injection in 1889 and 1890. This was despite the fact that the culture of experimentation with Brown-Séquard's elixir, and especially Hammond's early work, had "awakened a great deal of interest in high medical circles."[346] It would take more than testicular injections to cement Brown-Séquard's method in the American medical imaginary, but fortunately for Brown-Séquard and his proponents, a new glandular drug was on its way.[347]

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[344] Loomis, "An Experimental Study of the Brown-Séquard Theory," 205.

[345] For the month of August 1889 alone, I have counted reports of seventy-two doctors using Brown-Séquard's elixir from around the United States, as evidenced by quips and articles in the lay press. Most of these doctors were general practitioners. There were likely more doctors who were experimenting with Brown-Séquard's method but whose efforts went unreported. J. M. D. Olmsted, one of Brown-Séquard's earliest biographers, claims that there were 12, 000 physicians internationally working with Brown-Séquard's elixir by the end of 1889, but it is not clear how Olmstead came by this number. See Olmsted, *Charles-Edouard Brown-Séquard, a Nineteenth Century Neurologist and Endocrinologist*, 209.

[346] "The Doctors Disagree," *St. Paul Daily News*, August 8, 1889.

[347] See Anon, "Brown-Séquard's Rejuvenator Once More." This anonymous author writes: "The newspapers have for a long time been silent on the subject of the rejuvenation of old men by means of the injection of testicular juice, and many people have doubtless forgotten that such a thing was ever talked about; but the venerable discoverer of this odd form of stimulant has by no means forgotten it, and his faith in its efficacy grows stronger every day. He has recently published a brochure recounting the details of the method and producing additional evidence of its value." For Brown-Séquard's attempts at boosting others, see "The Ovarian Juice in Therapeutics," *The Medical Record* 37, no. 19 (May 10, 1890): 529–30.

The Arrival of Thyroid Therapy, 1891-1894

By 1891, Brown-Séquard's injections had not yet inspired a medical "movement" in America, and perhaps they never would have if not for a critical development underway in British physiological circles. In October of that year, physiologist George Murray had reported that subcutaneous injections of thyroid juice could cure myxedema—a thyroid disorder characterized by swelling of the face, neck and limbs, dryness of the skin, hair loss, and slowness of movements and speech. Murray reasoned that this disease was caused by the absence of "some substance which is present in the normal thyroid gland," and that treating the patient with healthy thyroid extracts could ameliorate the illness.[348] Murray used the fresh thyroid glands of sheep, which were removed and prepared "as soon as possible" after the animal's slaughter. He let the glands soak overnight in a vial of pure glycerine and carbolic acid, presumably to sterilize the tissue. The juice was then wrung out by hand through a clean handkerchief and made ready for injection.[349] Murray gave a series of shots to his patient between the shoulder blades, infrequently, over a three-month period, and noted the remarkable amelioration of her symptoms: improved speech, decreased swelling, moist skin, easier movements, returned menstruation. Murray suggested that it was the first effective treatment of myxedema in humans. "It is not wise to draw many conclusions from a single case," he cautioned, but "others may be induced to give the treatment a fair trial."[350]

Murray did not mention Brown-Séquard in his landmark myxedema study of 1891,[351] and Brown-Séquard did not have any part in his experiments, but circumstantial evidence

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[348] George R. Murray, "Note on the Treatment of Myxœdema by Hypodermic Injections of an Extract of the Thyroid Gland of a Sheep," *The British Medical Journal* 2, no. 1606 (1891): 796–97.
[349] Murray, 797.
[350] Murray, 797.
[351] There is circumstantial evidence to suggest that Murray did not want to associate with Brown-Séquard. His famous article, "Note of the Treatment of Myxoedema by Hypodermic Injections of an Extract of the Thyroid Gland of a Sheep," did not mention Brown-Séquard, which is odd, given that Murray was almost certainly aware of Brown-Séquard's work by 1891, and aware that his own experiments with subcutaneous injections of thyroid extracts were methodologically and theoretically aligned with Brown-Séquard's experiments.

suggests that Murray was inspired by Brown-Séquard's theories.[352] This is because months before Murray's important thyroid paper, Brown-Séquard had signaled that thyroid glands, like testicles, might also contain a powerful substance that could be harnessed therapeutically. Along with his assistant Jacques-Arsène d'Arsonval, he expounded this idea in an ambitious paper to the Société de Biologie in April 1891, which argued that possibly all glands and all tissues of the body—not just testicles—secreted something powerful into the blood and, as with testicles, should be investigated for their therapeutic potential.[353] This idea came to them after experimentation with various tissues and organs in the lab. Brown-Séquard and d'Arsonval's exact wording in the April 1891 paper was this:

> This observation made at various times on a large number of animals and for most tissues or organs (liver, kidney, brain, bone marrow, thyroid gland, adrenal capsules, pancreas, muscles, etc.) has enabled us to resume this research of a vital interest. The question has therefore widened and now we believe that all tissues, glandular or not, give something special to the blood, that every act of nutrition is accompanied by an internal secretion. We therefore believe that all the tissues can and should be employed in special cases a mode of treatment; that there is, in a word, a need to create a new therapy whose medicines will be products produced by the different tissues of the organism.[354]

In 1889, Brown-Séquard had attributed the powerful effects of testicular extracts to the "nutritive modifications" that were exacted on the body "by some of the principles contained in the injected fluid."[355] This 1891 paper, however, specifically connected his therapeutic idea to the concept of "internal secretions"—an older but specific physiological theory,

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[352] This is also the opinion of Brown-Séquard's most recent biographer, Louis-Cyril Celestin, who argues that Murray had "acquainted himself" with Brown-Séquard's work, although Celestin does not offer any specific evidence to support this claim. See Celestin, *Charles-Edouard Brown-Séquard*, 210–11.
[353] Charles Brown-Séquard and Jacques Arsène d'Arsonval, "De l'injection des extraits liquides provenant des glandes et des tissus de l'organisme comme méthode thérapeutique," *C R Soc Biol*, April 18, 1891, 248–49.
[354] Brown-Séquard and d'Arsonval.
[355] Charles Brown-Séquard, "Note on the Effects Produced on Man by Subcutaneous Injections of a Liquid Obtained from the Testicles of Animals," *The Lancet*, July 20, 1889, 105–7.

elaborated at least as early as Claude Bernard, that the glands of the body secreted something material and necessary into the blood.[356]

Whether Murray's work was inspired by this paper or not, American doctors began to explore thyroid therapies as a new iteration of Brown-Séquard's idea. American journals reported on new research on thyroid therapeutics alongside commentaries about Brown-Séquard's testicular injections, [357] and began to pick up the stories of lesser-known European investigators who were experimenting with other animal organs and glands, such as pancreas extracts for the treatment of diabetes and brain extracts to treat nervous disorders.[358] From 1893, medical periodicals started to gesture for the first time to an emerging therapeutic movement of "physiological remedies" that used "organic extracts" and "animal extracts" to treat an array of human disease. Brown-Séquard's publications were dissected for their theoretical content, especially his and d'Arsonval's argument that *all* organs and *all* tissues of the body emitted internal secretions into the blood, and could be put to therapeutic ends.[359]

Brown-Séquard's work was newly interesting to American doctors because thyroid therapy appeared to work miraculously in the clinic. Physician after physician repeated Muray's experiments and also found that thyroid extracts were a remarkable treatment for myxoedema. By 1893 and 1894, medical journals began reporting in earnest on the new

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[356] For a concise and useful history of the theory of internal secretions, see Swazey and Reeds, "Today's Medicine, Tomorrow's Science." Note also that Brown-Séquard himself had contributed to this theory in earlier work, done in the 1850s, on the physiology of the adrenal gland. I have addressed this in an earlier paper. See Patrick M. Walsh, "Experimenting with 'Life' in Nineteenth-Century Physiology: Brown-Séquard's Method for Characterising Blood," *Australian Feminist Studies* 34, no. 99 (January 2, 2019): 73–92, https://doi.org/10.1080/08164649.2019.1605487.

[357] See James J. Putnam, "Recent Observations on the Functions of the Thyroid Gland; and the Relation of Its Enlargement to Graves's Disease; Also Remarks on the Therapeutic Use of Sheep's Thyroids and of Other Organic Extracts," *Boston Medical and Surgical Journal* 125, no. 23 (February 15, 1894): 153. He wrote: "It was impossible that the wonderful discoveries with regard to the effects of thyroid extracts in myxoedema should have failed to renew the interest in the use of the other organic extracts (of testicle, brain, spinal cord, etc.) suggested by Brown-Séquard and D'Arsonval, by Babes, and by Althaus…" (pp. 155-56).

[358] For example, see "The Injections of Organic Liquids and Their Utility in Therapeutics," *Boston Medical and Surgical Journal* 123, no. 2 (January 12, 1893): 46–47.

[359] See Brown-Séquard and d'Arsonval, "De l'injection des extraits liquides provenant des glandes et des tissus de l'organisme comme méthode thérapeutique," April 18, 1891; Brown-Séquard and d'Arsonval, "Additions à une note sur l'injections des extraits liquides de divers organes, comme méthode thérapeutique."

thyroid therapy. By the mid 1890s, up to half a dozen lengthy reports on thyroid therapy would appear in each issue of the medicals journal I surveyed, a sharp increase from the average of one or two articles that appeared per issue on Brown-Séquard's testicular extracts.[360] By 1897, the volume of publications on thyroid therapy had doubled, with an average of twelve to fifteen articles appearing in each and every issue. This surge in popularity did not come as a surprise to doctors on the ground, who were every day working with thyroid extracts and noting their extraordinary success in myxedematous patients. According to Dr. Wharton Sinkler, a Professor of Nervous Diseases and neurologist at the Philadelphia Hospital, "one of the most interesting and noteworthy events in medicine in the last decade is the treatment of myxedema by the internal administration of thyroid gland."[361]

Even *JAMA,* a journal most reticent to recognize Brown-Séquard's testicular extract therapies, began to relent. In 1893, an editorial appeared in the journal acknowledging that "an intense interest in [thyroid therapies] is apparent on the part of the British medical profession, as is evident from the fact that at least a dozen articles have appeared in the leading journals in the last three months. The reports of the cases thus far recorded are very favorable, and the results are astonishing."[362] In the next issue of *JAMA,* there was another article on thyroid therapy noting that "recent observations" had shown that thyroid gland therapy was "quite efficient" in treating myxedema.

The efficacy of thyroid therapy also gave university-based physicians a license to explore the therapeutic potential of myriad organic extracts, following Brown-Séquard and d'Arsonval's suggestions in their 1891 paper. For example, Dr. Solomon Solis-Cohen, a

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[360] Curiously, and as compared to Brown-Séquard's elixir, the thyroid therapy revolution was hardly reported in the lay press. That is to say, as medical journals start to take more interest in glandular therapeutics, the lay press started to lose interest. This perhaps is an indication of the orthodox reception of thyroid therapy.

[361] Wharton Sinkler, "Myxedema and Its Treatment by Thyroid Extract," *The Philadelphia Polyclinic* 3, no. 15 (April 1894): 141.

[362] Anon, "The Treatment of Myxoedema by Thyroid Extract and the Functions of the Thyroid Gland," *JAMA* 20 (February 11, 1893): 161.

Professor of Clinical Medicine and Applied Therapeutics at the Philadelphia Polyclinic, became heavily involved in glandular research during the thyroid therapy rush of 1893. That year he published a lengthy commentary which argued that the age-old method of using animal extracts as medicine had undergone a "revival" first through Brown-Séquard testicular injections and next through the work of British physicians on thyroid glands.[363] He claimed that recent years had seen experiments with pancreas extract for diabetes, nerve tissue for epilepsy, and even thymus gland for paralysis. Dr. James J. Putnam, from Harvard's medical school, agreed that doctors now had cause to reinvest in the Brown-Séquard idea about the therapeutic potential of the glands and tissues of the body, and reported that doctors had found good effects from using testicular injections to treat eczema, leukoderma and icthyosis.[364] That a new era was dawning in the field of glandular therapeutics was also evident in the changing tone of even the most sarcastic editorials, which still ridiculed Brown-Séquard for being a senile quack, but were forced to admit that "…the pollen [of his theory] has in some cases fallen on fertile soil," citing as examples reports from European medical journals on injections of "nervous matter" for the treatment of tabes (chronic wastage) and neurasthenia, and the treatment of acromegaly by the injection of the pituitary glands from sheep.[365]

Why did thyroid therapies attract more support from doctors than testicular injections? There were important differences between the two therapies. Where the testicular injections had been marketed by Brown-Séquard and his followers as *general* treatment for a range of diseases, from paralysis to asthma, Murray's thyroid therapy was framed as a highly specific treatment for myxedema. Murray's therapy also worked quite consistently and

[363] Solis-Cohen, "The Therapeutic Properties of Animal Extracts," November 1893. He likened the age-old method of using animal extracts to a bygone era of "witchcraft" when a "fox's liver" could "cure a royal princess" (p. 309).
[364] Putnam, "Recent Observations," 155.
[365] Anon, "Is the Millennium at Hand?," *The Medical Record* 42, no. 15 (October 8, 1892): 423–24.

dramatically in patients with myxedema, as noted by American physicians, and in some cases led to stunning cures. Brown-Séquard's testicular injections, by contrast, seemed to work only some of the time and in some people. Adding further to the appeal of thyroid therapy, Murray had a concrete answer for why thyroid therapy was successful: myxedema was caused by loss of function of the thyroid gland and injections of healthy thyroid extract could make this better. Brown-Séquard had never been able to provide such a concrete explanation for why testicular extracts worked the way they did; according to him, the study of internal secretions was in its infancy, and there were likely many systemic factors contributing to the general tonic effects of reproductive tissue.[366]

Thus, for physicians who were skeptical of general panacea treatments, as Brown-Séquard's injections were often interpreted, and who were scandalized by the notion of treating patients with reproductive tissue, thyroid injections were a much safer horse to bet on. In the words of a Dr. Pearce Bailey, a New York City neurologist who reflected on the arrival of thyroid therapy in a 1897 issue of *Science Monthly*, "thyroid [medication] forms one of the few medicinal agents in our possession which are not given on purely empirical grounds."[367] While there were certainly still skeptics of the new thyroid therapy who penned sneering editorials that described thyroid extracts as just another medical fad, and "a dreary waste of experiments" to use one author's phrase,[368] they were considerably outnumbered by doctors who were keen to investigate thyroid drugs and to trial them in patients.

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[366] Brown-Séquard approached the study of glands as a new field of physiological inquiry. For his theoretical sketches, which dealt with the relationship of the glands to the blood, and his thoughts on secretions, see Charles Brown-Séquard, "On a New Therapeutic Method Consisting in the Use of Organic Liquids Extracted from Glands and Other Organs," *The British Medical Journal*, June 3, 1893, 1145–47.

[367] Pearce Bailey, "The Thyroid Gland in Medicine," *Bismarck Tribune*, September 16, 1897. Originally published in *Science Monthly*. In this article, Bailey described the thyroid therapy as a "sovereign remedy" because the physician knows "the reasons for the brilliant results of its proper application." What was the reason? Bailey and others believed that the thyroid gland emitted a secretion into the bloodstream that was essential to health and wellbeing, and the pathology resulted when the thyroid gland could no longer emit this secretion. Yet, as the final part of this chapter will explain, there was still confusion in the scientific and medical community about how exactly "internal secretions" functioned in the body and blood.

[368] George T. Welch, "Therapeutical Superstition," *Medical Record* 44, no. 2 (July 8, 1893): 35.

What proponents of thyroid therapy had in common with early followers of testicular extracts, however, was the considerable labor and clinical creativity they deployed to determine, experimentally, whether thyroid extracts had value as new medicine. This involved reading published clinical literature, producing extracts in the clinic, conducting methodical tests on patients, and then reporting on the successes and failures for the benefit of the medical community. Thyroid therapy had more support from physicians from the very beginning, as compared to testicular extracts, but to use thyroid extracts successfully in the clinic still meant that doctors had to roll up their sleeves, formulate the drug, and engage in a lengthy process of trial and error in treating ailing patients.

One of America's early proponents of thyroid therapy was Francis P. Kinnicutt, a physician at St. Luke's Hospital and the Presbyterian Hospital in New York.[369] In the fall of 1893, he published a lengthy review of the physiological and clinical literature on thyroid therapy and included as an appendix all the studies that had thus far been published. At his time of writing, sixty-seven cases of myxedema and cretinism, a thyroid disorder in children, had been successfully treated by thyroid drugs, many with "brilliant results."[370] Kinnicutt shared his own experiences of using thyroid extracts in a typical myxedema case: a 49-year-old housewife, referred to him by a Dr. Elizabeth Cushier of New York City, who was first admitted to the wards of St. Luke's in October 1892. Kinnicutt used this case to experiment with a new mode of drug delivery: thyroid feeding. This method involved the doctor "feeding" patients with raw and sometimes cooked thyroid gland—a simple act for the doctor, but an often-repulsive experience for patients, who had to chew and swallow raw animal organs. This new method had been first trialed by British physician, MacKenzie who,

[369] Francis P. Kinnicutt, "Myxoedema--The Functions of the Thyroid Gland, and the Present Method of Treatment of Myxoedema," *The Medical Record* 44, no. 15 (October 7, 1893): 449–55.
[370] Kinnicutt, 450.

out of sheer frustration for not being able to access thyroid injections, asked his patients to try ingesting thyroid tissue by mouth.[371]

Kinnicutt was intrigued both by Murray's new treatment for myxedema and by "feeding" as a new mode of drug delivery.[372] He began his treatment regime by prescribing his patient a sandwich of "minced raw thyroid gland of a sheep," to be eaten once a day for six days. It did not alleviate her symptoms. Next, he dropped the sandwich buns and instead administered spoonfuls of minced thyroid mixed with glycerine, for four days. But this didn't work either. Kinnicutt then doubled the dose of thyroid gland, which finally issued a reaction from his patient—her temperature increased, as did her pulse. He continued this treatment for twenty-three days, and by the end of this period, "the improvement in the patient's condition was very striking."[373] Despite her improved condition, which included reduced swelling and improved speech, Kinnicutt's patient grew to intensely dislike eating raw thyroid glands. In Kinnicutt's words, "the raw gland had, however, become very distasteful, and she could be persuaded only with difficulty to take it." After many months of continued treatment and improved conditions, Kinnicutt shifted his treatment to a more palatable option: drinking thyroid juice mixed with water or milk to spare his patient "digestive disturbance."[374] When she experienced a full recovery, after months of treatment, Kinnicutt was sufficiently

[371] Thyroid injections, like testicular injections, involved a lengthy production process which involved sourcing raw tissue from a slaughterhouse or butcher, grinding this up in the clinic, and then preparing it into a form that was injectable. In this early period, there were wholesalers of thyroid glands (usually physicians who acted as intermediaries between slaughterhouses and the medical community), but I have not found evidence that there were wholesalers of thyroid injections.

[372] Kinnicutt likely could have taken the time to make thyroid injections himself, but he decided to use the feeding method in the interests of science. He explained that physicians had expressed concern that stomach juices would render ineffective any material ingested for therapeutic benefit, and his experiments could help settle this debate. Kinnicutt used Dr. George Crary as his supplier of glands. See M. Allen Starr, "A Contribution to the Subject of Myxoedema: With the Report of Three Cases Treated Successfully by Thyroid Extract," *The Medical Record* 43, no. 23 (June 10, 1893): 705–8.

[373] Kinnicutt, "Myxoedema," 452.

[374] Kinnicutt, 453.

impressed to write that "the future history of the cases of myxoedema and sporadic cretinism…will be watched with interest."[375]

Kinnicutt's experience is typical of doctors in the mid-1890s who were inspired to prescribe thyroid extracts: in this highly experimental phase, doctors tried all manner of approaches to getting thyroid extracts into their myxedematous patients. Some made and used subcutaneous injections from thyroid tissue.[376] Others opted for feeding treatments, which were simple to administer and less time consuming to prepare. When patients baulked at the idea of eating foul tasting preparations, doctors explored more appetizing options. According to *JAMA,* some doctors prepared glands up in hot soup, others "minced and mixed" it with currant jelly, and some ever tried to fry them in hot oil like a sweetbread.[377] Dr. Ethel D. Brown, a New York physician, mixed thyroid extract with whiskey or a beef-tea, which she said helped make the medicine go down.[378] There were also reports coming in from doctors who were using thyroid therapies on non-thyroid related disorders, such as Dr. J. V. Shoemaker from Philadelphia who successfully treated a case of psoriasis with a daily dose of thyroid gland that was "lightly fired" and taken at noon.[379]

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[375] Kinnicutt, 453.

[376] For example, see Starr, "A Contribution to the Subject of Myxoedema: With the Report of Three Cases Treated Successfully by Thyroid Extract."

[377] Anon, "The Treatment of Myxoedema by Thyroid Extract and the Functions of the Thyroid Gland." See also "Thyroid Feeding in Myxedema," *JAMA* 21 (July 29, 1893): 150. For the original article, see J. W. Alexander, "Note on a Case of Myxoedema Occurring in an Insane Patient," *Medical Chronicle: A Monthly Record of the Progress of the Medical Sciences* 18, no. 3 (June 1893): 175–76.

[378] Ethel D. Brown, "A Case of Myxoedema-- Three and a Half Months' Treatment with Thyroid Glands," *The Medical Record* 44, no. 5 (July 29, 1893): 142–43. Patient voices are usually absent from medical literature in the 1890s, but when these sources are read against the grain, we can see how patients shaped how thyroid drugs were prepared by doctors. If a patient refused to chew and swallow on command, doctors were left with little choice but to alter their approach, else face the failure of their clinical trial and treatment regime. This style of patient feedback is particularly evident in Kinnicutt's account, where we can see the doctor making an appetizing cocktail of thyroid "juice" and milk to appease his patient. Doctors knew that a new drug was only useful in a clinical setting if it was both readily and cheaply available, and if patients agreed that it was a drug worth taking.

[379] "Dr. J. V. Shoemaker, of Philadelphia, Read a Paper on Psoriasis with Special Remarks Upon Etiology and Treatment," *JAMA*, June 2, 1894, 846.

There was a very practical reason for why doctors persisted with feedings treatments, variously flavored.[380] Making up a simple thyroid sandwich required much less labor than preparing a hypodermic injection, and it was a good alternative drugging option for time-poor physicians. In reading through physician testimonials from this period, we get a clear sense of exactly how time-consuming the new glandular therapeutic were to produce. In an article submitted to the *Medical Record* in 1893, Dr. M. Allen Starr, a professor at the College of Physicians and Surgeons, explained the process, which he had outsourced to a physician colleague, Dr. Crary.[381]

> The extract was prepared by Dr. Crary by obtaining the glands of the sheep at the slaughter-house, which he did with much difficulty, as it was found that the butchers in killing the sheep, cut the throat of the animal at such a place as to divide these glands [the thyroid] in half, and as in many sheep they are very small, weighing only ten grains, it was necessary to make careful dissection of the two portions of the severed neck in order to find them. The butchers were unaware of their existence, and when requested to furnish the gland uniformly produced the thymus gland, which they term the throat sweetbread.[382]

Starr explained that Crary was ultimately successful in finding "the real thyroid," as confirmed by a contact, Dr. T. Mitchell Prudden, who conducted microscopical examinations of the tissue "to be sure we were dealing with the right gland."

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[380] Crary also opted for the feeding method because "administration by the stomach was considered to be safer than by hypodermic injection." As doctors knew from the days of experimenting with testicular injections, the jab was often followed by abscesses, fever, and sensitivity at the injection site. Crary also gave a third and fourth reason for opting for the feeding method over injection: it was much easier to adjust the drug dose (simply by changing to weight of tissue that was eaten), and patients could administer the drug to themselves at home without the doctors and their syringe. What's more, thyroid feeding worked wonders in his patients. Crary said that patients started to improve after just two weeks of feedings, and after four months, they could be "cured." George W. Crary, "A Case of Myxoedema, Treated with Thyroid Extract by the Stomach, and a Description of the Method of Preparing the Extract," *The Medical Record* 43, no. 24 (June 17, 1893): 739, 742.

[381] See Starr, "A Contribution to the Subject of Myxoedema: With the Report of Three Cases Treated Successfully by Thyroid Extract"; Kinnicutt, "Myxoedema." Dr. George M. Crary was also known to supply Kinnicutt and others with raw thyroid tissue, as Starr explains in this article.

[382] Starr, "A Contribution to the Subject of Myxoedema: With the Report of Three Cases Treated Successfully by Thyroid Extract," 707. See also "The True Sweetbread," *The Medical Record* 43, no. 25 (June 24, 1893): 784. See this article for instruction on how to identify the thymus gland, and suggestions as to why butchers found it hard to identify.

Next came the difficulty of preparing the glands. Starr explained that after dissecting the correct glands, Crary engaged in a lengthy process of washing the fresh tissue, sometimes twice, in "saturated solution of boracic acid" to strip away the fat and remove the gland from its attached vessels and connective tissue. The tissue was then weighed, chopped very finely, and then left to sit for four days in a solution of "German doubly distilled" glycerine. Next came the filtering of the liquid which, if done correctly, would look like a "red sirup."[383]

In a separate publication, Crary himself continued to describe his process, following Starr's account, and included more detail about his intense frustration with the local butcher, who kept giving him thymus glands instead of thyroid glands, and how he was forced to "strike a deal" with the slaughterhouse instead.[384] Cray begroaned the many times he had to wash his hands throughout the process of handling the fresh tissue, and how he had to repeatedly sterilize his instruments to ensure aseptic practice. He emphasized the importance of making the thyroid extract within twelve hours of the animal being killed—else the glands would lose their physiological activity—and he appeared stressed about this tight manufacturing schedule. It was a schedule that he described doggedly, almost dourly, as if wondering how he, a physician, had wound up spending his days fussing over animal meat.

There was another real barrier to making a good glandular extract, according to Cray, and this had to do with standardization. Not all thyroid glands were made equal, he explained. Some were big, some were small, and some were diseased, being full of cysts "with broken down cheesy contents." To achieve a high-quality extract, Crary had to select the right type of gland—free from cysts and of the right weight—but this could be a time-consuming process. Of the 263 glands that he had worked with so far, the lightest gland he had found

[383] Starr, "A Contribution to the Subject of Myxoedema: With the Report of Three Cases Treated Successfully by Thyroid Extract," 707–8.
[384] Crary, "A Case of Myxoedema."

was just ten grains in weight, and the heaviest was 720 grains.[385] Most weighed about eighty-four grains. He was troubled by this variability: "The glands varying so enormously in their weight, the number used is not a sufficiently accurate basis to go upon in regulating the strength of the extract, and hence I have fixed upon an arbitrary standard of twenty-four grains of gland to one drachm of glycerine."[386]

After stepping through Crary's account of the painstaking process of making thyroid injections, it is no wonder why doctors opted for treatment-by-feeding. Working physicians were confronted with limited time and resources, and feeding regimes were by far the easiest way of getting fresh thyroid into the bodies of myxedematous patients. There was still no consensus on exactly how this new drug should be delivered into the body—In a burger? In a soup? With whiskey? —and physicians still had big questions about dosage and treatment protocols. In lieu of a clear clinical directive, doctors made dose adjustments on the fly, treated for as long as they needed to, and consulted their colleagues for support.

Thus, while medical periodical literature suggests that testicular injections had retreated almost into obscurity by the mid-1890s in America, it also reveals that physicians who worked with thyroid glands adopted from the testicular craze a culture of making their own glandular drugs and testing it in the clinic.[387] It was a difficult and messy business, as we learned from Crary, and supply of the medicine was sometimes limited, as reported by Dr. Rogers, a Superintendent of Northern Indiana Hospital, who complained that their treatment

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[385] Crary, 742.

[386] Despite his drug production difficulties, Crary ultimately triumphed. He produced thyroid medication that worked. Submitting his results to the New York Academy of Medicine, and to the *Medical Record*, he claimed that his results "add[ed] [their] weight to the testimony already adduced, especially in English, as to the efficacy of the administration of the thyroid glands of the sheep in the treatment of myxoedema…" See George H. Crary, "Myxoedema, Acquired and Congenital, and the Use of Thyroid Extracts," *The Medical Record* 44, no. 23 (December 2, 1893): 725; Crary, "A Case of Myxoedema," 739.

[387] Before the year of 1895, there are only rare reports from doctors who opted for commercial preparations over physician-prepared dugs.

plans were thwarted because they could not "secure a supply" of thyroid medicine. [388] But this did not deter doctors from their mission to make new and effective drugs for patients in need, even if their first attempts did not yield promising results.

Sifting through physicians' grisly descriptions of preparing glandular drugs from raw animal materials begs an obvious question: why did physicians become involved in the messy business of drug production at all? Why not buy their drugs from suppliers or go to the commercial marketplace?[389] Doctors' hands-on approach to drug production can be partly explained by the newness of these drugs. So called "biological" drugs made from animal products, such as Brown-Séquardian extracts and Pasteurian vaccines, were a new class of scientific medicine in the late 1880s and early 1890s, and physicians could not simply source them from the corner-store apothecary, at least not in the very early years while they were still in development.[390] When commercial glandular preparations did start to become available on the medical marketplace in the early 1890s, physicians still opted for their own preparations because they lacked trust in "patent" drugs. As many historians have noted,

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[388] "A New Discovery in Medicine: An Indianian Secures a Preparation That Greatly Aids Cataleptics," *Charleston Tri-Weekly Courier*, March 25, 1896. Originally published in *Chicago Times Herald*. Rogers had been using a preparation made from "the thyroid glands of sheep." Presumably, Rogers was trying to "secure a supply" of thyroid medicine because he did not want to make it himself. Possibly, Rogers was having difficulty accessing raw materials from the slaughterhouse, or elsewhere. Dr. Oscar Coleman de Wolf, ex-commissioner of health of Chicago, suggested that this might be a barrier to entry for some physicians, noting that his own "extensive and careful experiments" with glandular extracts were aided by his access to the Chicago stockyards. See "Dr. Todd and the 'Elixir of Life': His Interesting Experiments with the New Brown-Séquard Discovery," *Chicago Daily Tribune*, August 13, 1889. (Note that Dr. De Wolf soared to national importance through his revolutionary reforms of the meatpacking industry). Dr. B. Sherwood Dunn of Los Angeles, in his writings on physicians' experiments with ovarian extracts, also made mention of the "difficulty of obtaining the fresh organ." This led physicians to prefer powdered forms of ovarian extract, presumably bought on the commercial marketplace. See B. Sherwood Dunn, "Conservation of the Ovary," *The American Journal of Obstetrics and Diseases in Women and Children* 36 (1897): 571–75.

[389] The next chapter shows that this did eventually happen: over the course of the 1890s, doctors did start to eschew physician-prepared glandular drugs in favor of commercial preparations. But in the period between 1889 and 1894, commercial preparations were only rarely mentioned in physicians' reports. The clear default in the early 1890s was for physicians to simply make the drug themselves.

[390] For a history of biological drugs, see Schwerin, Stoff, and Wahrig, *Biologics*.I make this claim with a caveat. Homeopathic remedies were available, as Dr. Conan pointed out to Brown-Séquard in 1889 (see Chapter 1). Trade ephemera also reveals that desiccated thyroid extract was available for purchase from some commercial manufacturers before Brown-Séquard's movement that started in 1889. But Brown-Séquardian extracts were marketed by him and his followers, and understood by doctors, as materially different to extant preparations. As Brown-Séquard argued, the difference lay in how they were prepared, and the physiological theory that informed their use.

American doctors generally suspected commercial preparations for being fraudulent and possibly dangerous in the 1890s.[391] There was possibly even more reason to be skeptical of commercial glandular reparations, as druggists and pharmacists were accustomed to creating drugs from plants, not animal products, and might make amateur errors. It thus made sense for doctors to continue producing these drugs while the field was so new, especially given that Brown-Séquard's recipe was, in theory, simple enough to follow.

Doctors' willingness to make Brown-Séquardian drugs can also be explained by the highly experimental culture in which physicians found themselves working vis-à-vis glandular therapies. By preparing glandular drugs themselves, doctors had ultimate control over drug design and dosage, which was important when it came to patient testing. If a patient responded badly to a drug, a doctor could quickly adjust it and try a different approach. If a patient responded well, the doctor could strengthen the dose in the attempt to make the effect even stronger. Thus, having control over drug production meant that doctors could experiment quickly and liberally with animal tissues and build clinical knowledge about glands. As the next section shows, this culture of experimentation only intensified in the second half of the 1890s, as more glands and tissues became drug candidates.

The Theory and Practice of Using Animal Extracts

The arrival of thyroid therapies had two key effects on the bourgeoning field of glandular therapeutics. Firstly, it functioned as a wrench that pried open the gate to broad experimentation with animal glands in the orthodox medical community—a gate that had been held firmly shut for those who were preoccupied by the negative reaction to Brown-

[391] Historians of pharmacy, especially Joseph Gabriel and Jonathan Liebenau, describe the orthodox doctors' aversion to "patent" medicines in the nineteenth century, and how their attitudes slowly changed toward the turn of twentieth century. Gabriel, *Medical Monopoly*; Liebenau, *Medical Science and Medical Industry*. The transformation of American doctors' attitudes toward commercial glandular preparations will be addressed at length in the next chapter.

Séquard's testicular extracts.[392] Drugs made from animal organs and glands started to proliferate in the middle of the 1890s, as evidenced by entries in medical journals that were sometimes listed under index terms "animal extracts," "organ extracts" or "animal juices."

Secondly, and in response to this proliferating experimental and clinical field, thyroid therapies more clearly established the boundaries of orthodox practice with respect to the production and prescription of animal organs and tissues. For example, medical periodical literature reveals that some doctors who were convinced of the merits of thyroid therapy remained thoroughly *unconvinced* of the merits of any other animal extract treatment, such as the use of muscle extract for muscular dystrophy and the use of lung tissue to treat pulmonary disorders.[393] Conservative thyroid-therapy proponents did all they could to shore up the legitimacy of their own use of thyroid therapy, while delegitimizing the use of any other animal extract, which they claimed had no place in clinical practice.

There is no better case to demonstrate this form of professional gatekeeping around the "right" and "wrong" type of animal extracts than the controversy of Dr. William A. Hammond, the highly celebrated ex-Surgeon General of the Civil War who rebranded himself in the early 1890s as glandular extract entrepreneur. As historian Bonnie Blustein explains, Hammond became embroiled in a terrific scandal in 1893 when he was exposed for first establishing a for-profit company that sold myriad organ extracts, including "cerebrine" (brain extracts) and "cardine" (heart extracts), and then refusing to admit fault when a

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[392] See description of thyroid therapies in "Science & Discovery: Antitoxins," *Weekly Rock Mountain News*, July 15, 1897. Not mentioning Brown-Séquard or testicles at all, this article states: "Another new method of medication, which has come into use in the last few years, is the introduction into the system of certain animal juices and extracts of various organs to supply the want to similar substances, the manufacture of which is suppressed or diminished by disease. The pioneer in this therapeutic advance was Dr. George Murray of Newcastle, who has just proved that myxoedema and cretinism…can be cured by supplying the economy with extract of the corresponding organic of a sheep. The success of this treatment has led to what the profane might be disposed to call a "boom" in animal extracts: the brain, the heart, the lung, the kidney, the spleen, the pancreas, and every gland and nearly every tissue in the body…"

[393] See critical commentary about the "i-n-e" compounds, which is an allusion to W. A. Hammond's extracts. William Krauss, "What the Newer Therapeutic Procedures Have Done for Neurology," *Boston Medical and Surgical Journal* 11, no. 23 (December 11, 1893): 711–15.

committee of self-appointed investigators discovered that these preparations were completely inert.[394] Orthodox physicians were appalled by Hammond's conduct, referring to him as the "Great Retired"—a derogatory term that mocked his advanced age and fall from grace in respectable society. Not only did they oppose his overtly commercial intentions, doctors also objected to his rapid development of diverse extracts—from the stomach, bone marrow, ovaries, and pancreas—without any apparent physiological or experimental rationale. Solis-Cohen publicly reprimanded Hammond for bringing to glandular therapeutics its "greatest notoriety" yet.[395] He also set out to explain, with physiological reasoning, why "cerebrine" and "cardine" were so very different from thyroid glands.[396]

> Between such organs as, for example, the brain and the thyroid gland, there are many and great differences. One of these differences is all-important: The thyroid gland is a secretory organ; the brain is not. Without entering into a discussion of the exact nature of the process, concerning which the evidence is not clear, it is sufficient to know that clinical and experimental observations are at one in demonstrating that the thyroid gland manufactures some substance which, but its function in the economy, prevents the occurrence of the symptom complex termed myxedema or cachexia strumipriva…the brain, so far as we know, secretes nothing physical... consequently, there is nothing in the whole nosology which, on theoretic grounds, the administration of brain extract could be expected to remedy. Similarly, the heart, so far as we know, secretes nothing...[397]

Following his own advice and physiological logic, Solis-Cohen built up a portfolio of experiments starting from 1893 with glands and tissues that were known to issue secretions, such as thyroid glands and adrenal glands, and in turn rejected the brain and heart as appropriate subjects of investigation because they "secret[e] nothing." He and the Polyclinic continued to criticize Hammond. An unsigned article from the *Philadelphia Polyclinic* aptly

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[394] See Blustein, *Preserve Your Love for Science*, 209–11; G. Archie Stockwell, "Correspondence: 'Cerebrine' and the Veracity of William A. Hammond," *The Medical Age* 11, no. 24 (December 26, 1893): 747–49; Anon, "A Very Pretty Quarrel," *Bulletin of Pharmacy* 7, no. 8 (August 1893): 378; Anon, "Wonders Never Cease," *The Medical Age* 11, no. 14 (July 25, 1893): 434.
[395] Solis-Cohen, "The Therapeutic Properties of Animal Extracts," November 1893.
[396] Solis-Cohen.
[397] Solomon Solis-Cohen, "Medical Progress: The Uses of 'Organic Extracts,'" *The Medical Age* 12, no. 1 (January 10, 1894). This excerpt is just one example of the kind of commentary that appeared in medical journals in the year 1894, in the wake of the Hammond controversy.

captures a stance that was shared by proponents of the "secretions-only" approach to therapy. It read: "That any sane physician could seriously advance the idea that diseases of the heart are to be treated with extract of cardiac muscle, disease of the brain to be treated with extract of brain substance, disease of the kidney to be treated with extract of kidney substance, taxes one's credulity to the utmost."[398] Thyroid drugs gave champions of orthodox medicine a cause to rally behind. To such champions, it was the first piece of evidence that there was a therapeutic future in animal organs and glands, and they did not want drug-happy individuals and companies getting in the way of real, "rational" medicine.

But what was "rational" medicine? For some pundits, "rational" meant having a physiological reason for using a particular glandular drug to treat a particular disease and having experimental evidence to back it up. An (unnamed) medical commentator explained what this meant in an article published with the *Boston Medical & Surgical Journal* in 1895. According to them, thyroid therapy was "rational" because it treated a deficiency of a thyroid secretion in the body, as in myxedema. The commentator went on to explain that:

> For most of the glands, however, this [secretion-pathology connection] is a mere hypothesis, and we need more experimental evidence before employing these extracts, of whose composition and action we know nothing, in the treatment of disease. Preparations from the non-glandular tissues, the brain, the [spinal] cord, the heart, and the muscles, are different. There is no evidence that they furnish any necessary substance to the economy, and the use of them in therapeutics has as yet not even a rational hypothesis to support it.[399]

Yet, despite what this commentator was suggesting about the "rationality" of using thyroid therapy vis-à-vis other glandular drugs, given knowledge of the thyroid "secretion" and its connection to thyroid-related diseases, the reality was a little more complicated. In the 1890s, there was not yet consensus among physiologists and physicians about how internal secretions functioned in the body. As historians Swazey and Reed note, there were in fact two

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[398] Anon, "Organo-Therapy," *The Philadelphia Polyclinic* 4, no. 40 (October 1895): 409–10.
[399] "Animal Extracts," *Boston Medical and Surgical Journal* 132, no. 3 (January 7, 1895): 66–67.

schools of thought in the 1890s when it came "disease and the ductless glands."[400] We have already been introduced to one major school of thought through the views of Solis-Cohen, who subscribed to the "internal secretions" theory of glands. In 1894 he argued that the thyroid emitted a specific "[internal] secretion" into the blood, that diseases such as myxedema were caused by the "under-" secretion of this gland, and that injections or feedings of healthy thyroid extract could ameliorate this disease by replacing the specific secretion that was lacking. But there was a second compelling theory for how glands and organs functioned in the body, and it was equally as popular among American physicians in the 1890s. This second camp held that organs and glands functioned by neutralizing toxins or "poisons" that circulated naturally within the body—"auto-toxins"—as well as toxins that were introduced by an infection with a pathogen (such as bacteria or a virus). According to this theory, which has been described by some as "autointoxication,"[401] a disease state is caused by a breakdown of the antitoxic functions of an organ or gland, which would result in the buildup of toxins in the body—its "auto-intoxication." Proponents of this theory hypothesized that autointoxication, or "toxaemic conditions,"[402] could be ameliorated by treatments with the extracts of healthy organs and glands associated with a condition, such as

[400] Swazey and Reeds, "Today's Medicine, Tomorrow's Science." "Disease and the Ductless Glands" is the name of a particularly revealing chapter in Swazey and Reed's book, as it details the state of scientific and medical opinion on glands in the 1890s and beyond.

[401] For a more detailed description of "auto-intoxication," see parts of Christiane Sinding, "Clinical Research and Basic Science: The Development of the Concept of End-Organ Resistance to a Hormone," *Journal of the History of Medicine and Allied Sciences* 45, no. 2 (1990): 213, 214, 230. Sinding also includes an interesting comment on p. 200 about the conceptual linkages that formed between germ theory, immunology and endocrinology. See also Micaela Sullivan-Fowler, "Doubtful Theories, Drastic Therapies: Autointoxication and Faddism in the Late Nineteenth and Early Twentieth Centuries," *Journal of the History of Medicine and Allied Sciences* 50, no. 3 (1995): 364–90, https://doi.org/10.1093/jhmas/50.3.364. For a related discussion about autoimmunity and "auto-antibodies," see Warwick Anderson and Ian R. Mackay, "Immunological Thought Styles," in *Intolerant Bodies: A Short History of Autoimmunity* (Baltimore: Johns Hopkins University Press, 2014).

[402] This was Charles L. Dana's term. See Charles L. Dana, "Modern Pathology and the Pathology of Nervous Diseases, With Some Therapeutical Deductions and Experiments with Organic Extracts," *Boston Medical and Surgical Journal* 123, no. 20 (May 18, 1893): 490.

injections of healthy thyroid extract for the treatment of myxedema, which was known to be a thyroid-related disorder.[403]

The key tension between these two theories came down to disagreements over specificity. Doctors who subscribed to the internal-secretions theory were more likely to insist that thyroid extract, for example, should only be used for the treatment of myxedema, because it was known to be specifically linked to that disease state. Proponents of the auto-intoxication theory were more likely to view glands, especially the thyroid and adrenals, as having broad-spectrum antitoxic powers. This reasoning led to thyroid gland extracts in the 1890s being used for all manner of maladies, including lupus, psoriasis, diabetes and obesity.[404] As the next chapter will show, adrenal gland extracts were also used as a broad-spectrum drug, both for conditions that were specifically related to the glands (such as Addison's disease) and for diseases that were not, such as asthma and hay fever.

With this context, the definition of "rational" put forward by the commentator in the *Boston Medical & Surgical Journal* (*BMSJ*) takes on a different light. Thyroid therapy was preferred by some doctors, such as this commentator, because it made sense within the context of the internal secretions theory to which they subscribed, and because there was a large body of empirical evidence, gathered through experimentation, to support its use in the clinic. Under this worldview, it would be "irrational" to use other glands and tissues of the body in the clinic, or even to experiment with them, as they were known to give off internal secretions into the blood and there was little empirical evidence of their clinical utility.

Yet, other American doctors who leaned more toward the antitoxin theory of glands had a different understanding of what it meant to experiment "rationally." This was the case

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[403] Dana, 490.
[404] For example, see A. W. Sherman, "Thyroid Feeding in Obesity," *JAMA* 34 (March 24, 1900): 728–30; Theodore Diller, "Thyroid Feeding in the Treatment of Insanity.--Report of Ten Cases," *The Philadelphia Polyclinic* 5, no. 39 (September 1896): 381–84.

with Charles L. Dana, a professor of Nervous and Mental Disease at the New York Post-Graduate Medical School, who used brain extracts to treat paralysis, testicular extracts to treat epilepsy, and thyroid extracts to treat dementia. He knew his work would attract criticism from the kinds of doctors who only recommended the use of thyroid tissue for thyroid-related disorders and, in anticipating their feedback, he wrote this defense:

> I wish, in conclusion, to say with regard to this particular form of treatment [using organic extracts], that I have referred to it with some hesitation, owing to the decidedly bad odor attached to these methods…. Nevertheless, I am so firm a believer in the rationality of this method of therapeutics, or in this line of therapeutical investigations, that I am willing to brave some misunderstandings in connection with the use of such preparations. …the remarkable results obtained from the use of the thyroid gland in myxoedema is of itself abundant justification of this position. There is not reason why we should not be able to find some other glandular product which will have a beneficial effect in other toxaemic conditions.[405]

Dana's liberal experimentation with various organic extracts was rational, therefore, under the theory to which he ascribed. He also brought up another fine point that poked a hole in the logic of those who advocated for much more constrained experimentation: if one did not try out other glandular tissues in the clinic, then how would knowledge advance about them?

Judging by the ever-increasing volume of journal articles that were published about a wide variety of glandular treatments in the late 1890s, it seems that many more doctors sided with Dana's version of "rational" experimentation than the more conservative stance. For example, the 1896 and 1897 editions of *JAMA* are thick with articles and editorials about new drugs developed from all manner of animal tissues; on average, twenty articles about glandular therapeutics appear in each issue of the journal, which was up from a count of zero in the Brown-Séquard days. These articles were written by general practitioners, such as Dr. J. F. Jenkins of Tucumseh, Michigan, who prescribed the "uncooked adrenals of a sheep" to an Addisonian patient who "took it in the form of sandwiches."[406] And specialists, such as

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[405] Dana, "Modern Pathology and the Pathology of Nervous Diseases."
[406] J. F. Jenkins, "Some of Our Late Therapeutic Resources," *JAMA* 26 (January 4, 1896): 25–27. Given his location in Tucumseh, I have surmised that Jenkins is a country practitioner.

neurologist Dr. F. S. Pearce of Philadelphia who reported on his use of testicular injections for the treatment of both men and women suffering from locomotor ataxia, paralysis and neurasthenia.[407] It also included reports from medical professors at universities, such as Dr. William Osler of Johns Hopkins University, who shared his unsuccessful attempt at employing adrenal gland therapy in Addison's disease,[408] and Professor William E. Quine, of Chicago's College of Physicians and Surgeons, who reported on the uses of bone marrow extract for pernicious anemia, leukemia and "kindred disorders."[409]

Gynecologists and child disease specialists also took great interest in Brown-Séquardian remedies in the second half of the 1890s.[410] Reports about thyroid therapies appeared frequently after 1893, especially for the treatment of myxoedema in women and cretinism in children.[411] From 1896, reports started to emerge from doctors who had begun to use thyroid therapy more liberally—that is, for diseases other than myxoedema and cretinism—as well as a wide array of other animal extracts. For example, from 1896, it was common to see reports about thyroid therapy being employed to treat amenorrhea, and mammary gland extracts and parotid extracts being used as treatments for psoriasis and ovarian "troubles." [412] In 1896 and 1897, we also see the first reports of doctors regularly

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[407] F. S. Pearce, "A Clinical Report on the Use of Testicular Fluid Injections," *JAMA* 26 (June 13, 1896): 1175. He was careful to state: "[this report] is not entended [sic] to laud the remedy, but to present the clinical evidence of its limited usefulness in disease."

[408] William Osler, "A Case of Addison's Disease Treated with Suprarenal Extract; Death," *JAMA* 28 (March 6, 1897): 466. Osler's experimentation led to fatality in a patient, but it did not discourage him from further experimentation. To make his concoctions, he used the adrenal glands of pigs which he "thoroughly mashed with pestle and mortar" and then filtered to achieve "a rather cloudy, reddish, thick fluid [that had a] meat-like odor."

[409] William E. Quine, "Chairman's Address: The Remedial Application of Bone Marrow," *JAMA* 26 (May 23, 1896): 1012–14.

[410] *The American Journal of Obstetrics and Diseases in Women and Children*, which had not mentioned Brown-Séquard or his work in the early 1890s, began reporting on the success of thyroid therapies starting in 1896. To a lesser extent, a similar pattern can be observed in the reporting habits of American neurologists and alienists, who spent the first half of the 1890s not speaking very much about Brown-Séquard's work on glands, but then giving much more attention to animal extract therapies in the post-thyroid-therapy era.

[411] Cretinism was a thyroid-related disorder in children, resulting in delayed physical and cognitive development.

[412] For example, see "Brief of Current Literature," *The American Journal of Obstetrics and Diseases in Women and Children* 34 (1896): 430. See also John B. Shober, "The Use of Mammary Gland in the Treatment of

using ovarian extracts to treat menopause and ovarian deficiencies, broadly construed.[413] Even Brown-Séquard's name and work, which was markedly absent from *The American Journal of Obstetrics and Diseases in Women and Children* in the early 1890s, was invoked in a lengthy 1896 article written by David Tod Gilliam, Professor of Gynecology at the Starling Medical College in Columbus, Ohio. Gilliam, who wrote on the connections between ovaries and epilepsy in women, said that he agreed with Brown-Séquard that there was a connection between the "mind" and the "sexual glands," and even admitted that "I do not believe that Brown-Séquard was altogether dreaming when he promulgated the virtues of the seminal fluid."[414] At the 1897 meeting of the Association of Obstetricians and Gynecologists, Dr. B. Sherwood Dunn of Los Angeles also felt bold enough to throw his support behind Brown-Séquard, stating that he had been for some time "favorably disposed" to Brown-Séquard's hypothesis of glandular secretion, and that anyone who had lingering skepticism ought to take note of certain experiments made with "ovarian substance," which were given to patients who either lost ovarian function or were suffering from "troubles" associated with the ovaries.[415] In response to Dunn's paper, Dr. Albert Goldspohn of Chicago said that "Whatever the merits of the Brown-Séquard treatment may have been in the past, the glandular theory had much to speak for it clinically."[416]

The proliferation of experiments on animal extracts even had some of the gatekeepers themselves, including Solis-Cohen, becoming more relaxed about their narrow definitions of "rational" experimentation. In 1897, he described the remarkable results he had observed by

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Fibroids of the Uterus, and of Parotid Gland for Ovarian Disease," *The American Journal of Obstetrics and Diseases in Women and Children* 38 (1898): 352–55.

[413] See "The Treatment of the Disturbances of the Menopause," *The American Journal of Obstetrics and Diseases in Women and Children* 34 (1896): 302–3. See also "Vaginal Hysterectomy," *The American Journal of Obstetrics and Diseases in Women and Children* 37 (1898): 693.

[414] David Todd Gilliam, "Oöphorectomy for the Insanity and Epilepsy of the Female: A Plea for Its More General Adoption," *The American Journal of Obstetrics and Diseases in Women and Children* 34 (1896): 555–61.

[415] Dunn, "Conservation of the Ovary."

[416] See note about Dr. Albert Goldspohn in Dunn.

treating exophthalmic goiter and ataxia with thymus gland—an approach he could have easily dismissed, for there was nothing in the "nosology" to suggest "on theoretic grounds" that the secretions of the thymus were related to either of these conditions.[417] What motivated his interest in thymus gland was a report by a Dr. David Owens of Manchester, who had accidentally treated his goiter patients with feedings of thymus gland, not thyroid gland, and had observed "wonderful improvements." The mix-up was blamed on the local butcher, who sometimes confused these two organs when making his cuts—they were similar-looking and similar-sounding organs, and both were found in the neck of the carcass. This was apparently enough for Solis-Cohen to launch an experimental investigation to assess the merits of thymus gland treatment in various disorders which, he found, worked well enough in exophthalmic goiter.[418]

Why did broad experimentation with the new glandular drugs prevail in the medical community amid regular critique, gatekeeping and, if we consider the beginnings of the movement, unwanted sensation? I suggest that liberal experimentation was in fact fueled by the lack of consensus. The lack certainty about the therapeutic value of the glands and tissues of the body, and the apparent openness of the field—especially after the arrival of thyroid therapy—were ideal conditions for entrepreneurial doctors to make bold decisions both in the types of glands they developed into drugs and how they used them in the clinic. Another key factor driving doctors to experiment liberally was the uncertainty about how exactly glands functioned at a physiological level. In the absence of concrete physiological principles, doctors gave themselves creative license to search for new drug candidates in unusual places,

[417] Exophthalmic goiter was characterized by swelling of the neck (caused by an enlarged thyroid) and protruding eyes. See J. W. Thompson, "Exophthalmic Goitre, or Graves' Disease," *JAMA* 22 (1885): 597–98. Ataxia was characterized by poor muscle control, or "feebleness in the co-ordinating mechanisms" to use Solis-Cohen's definition in Solomon Solis-Cohen, "Vasomotor Ataxia: A Contribution to the Subject of Idiosyncrasies," *The American Journal of the Medical Sciences* 2 (1894): 130–46.
[418] Solomon Solis-Cohen, "The Treatment of Exophthalmic Goiter and Other Vasomotor Ataxis with Preparations of the Thymus Gland and of the Adrenals," *JAMA*, July 10, 1897, 65–67.

even if their reasoning was shaky. If brain tissue worked for epilepsy, why not lung tissue for "pulmonary affectations"?[419]

The absence of a clear physiological doctrine was also helpful in defending one's work from attack; physicians sometimes employed explanations from both schools of thought, as it suited their experimental program. Solis-Cohen himself used this strategy in his paper on the therapeutic utility of thymus extracts and adrenal extracts. He concluded his paper by suggesting that the physiological reasons for their action are unclear but that "I do believe that they are competent in the one case—thymus—chiefly by an antitoxic action, to counteract the exciting influences, and in the other case—adrenal—chiefly by opposing action upon the circulation to neutralize the effect of those influences."[420] Solis-Cohen was an arch defender of the "secretions" theory and all the physiological specificity that it implied, yet in this instance he deployed the much more general auto-intoxication theory to explain his use of thymus extracts and adrenal extracts. Solis-Cohen even seems to have taken the theoretical no-man's-land as an excuse for simply doing the experimental work that he wanted to do, without apology. Privileging liberal experimentation in a moment of theoretical uncertainty might seem like a hypocritical position for Solis-Cohen to adopt if one considers his criticism of Hammond earlier in the decade, but it was the path that allowed him to continue working on the thymus gland and adrenal gland as new and untested drug candidates. To wait for a physiological doctrine to solidify in the medical community would mean not getting potentially useful treatments into the clinic.

When more concrete answers were called for, doctors turned to each other for counsel. Such discussion was particularly evident at conferences and proceedings of medical societies, where doctors came together to share results, to review the field, and to ask hard

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[419] Anon, "The Latest in Organ Therapeutics: Extract of Lung Tissue," *The Medical Age* 28 (February 20, 1897): 368.
[420] Solis-Cohen, "The Treatment of Exophthalmic Goiter," 67.

questions. This was the case at the 1894 meeting of the American Neurological Association, where neurologists questioned if there really was a rational basis for thyroid treatment in neurological conditions such as dementia.[421] Such dialogue was also apparent at the 1896 meeting of the New York Neurological Society,[422] where a robust conversation took place concerning the merits of thyroid treatment for various kinds of thyroid related disease, including myxedema, goiter, cretinism, and Basedow's disease. Over a dozen doctors from around the country, who appeared to be advocates of the "secretion" hypothesis, attempted to distinguish between diseases that were caused by over-secretion of the thyroid gland and those caused by under-secretion. This question had come to the fore because of the truly variable results in treatments of thyroid-related disorders. Initially, it was assumed that feedings or injections of thyroid extracts would be a one-size-fits-all drug, as far as thyroid disorders were concerned. But Basedow's disease and some cases of goiter seemed to not respond at all to thyroid treatments. Here, a lack of response led some members of the community to suggest a theory of over-secretion—perhaps treatments didn't work because in some cases disease was caused by *too much* thyroid secretion in the bloodstream.

To have these kinds of discussions, clinicians collected and shared data with each other, which were pieced together from medical periodicals, anecdotes, and personal experience in the clinic. They had to trust the knowledge that was built in the clinic and to use medical reasoning to determine the value of the treatments they were employing. As one commentator put it in 1896, developing new knowledge about glands in the late 1890s could be "accomplished by concerted efforts, in experimental research and the clinic." But importantly, he continued:

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[421] "American Neurological Association: Twentieth Annual Meeting, Washington, D.C., May 30, 21 and June 1, 1894," *Boston Medical and Surgical Journal* 131, no. 13 (n.d.): 318–21.
[422] "New York Neurological Society, Stated Meeting," *Boston Medical and Surgical Journal* 134, no. 22 (n.d.): 540–43.

> Separat[ing] the wheat from the chaff is not by way of the laboratory alone. Physiologic chemistry and experimental physiology may separate the secretions of the organs into their components and determine their toxic processes, but, after all, it is the practicing physician who applies the facts they discover. He must be neither too skeptical nor too confiding, but remember what Dedalus said when he entrusted his wings to his son: "In medico tutissimus ibis."[423] (you will go most safely by the middle course.")

By 1896, American doctors were well accustomed to going by the "middle course," and building their own picture about how glands and organs functioned in the body. Without recourse to physiological doctrine, it was left to them to make a new clinical field and to build knowledge about a new class of drugs.

Conclusion: Becoming Mainstream

This chapter began with a key question: how did Brown-Séquardian therapeutics shift from the margins to the mainstream of medical practice in America, from 1889 to 1900? The sources that I have consulted reveal that doctors were at the heart of this change. Their testimony over the course of the decade points to a gradually shifting attitude toward the utility of drugs made from animal glands and organs. What began as a stunning, scandalous, and laughable idea at the start of the decade looked much more like cutting-edge medical science by the end of the decade. It is true that there were many failed therapies, including Brown-Séquard's testicular injections and Hammond's various extracts, and doctors had by no means declared by the turn of the century that animal extract therapy was an unqualified success in the clinic. It would take much longer for this kind of certainty to coalesce about the therapeutic value of glands and tissues of the body as a new class of medicines. But the 1890s did see some veritable medical breakthroughs with animal extracts; thyroid therapy was widely regarded as an exciting realization of what the method of Brown-Séquard could yield, and adrenal gland extracts were also emerging as the next most promising drug candidate, as

[423] F. Kraus, "The Present Status of Animal Therapeutics," *JAMA* 26 (March 14, 1896): 528–32.

the next chapter will fully elaborate. Beyond these two therapies, there was a growing acceptance by 1900, among even the most skeptical of American doctors, that there might just be something of value in Brown-Séquard's original idea.

What occasioned these slowly turning tides of medical opinion in America? This chapter has argued that it came down to the work that doctors did in the clinic. Doctors who toiled with glands and tissues in the 1890s worked hard to build something from nothing. They identified new drug candidates, recruited patients, and treated them, sometimes with revolting products. To be a practitioner who prescribed these drugs in the 1890s also meant bearing the responsibility of drug production. Sometimes this meant a trip to the slaughterhouse, sometimes to the butcher, and sometimes to a supplier, like Dr. Crary, who took it upon himself to act as an intermediary between carcass and clinic.

Indeed, and despite being chastised by Brown-Séquard in the early 1890s, American doctors had done exactly what Brown-Séquard had asked of them. They used a critical and experimental gaze to build new knowledge about the glands and tissues of the body. Through their work, they identified new drug candidates, and found new confidence in the utility of some animal extracts in the clinic. What's more, American doctors who wrote into medical periodicals shared Brown-Séquard's skepticism of commercial drugs on the medical marketplace—at least before 1895. They instead used his recipe and made glandular drugs by hand as Brown-Séquard had instructed.

As the next chapter will show, however, the sands were shifting in America. The manufacturing problem wrestled with by Brown-Séquard and d'Arsonval came to bother American physicians who wanted to use glandular drugs in the clinic. Making glandular drugs by hand was becoming a tiresome and thankless task, for doctors did not have the time or resources to drive out to the slaughterhouse, crush up raw tissues, and drip-drip the fluid mixtures through a paper filter. But what were they to do? Who else would produce glandular

drugs, if not physicians themselves? The next chapter will show how the American medical community settled on a solution in the first decade of the twentieth century that might have made Brown-Séquard turn in his grave: the drug company, and not physicians themselves, would become the new producers of glandular drugs.

Chapter 4: The Rise of the Company: How American Endocrinology Became a Pharmaceutical Industry, 1893-1910

When Brown-Séquard's glandular therapy movement spread from Paris to the United States in the early 1890s, and American physicians began using glandular products for the first time in the clinic, drug companies were strikingly absent from physician conversations about how to produce this new line of drugs. As I showed in the previous chapter, the burden of drug manufacturing largely fell on the shoulders of practicing physicians, as Brown-Séquard had divined it. They first sourced raw glands and tissues from slaughterhouses, butchers, or physician-suppliers. Next, they ground them up in mortar-and-pestles, mixed them with a sterile liquid (usually glycerin), and passed them through a simple filtration device, which left a rosy-pink liquid extract. Finally, doctors would inject this liquid into their patients, and hope it would ameliorate or even cure disease. Doctors who felt lazy or time-poor would attempt to source pre-prepared products from physician-friends. If that failed, they sometimes asked their patients to simply eat raw and unprocessed glands, which could be placed between sandwich buns, or prepared in a soup or with whisky, to help make the drug more palatable.

By 1910, however, physician-made glandular products had been almost completely replaced by commercial drugs. Doctors had stopped preparing thyroid gland burgers and instead prescribed thyroid pills, which they bought directly from pharmaceutical companies in bottles of 100 or 500 tablets. Suprarenal products came to be prescribed as "desiccated" powders, crushed and dried in huge industrial vats at drug companies, or purified and diluted by chemists in a solution of liquid "Adrenalin." Even the less commonly prescribed glandular products, such as those developed from the thymus, ovaries, and pituitary gland, were almost always administered by doctors as powdered extracts sourced from manufacturing firms.

The medical community's transition to using commercial glandular products occurred progressively between about 1900 and 1910. To be sure, some doctors began

tentatively turning to the market in 1893, when the first thyroid gland tablets were rolled out by Michigan-based Parke, Davis & Co. and other companies,[424] but most doctors used raw extracts that they had prepared themselves or sourced from colleagues. Commercial drugs gained popularity by the end of the 1890s, as more glandular products came on the market, but it was not uncommon to still see physicians writing into medical journals about their practice of filtering and sterilizing raw animal tissue. An obvious tipping point occurred in the early 1900s, after the release of Parke, Davis & Co.'s landmark "Adrenalin" solution, which is a phenomenon that will be given close attention in this chapter. By 1910, doctors rarely prepared glandular products themselves in clinic, or liaised with butchers or slaughterhouses; the manufacturing house had become their go-to producer and wholesaler of drugs.[425]

Curiously, physicians turned to the market for glandular products despite evidence that more than half of the preparations were "worthless, and perhaps even dangerous," a phrase used by W. H. Schultz, a pharmacologist at the Hygienic Laboratory, Public Health and Marine-Hospital Service (Washington, D.C) who, in 1909, conducted a study on the quality of suprarenal gland preparations available on the "open market."[426] Confronted with buyer's dissatisfaction, such as through the purchase of a dud drug, or after reading a damning exposé of a company or product penned by colleagues or government employees, American doctors responded by urging drug companies to improve. As the editors of the

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[424] Kraus, 530.

[425] When they occasionally reverted to this outdated practice, they usually provided some explanation for why they had deviated from the new norm of buying and prescribing commercial preparations. For example, some doctors compared the efficacy between fresh glands made in clinic, and solutions or extracts that were bought on the market. For example, see "Treatment of Goitre by Thyroid Extract," *JAMA* 26 (May 16, 1896): 980–81. This source offers a report of one doctor, albeit based in Germany not the U.S., who treated their cases "partly by fresh glands and partly by tablets," and they found "fresh gland more effective than tablets." Other doctors made products in clinic because they were not yet commercially available, such as Cornell's Dr. Beebe who made an anti-thyroid serum in the 1900s and later enlisted Parke, Davis & Co.'s assistance in producing the drug on a commercial scale (1912). See Harvery Merker, Interview with Dr. Harvey Merker, interview by Gertrude Losie and Dr. Moore, July 6, 1961, 19, C38(a), Kremers Reference Files.

[426] W. H. Schultz, "Quantitative Physiological Activity of Some Commercial Solutions of Epinephrin," *Hygienic Laboratory Bulletin* 61 (January 1910): 7–26.

Journal of the American Medical Association (*JAMA*) wrote in response to Schultz's study—which was one of many similar studies conducted by the government and the American Medical Association (AMA)[427]—it was "clearly the duty of the manufacturers to devise some means of preventing [the circulation of poor quality drugs], either by greater care in the manufacture, by a system of recalling the preparations after a certain date…or by giving the pharmacist more explicitly directions as to how to keep them."[428]

This dramatic evolution in the manufacturing and prescribing habits of doctors is the focus of this chapter. What conditions led to the doctor's progressive retreat from their own role as drug producers, and their apparent embrace of purchasing commercial preparations, warts and all? We might assume that the pharmaceuticalization of endocrine drugs was a foregone conclusion: that powerful market forces simply pulled physicians, almost by gravitational force, into the orbits of manufacturing firms. American pharmaceutical companies were gaining in number, size and prominence in the years after the Civil War, and the proprietary drug market was expanding, despite the medical community's condemnation of "patent" medicines. According to historian of pharmacy Jonathan Liebenau, whose *Medical Science and Medical Industry* (1987) is still an authoritative account of the rise of commercial pharmaceutical manufacturing in the U.S., American physicians had come to accept by the end of the nineteenth century that preparations produced by some companies were generally of a higher quality than medicines they could have sourced from the corner-

[427] W. A. Puckner, "Pharmacology: Reed and Carnrick Methods: An Examination of the Claims Made for Trophonine, Protonuclein, Nephritin and Peptenzyme," *JAMA* 49 (October 5, 1907): 1198–1203; "Standardization of Suprarenal Products," *JAMA* 47 (September 22, 1906): 944; W. A. Puckner, "Pharmacology: Liquid Combinations Containing Pepsin and Pancreatin: Report on the Council on Pharmacy and Chemistry of the American Medical Association," *JAMA* 48 (February 2, 1907): 434–35. "Activity of Commercial Suprarenal Preparations," *Journal of the American Medical Association* 54, no. 9 (February 26, 1910): 710; Reid Hunt and Atherton Seidell, "Commercial Thyroid Preparations and Suggestions as to the Standard of Thyroid," *JAMA* 51 (October 24, 1908): 1385–89. W. A. Puckner and W. S. Hilpert, "The Presence of Sulphitein Commercial Solutions of Suprarenal Alkaloid," *JAMA* 51 (October 31, 1908): 1525.

[428] "Activity of Commercial Suprarenal Preparations."

store pharmacist.[429] The best preparations came from so-called "ethical" manufacturers, such as Philadelphia's H. K. Mulford and Detroit's Parke, Davis & Co., druggists that successfully marketed themselves to orthodox physicians as scientific operators that produced cutting-edge "scientific" medicines.

Historian of pharmacy Joseph Gabriel, who builds on Liebenau's work in his landmark *Medical Monopoly* (2014), explains how ethical manufacturers—and especially Parke, Davis & Co.—were successful in convincing American doctors that their manufacturing efforts were about scientific innovation and not about profit.[430] They deferred to doctors' authority, publicly eschewed patent drugs and the patenting system in general, and were restrained producers and advertisers of new medicines. It was, in part, through the campaigns of self-proclaimed "ethical" manufacturing companies, Gabriel argues, that American physicians overcame their reluctance to purchase and prescribe company-produced preparations, and slowly put their support behind a corporate model of drug production.[431] By the interwar period, the transformation was complete: American physicians were faithful patrons of big pharmaceutical companies. Other historians have given similar narratives of the slow but steady integration of pharmaceutical companies with scientific and medical practice, especially by the interwar period, as the introductory chapter detailed. [432]

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[429] See Liebenau, *Medical Science and Medical Industry*, 20.

[430] Gabriel, *Medical Monopoly*. This chapter as builds on Gabriel's work on ethical manufacturers of drugs, which includes this monograph as well as several articles. See: J. M. Gabriel, "A Thing Patented Is a Thing Divulged: Francis E. Stewart, George S. Davis, and the Legitimization of Intellectual Property Rights in Pharmaceutical Manufacturing, 1879-1911," *Journal of the History of Medicine and Allied Sciences* 64, no. 2 (October 23, 2008): 135–72, https://doi.org/10.1093/jhmas/jrn075; Joseph M. Gabriel, "The Testing of Sanocrysin: Science, Profit, and Innovation in Clinical Trial Design, 1926–31," *Journal of the History of Medicine and Allied Sciences* 69, no. 4 (October 1, 2014): 604–32, https://doi.org/10.1093/jhmas/jrt040; Gabriel and Holman, "Clinical Trials and the Origins of Pharmaceutical Fraud." See also McTavish, *Pain and Profits*, 6, 46–48. On p. 6, they argue that "ethical" meant that a company only advertised to physicians, not the lay public. See also pp. 46-48, in which McTavish and McTavish introduce the plight of the "ethical" manufacturer of drugs, who sought to make a profit while disguising their imperative to make money.

[431] Gabriel, *Medical Monopoly*. Gabriel gives other reasons for historical change, too, such as the flow of new drugs and norms to America from Europe, especially Germany.

[432] See Swann, *Academic Scientists and the Pharmaceutical Industry*; Parascandola, *The Development of American Pharmacology*. For a detailed account of how a university and drug company collaborated during the

Yet, within these narratives of the industrialization and pharmaceuticalization of drug production, we rarely hear from doctors themselves, and especially not in the realm of endocrinology. Did doctors turn to commercial glandular preparations of their own accord? Were they cajoled by companies, or compelled to "go corporate" because of economic incentives? Did they willingly give up the burden (and opportunity) of drug production, or was it taken from them by companies who sought to create a market monopoly? Early endocrinology provides an ideal case study for exploring how doctors experienced the rise of a pharmaceutical industry, for we can observe how physicians transitioned from a drug supply chain that was predominantly controlled by the medical community to one that was predominantly controlled by manufacturing companies.[433] This transition also marks the dawn of the endocrine pharmaceutical industry as we know it, and my account of it will be the first history, as far as I am aware, to offer a detailed analysis of this critical juncture point in the U.S. as it occurred in the 1890s and turn of the century.[434]

To tell this story, I offer the perspectives of both drug company and doctor. I first introduce Parke, Davis & Co. as an "ethical" outfit, and especially its influence in pioneering

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discovery of insulin, see Katherine Badertscher and Christopher J. Rutty, "Insulin at 100: Indianapolis, Toronto, Woods Hole, and the 'Insulin Road,'" *Pharmacy in History* 62 (2020). See also: Bliss, *The Discovery of Insulin*.

[433] McTavish & McTavish suggest that the lack of physician voices in the literature could be due to a source problem. They write "on the whole, doctors simply do not tell us about their interactions with pharmaceutical firms or how, once they had gone into practice, they discovered new products or new therapeutic methods." See McTavish, *Pain and Profits*, 49. In my research, I have found that while American physicians are not especially forthcoming about their personal interactions with pharmaceutical companies, they do give many hints in medical periodical literature of their purchasing practices. In published clinical reports, doctors would often list names of companies next to the drug they used. Eg."Thyroid extract, P. D & Co." When doctors did not list the company from which they bought glandular preparations, they would often still betray their purchasing practices by stating that they had opted for a "powdered" or "desiccated" extract instead of a "fresh" glandular preparation. "Fresh" extracts were prepared by physicians, while "powdered" and "desiccated" extracts were almost always prepared by commercial companies.

[434] Other histories of endocrinology explore the pharmaceutical industry in the interwar years. See Oudshoorn, *Beyond the Natural Body*; Watkins, *The Estrogen Elixir*; Medeiros, *Heightened Expectations*; Christer Nordlund, *Hormones of Life: Endocrinology, the Pharmaceutical Industry and the Dream of a Remedy for Sterility, 1930–1970* (Sagamore Beach, Mass.: Science History Publications, 2011); Nicolas Rasmussen, "Steroids in Arms: Science, Government, Industry, and the Hormones of the Adrenal Cortex in the United States, 1930-1950," *Medical History* 46, no. 3 (2002): 299–324, https://doi.org/10.1017/S0025727300069374. Scholars who have looked closely at endocrinology in the 1890s, namely Merriley Borell and Cornelius Medvei, have not been concerned with drug companies. See Medvei, *A History of Endocrinology*; Borell, "Brown-Séquard's Organotherapy."

methods for standardizing drugs. I then give special attention to how the company communicated with physicians through promotional material, with the aim of showing Parke, Davis & Co.'s self-fashioned scientific aesthetic and how the company might have been perceived by physicians. The second half of the chapter gives voice to physicians, with the aim of exploring their reasons for doing away with DIY preparations and turning instead to the market for glandular drugs. Through these accounts I build an argument about practicing physicians, who played a large part in ushering in these dramatic changes to glandular product manufacturing. I argue that American doctors, in the interests of improving glandular therapies, actively facilitated the production of mass-produced glandular products, provided it was done right and produced by the right company. I show how some doctors even started to rub shoulders with Parke, Davis & Co. executives in the interests of improving the clinical utility of the new "Adrenalin" drug. In turn, Parke, Davis & Co. helped physicians raise their expectations of what glandular products could be, and how they should be prepared. The nineteenth- and twentieth-century drug manufacturer is sometimes characterized by historians as a corrupting force in American medicine and often excluded from accounts of scientific and medical progress.[435] I have found a rather different story in the archive. Physicians' testimony and company records reveal that Parke, Davis & Co.—as the leading manufacturer of glandular products—was critical to the development of clinical endocrinology.

[435] Old and new literature characterizes pharmaceutical companies variously as a corrupting, exploitative and/or violent force in American science and medicine. See Young, *The Toadstool Millionaires*; Greene, *Prescribing by Numbers*; Abena Dove Osseo-Asare, *Bitter Roots: The Search for Healing Plants in Africa* (University of Chicago Press, 2014), https://doi.org/10.7208/9780226086163; Gabriel and Holman, "Clinical Trials and the Origins of Pharmaceutical Fraud." Other times, pharmaceutical companies are simply absent from accounts of scientific progress at the turn of the century. See Bynum, *Science and the Practice of Medicine in the Nineteenth Century*; Warner, "Ideals of Science and Their Discontents in Late Nineteenth-Century American Medicine"; Marks, *The Progress of Experiment*.

Setting Down Standards

Who were Parke, Davis & Co.? By the early 1890s, when they first invested in the glandular product market, the Michigan-based company was a well-known chemical manufacturing house that had earned respect from the American medical community for pioneering a technique for the chemical standardization of drugs.[436] This "chemical assay," developed in the late 1870s, attempted to measure by chemical means the exact weight of the "active principle" in a preparation, with the goal of achieving a uniform and predictable strength in the drugs that went to market. Drug variability was a perennial problem in nineteenth-century America, and physicians complained that commercial preparations were either far too weak to be effective or "death-threateningly strong."[437] Circumventing the market altogether, doctors would often use their own compounding skills to create drugs of an appropriate strength, or source drugs from a local compounding pharmacist whom they trusted. Yet, compounding still yielded highly variable drugs and American physicians were left frustrated. According to Johnathan Liebenau, physicians' desire for standardization manifested in the first attempts at creating a nationally-recognized pharmacopeia, beginning in the early nineteenth century. Yet even when the first United States Pharmacopeia become available in 1821, clear drug standards were still not achieved; drugs names and formulas were listed in the Pharmacopeia based on the collective empirical experiences of a committee of physicians, not through scientific, pharmacologic testing.[438]

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[436] Parke, Davis & Co. was opened in 1862 in Detroit by Samuel P. Duffield. He was joined by Hervey Parke and George S. Davis in 1866 and 1867, and company was launched. For an early history of the company, see: Milton L. Hoefle and Warner Lambert-Parke Davis, "The Early History of Parke-Davis and Company," *Bulletin for the History of Chemistry* 25, no. 1 (2000): 28–34.

[437] Hoefle and Davis, 30.

[438] Liebenau, *Medical Science and Medical Industry*, 20–21. See also Glenn Sonnedecker, "The Founding Period of the U.S. Pharmacopeia: II. A National Movement Emerges," *Pharmacy in History* 36, no. 1 (1994): 3–25; Glenn Sonnedecker, "The Founding Period of the U. S. Pharmacopeia: III. The First Edition," *Pharmacy in History* 36, no. 3 (1994): 103–22. The first edition of a national pharmacopeia was published in 1820, according to Sonndecker (p. 107).

When Parke, Davis & Co. announced a method of chemical standardization in 1879, the company was thus proposing that it had the scientific means to test the activity of drugs before they were released on the market. The company presented the chemical assay as a way for physicians to distinguish the supposedly higher-quality Parke, Davis & Co. products from the "astounding multiplicity of forms and shapes [of drugs]" that existed within medical practice.[439] According to Parke, Davis & Co., the new chemical standard yielded "normal liquids" that could be relied upon.[440] For those physicians who believed in the utility of the chemical assay, there was now a concrete incentive to buy from a manufacturing firm and, specifically, to buy from Parke, Davis.[441]

The chemical assay proved useful in standardizing products with known chemical properties, but quite powerless in standardizing drugs whose "active principles" were not yet identified, such as Parke, Davis & Co.'s new line of "biological products," which were launched in the early 1890s and included glandular extracts and vaccines. This led to the company pioneering another standardization method in the late 1890s: the "physiological assay," or "bioassay." It attempted to establish "normal" doses of the new range of biological products by quantifying physiological reactions of lab animals to these drugs. This varied for each drug: changes in blood pressure became the yardstick for adrenal gland preparations; for antitoxins, it was the minimum dose required to neutralize a lethal dose of toxins; for ergot, it was the changing color of a cock's comb.[442]

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[439] Medical man quoted in Liebenau, *Medical Science and Medical Industry*, 21.
[440] Peter Stechl, "Biological Standardization of Drugs before 1928" (University of Wisconsin-Madison, 1969), 10.
[441] Hoefle and Davis, "The Early History of Parke-Davis and Company," 30. For more context on the relationship between physicians and pharmacists in the early to mid nineteenth century, and the effect of the chemical manufacturing revolution, see Edward Kremers and George Urdang, *Kremers and Urdang's History of Pharmacy*, ed. Glenn Sonnedecker, 3rd ed. (Philadelphia; Montreal: J. B. Lippincott Company, 1963), 263–67. See also John Parascandola, "The Pharmaceutical Sciences in America, 1852-1902," *Journal of the American Pharmaceutical Association* 40, no. 6 (2000): 733–35. He wrote: "Companies that could promise to deliver standardized preparations had an edge in winning the confidence of the public and the health professions."
[442] Stechl, "Biological Standardization of Drugs before 1928," 59–99, esp 83, 84.

The bioassay was a technique pioneered by Dr. Elijah Houghton, a faculty member at the University of Michigan Medical School who was poached by Parke, Davis & Co. in 1894, along with Charles McClintock—another Michigan faculty member—to launch the company's new "biological laboratory." Shortly upon arriving at the company, Houghton was successful in running his first physiological assay, which was applied to vegetable drugs, including ergot and heart tonics, then to the "biological" drugs, including antitoxins and preparations of suprarenal glands.[443] Even though it took much longer to make bioassays work in some glandular products, such as thyroid extracts,[444] Houghton's new method brought the company even further esteem both in the U.S. and Western Europe.[445] According to Peter Stechl, who wrote his dissertation on the topic, manufacturing firms, especially Parke, Davis & Co., led the way in biological standardization in the U.S., and regarded themselves as more progressive than even the U.S. Pharmacopoeia, which initially resisted the new "biological methods."[446]

The company's biological laboratory, too, attracted widespread acclaim. It was directed by Houghton and McClintock, who retained very close ties with the medical school at the University of Michigan,[447] recruited university-trained scientists to work in their midst, and worked hard to grow the scientific capabilities of the company. According to Harvey Merker, a retired company worker reflecting on the nearly fifty years he spent working at Parke, Davis, Houghton and McClintock employed "not over half a dozen" technically

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[443] See Jonathan Simon's chapter, "Standardization and Clinical Use," in Schwerin, Stoff, and Wahrig, *Biologics*.
[444] See Hunt and Seidell, "Commercial Thyroid Preparations and Suggestions as to the Standard of Thyroid."
[445] For an example of how the company mobilized the new physiological assay to their own commerical advantage, see publications such as: E. M. Houghton, "An Indispensable Part of Drug Valuation: Physiological Assay Necessary to Pharmaceutical Research--Where the Chemical Test Is Futile, the Animal Test Affords the Only Safeguard--the Bases of the Newer Pharmacy," *Bulletin of Pharmacy*, 1899, 418–20.
[446] Stechl, "Biological Standardization of Drugs before 1928," 110–11.
[447] The next chapter will detail in depth Houghton's connection to the University of Michigan Medical School and the Detroit College of Medicine and Surgery, which carried on well after he began his employment at Parke, Davis & Co. For context on Houghton's career, see "Dr. Houghton Retires," *The Firing Line* 15, no. 5 (May 1929): 177–78.

trained people to work in their laboratory when it opened in 1895, but this number steadily grew throughout the 1890s.[448] In 1902, the company built a research laboratory valued at a quarter of a million dollars,[449] whose launch was noted in national journals.[450] Parke, Davis & Co.'s first farm was described in 1898 as a "veritable menagerie" of animals, for it housed a number of horses (for serum production) as well as laboratory animals for physiological and pharmacological testing.[451] By 1908, the farm was upgraded to a 700-acre-large estate in the outskirts of Detroit which kept "hundreds" of horses and "thousands of guinea pigs, rabbits, dogs, roosters and calves."[452] By 1932, Parke, Davis & Co. employed between three and four thousand people and produced over 2,000 products.[453]

The company's success in drug manufacturing was also reflected in their widening national and international footprint. It started manufacturing in Canada in 1887, opened branches in Kansas City (1890), London, England (1891), Simla, India (1899), Chicago and St. Louis (1901), Sydney (1902), Petrograd (1903) and depots in Boston and Indianapolis (1903). By 1909, it had opened more branches in New York, Boston, Baltimore, New Orleans, Minneapolis, Tokyo and Buenos Aires.[454] In 1911, it launched a Seattle branch followed by more depots in Pittsburgh (1913) and Cincinnati (1914), and a branch in Havana (1916).[455] This all goes some way to demonstrating the profile of this manufacturing house, the company's quite visible position at the vanguard of medicinal manufacturing, and its

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[448] Merker, Interview with Dr. Harvey Merker, 10.
[449] "Parke, Davis & Company (History)," 1932, 5–6, 12, Parke, Davis & Co. C38 (a) I, Kremers Reference Files.
[450] "Notes and News," *Am. Jour. Pharm.*, November 1903, 551–52.
[451] "Infinitely Little Equipment and Processes of Production in Antitoxin Plant, 1898.," 1898, NMAH.AC.0001_B414F34, SI, Parke Davis Collections.
[452] "Parke, Davis & Company (History)," 5.
[453] "Parke, Davis & Company (History)," 7–8.
[454] "Advertisement: Ampoules of Adrenalin Chloride Solution," *JAMA*, 1909, 11. Note, this advertisement appears in the Advertising Section of the October to December issue. Available in the Medical Advertisements Collection at Ebling Library, University of Wisconsin-Madison.
[455] See "Parke, Davis & Company: Historical Highlights Year by Year: 1866 through 1959" (Parke, Davis & Co., n.d.), 3–5, C 38 (a) I: Parke, Davis & Co (General), Kremers Reference Files.

expertise in creating the new class of "biologics"—drugs made from animal products.[456] It was in this context of rising national and international prominence that Parke, Davis & Co. first entered the glandular product industry.

The Science of Selling Glandular Extracts

One only need glance at trade catalogues and advertisements to confirm that Parke, Davis & Co. hotly pursued developments in the field of glandular therapeutics between 1889 and 1910 and were quick to present a pharmaceutical product as a viable alternative to the raw extracts that were being used by doctors throughout the 1890s. The company's first glandular product was desiccated thyroid extract, appearing on the market in 1893, which closely aligned with developments in the medical community, as I outlined in the preceding chapter. Next came "saccharated" suprarenal glands in 1895,[457] and thymus gland extracts in 1896—again, two developments that track closely to physician's prescription activities in the realm of glandular products.[458] In 1901, Parke, Davis & Co. launched "Adrenalin Solution 1: 1000," which was a diluted solution of the concentrated "active principle" of the suprarenal glands.[459] For the rest of the decade, just three more glandular products were released by the company: Thyroidectin (1904),[460] an antitoxin-inspired therapy that targeted the "toxins" produced by an overactive thyroid; Pituitrin (1909), a drug processed from the extracts of the pituitary

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[456] See Hoefle and Davis, "The Early History of Parke-Davis and Company," 30. Hansen describes how Parke, Davis & Co.'s method of physiological standardization made it into British and American pharmacopeia. See Adolph M. Hanson, "Elijah Mark Houghton, Ph. C., M. D., American Scientist and Pioneer of Modern Pharmaceutical and Biological Chemistry," ca 1948, 5, Biographical Section: A2, Houghton, Kremers Reference Files. See article by E. M. Houghton himself, who pioneered the method of physiological standardization at Parke, Davis & Co.: E. M. Houghton, "Is Physiological Action Requisite as a Department of Pharmaceutical Research?," *The Pharmaceutical Era,* September 21, 1899, 399–400.

[457] Parke, Davis & Co. price lists from the 1890s and first years of 1900 are available at the Kremers Reference Files at the American Institute for the History of Pharmacy. See C38(a)I: Parke, Davis & Co in "Pabst Brewing & Co." For collections of company advertisements that were published in medical journals, see Ebling Library, University of Wisconsin-Madison. See also "Historical Highlights," 3.

[458] "Historical Highlights," 4.

[459] "Historical Highlights," 4.

[460] "Historical Highlights," 5. This was an "antitoxin" serum that was designed to counteract against the effects of thyroid hypersecretion.

gland;[461] and desiccated corpora lutea, which was developed from corpus luteum tissue (1910).[462]

Getting these drugs on the open market was one thing, but it was quite another to convince physicians to buy them. Physicians were already leery of the new and controversial glandular products movement (as outlined in the first three chapters) and became even more skeptical when they observed commercial preparations springing up on the marketplace. In 1894, for example, one editorialist, Dr. Albert Reynolds, scolded Armour & Company for distributing free thyroid extract samples to physicians and sarcastically recommended that the company "enlarge their field of usefulness" by offering physicians crushed perineal gland, liver and appendix—three glands the author clearly thought should not be made into therapies.[463] Another physician wrote in 1896 that "serotherapy and animal extracts seem to be the coming fad, though the quackish methods adopted by some of its promoters and manufacturers have somewhat chilled the ardor of the regular profession."[464] According to one anonymous author, publishing in the *Medical Age* in 1894, "no one really believes in animal extracts not even their sponsors, but this is an age of discovery and experiment, and some have not hesitated to make truth and honesty subservient to the mercenary instincts of the commercial sense."[465] Other physicians were more open-minded about what the market could offer, but still decided to run full scale testing of the new "commercial" preparations

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[461] "Historical Highlights," 5; F. O. Taylor, "American Chemical Industries- Parke, Davis and Company," *Industrial and Engineering Chemistry* 19, no. 10 (October 1927): 1205.

[462] There is evidence Parke, Davis & Co. was selling pancreatin somewhere between 1899 and 1907, according to a trade catalogue entitled *Medicinal Elixirs* (Parke, Davis & Co., n. d.). This source is undated, but we can use contextual information to date it to ca. 1900. (See back cover. The Simla branch opened in 1899 and was shifted to Bombay in 1907).

[463] "Objects to Animal Extracts," *JAMA* 23 (September 22, 1894): 475.

[464] "Prescription Writing and Pharmacy as Practiced in Our Large Hospitals and Dispensaries," *JAMA* 27 (July 18, 1896): 142. See also Solomon Solis-Cohen's assessment of the marketplace in Solomon Solis-Cohen, L. F. Appleman, and R. Max Goepp, "Suprarenal Extract in Addison's Disease," *American Medicine* 3 (April 12, 1902): 617–18. He wrote that "after the brilliant results obtained with thyroid extract, extravagant hopes were, as always, entertained of the possibilities of the new discovery extracts of every gland in the body were prepared by enterprising manufacturers… many of these preparations…have failed to realize the expectations of their advocates…" p. 617.

[465] "Animal Extracts," *Medical Age* 12, no. 8 (April 25, 1894): 225.

against their "fresh" preparations, with an eye to the efficacy and safety of open-market drugs, which suggests a reluctance to trust third party preparations over a drug that could be hand-made or sourced locally.[466]

To combat physician skepticism, and to guide doctors away from their practice of making DIY drugs, Parke, Davis & Co. waged a war of advertising. Notably, this advertising was less focused on promoting specific glandular products and more concerned with establishing Parke, Davis & Co. as a thoroughly scientific organization. Yes, the company wanted physicians to buy specific preparations, such as their desiccated thyroid extract or Adrenalin solution, but to do this, it first had to convince physicians that it was less like a commercial manufacturer and much more like a rigorous research institute.

Some of this advertising came in obvious forms, such as glossy pamphlets that were sent directly to physicians and universities, and restrained and respectable advertisements that appeared in the advertising pages of medical journals such as *JAMA* and *American Medicine*.[467] Other advertising strategies were much more subtle and possibly more compelling, such as company employees publishing frequently in elite scientific and medical journals including *The Journal of Physiology*,[468] *American Druggist*,[469] the *Journal of the*

[466] For example, see how Solis-Cohen shifts from using "fresh glands of recently slaughtered animals" and then "later, commercial preparations, desiccated powders, tablets, glycerine extracts and solid extracts." He said that preparations varied in nature, and so he "wrote to the leads manufacturers of American and England in order to get some idea of the manner in which the preparations on the market are made..." Solomon Solis-Cohen, "The Therapeutic Uses of the Thymus Gland," *JAMA* 35 (n.d.): 421.

[467] For example, see "Advertisement: Hayfever: Adrenalin Chloride Solution; Adrenalin Inhalant; Adrenalin Ointment," *JAMA* 49, no. 11 (1907); "Advertisement: Now Ready! Ampoules of Adrenalin Chloride: Solution 1: 10, 000," *JAMA*, 1909; "Advertisement: What Guaranty Have You," *American Medicine* 2 (1901): 17. The ad in the 1901 edition of American medicine stated: "What guaranty have you that a given serum or vaccine is safe? Behind our label are: Thirty years of reputation. A staff of expert bacteriologists, chemists and veterinarians. A corps of renowned consultants. The best of equipments. A readiness to incur any expense for proper safe-guards and tests." All advertisements cited here can be found in the Collection of Medical Advertisements at Ebling Library, UW-Madison.

[468] For example, see T. B. Aldrich, "The Active Principle of the Suprarenal Gland," *Journal of Physiology*, August 1901. Described in "Therapeutic Notes: Glimpses of the Parke-Davis Research Laboratories" (Parke, Davis & Company, March 1931), 62–63, C38(a), Kremers Reference Files.

[469] For example, see Houghton's paper "Physiological Testing" in July and September, 1911, and January and April, 1912. Described in "Therapeutic Notes: Glimpses," 62–63.

American Chemical Society,[470] and *The Lancet*. Some of these titles were scientific in nature and concerned Houghton's work on the physiological assay, but others actively engaged the ethical questions that the medical community was grappling with, such as Houghton's 1897 paper in *JAMA* entitled: "How Can We Increase the Therapeutic Reliability of Medicinal Agents?"[471] Parke, Davis & Co. was also adept at producing its own medical periodicals, namely *The Medical Age* (later *Therapeutic Gazette*) published by George S. Davis (one of the founders of the company), which published contributions from physicians who hailed from all around the country. Some historians have criticized these periodicals as being nothing more than company literature masquerading as medical literature;[472] yet, we can also see them as evidence of the company's success in productively engaging the American medical community through scholarly publishing.

Parke, Davis & Co. literature (in all its forms) usually made one of three marketing pitches. The first was to convince physicians that their company did not tolerate the fraudulent or unhygienic manufacturing practices that were so common at "proprietary" manufacturing firms. The next was to prey on doctors' own insecurities about their ability to make high-quality glandular drugs, and to present Parke, Davis & Co. as the more suitable manufacturer of biologics. The third was to invalidate the attempts of pharmacists who might deign to produce the new biological drugs in corner store workshops.[473]

The company made this multi-pronged argument by emphasizing the complexity of manufacturing high-quality biological products, the expensive infrastructure that was

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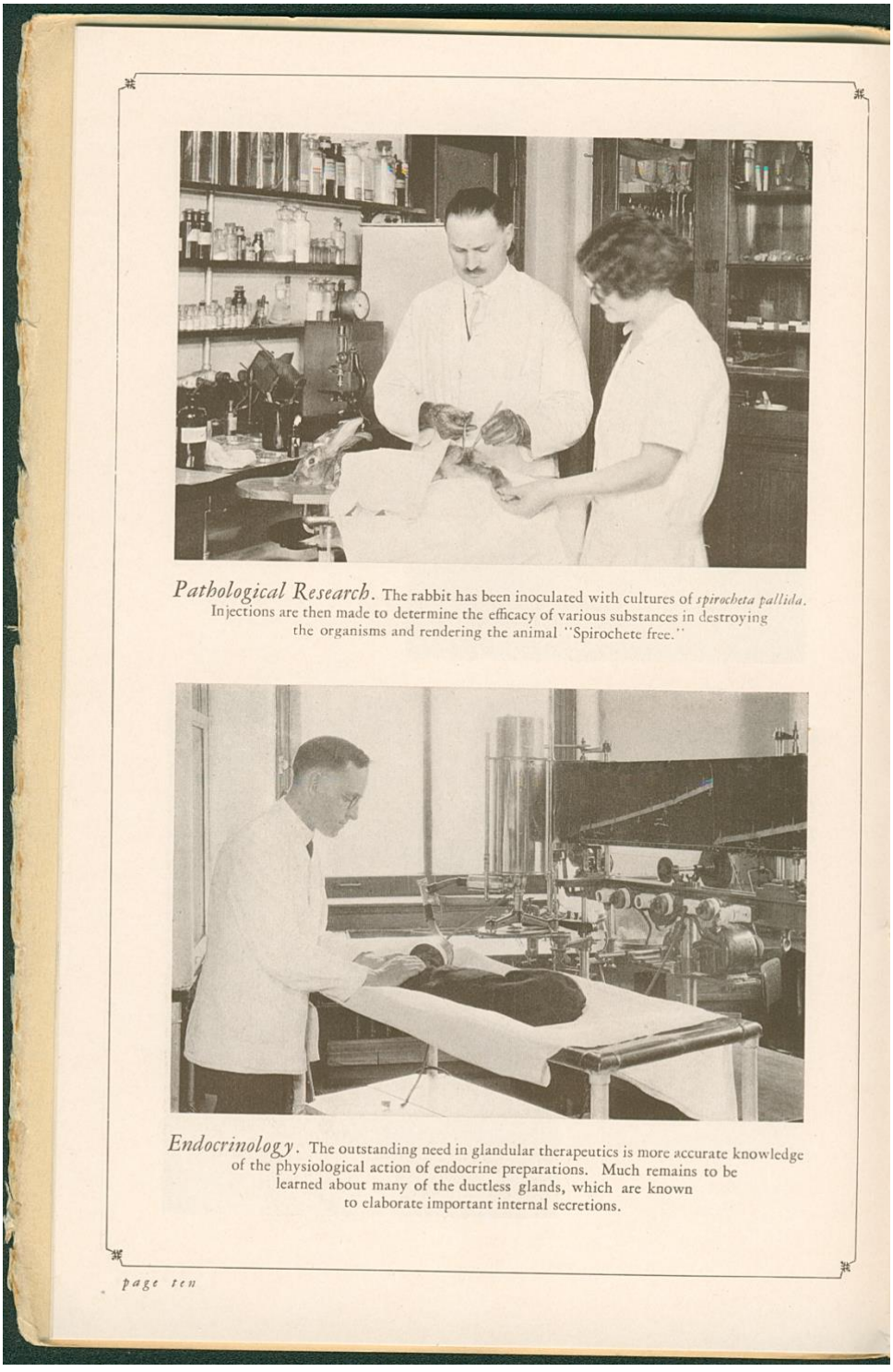
[470] For example, see Davis & Merker's paper "Chemical Changes in the Purification of Pepsin" in February 1919. Described in "Therapeutic Notes: Glimpses," 62–63.
[471] Mark E. Houghton, "How Can We Increase the Therapeutic Reliability of Medicinal Agents?," *JAMA*, April 3, 1897, 634–36.
[472] See Marks, ""Until the Sun of Science … "," 161. For an account of how Parke, Davis & Co. pioneered this type of "medical periodical" advertising, see Mahoney, *The Merchants of Life; an Account of the American Pharmaceutical Industry*, esp. 70, 71.
[473] I have found some evidence that physicians sourced glandular products from pharmacists. See "Gratifying Results," *Daily Inter Ocean*, August 13, 1889; "Elixir Horrors," *Atchinson Globe*, August 19, 1889.

required, and the expertise that was recruited to the company's campus to achieve scientific precision. For example, Parke, Davis & Co. pamphlets after 1894 almost always offered an "inside look" at their state-of-the-art biological laboratory, which they described as "sanitary," "aseptic," and surgically clean (see Figures 1 and 2). Some pamphlets portray the biological laboratory as a sterile operating theatre, with a team of workers donning crisp, white hospital gowns and bending over animals and organs that are laid out on sparkling counter tops.[474] These images are clinical, as if appealing to clinicians' sensibilities, and yet at the same time intimidating and remote, as if to communicate that Parke, Davis & Co. could create conditions of sterility and productivity that were not possible in the clinic.[475]

[474] Patrick M. Walsh, "A Bloody Business: American Vaccine Production at the Turn of the Twentieth Century," *Points* (blog), July 9, 2021, https://pointshistory.com/2021/07/09/a-bloody-business-american-vaccine-production/.

[475] The same pamphlets offer panoramic views of sprawling farmlands where Parke, Davis & Co. animals are left to graze; these bucolic images were designed to allay commonly held fears that animal *materia medica* would transmit animal disease to humans.



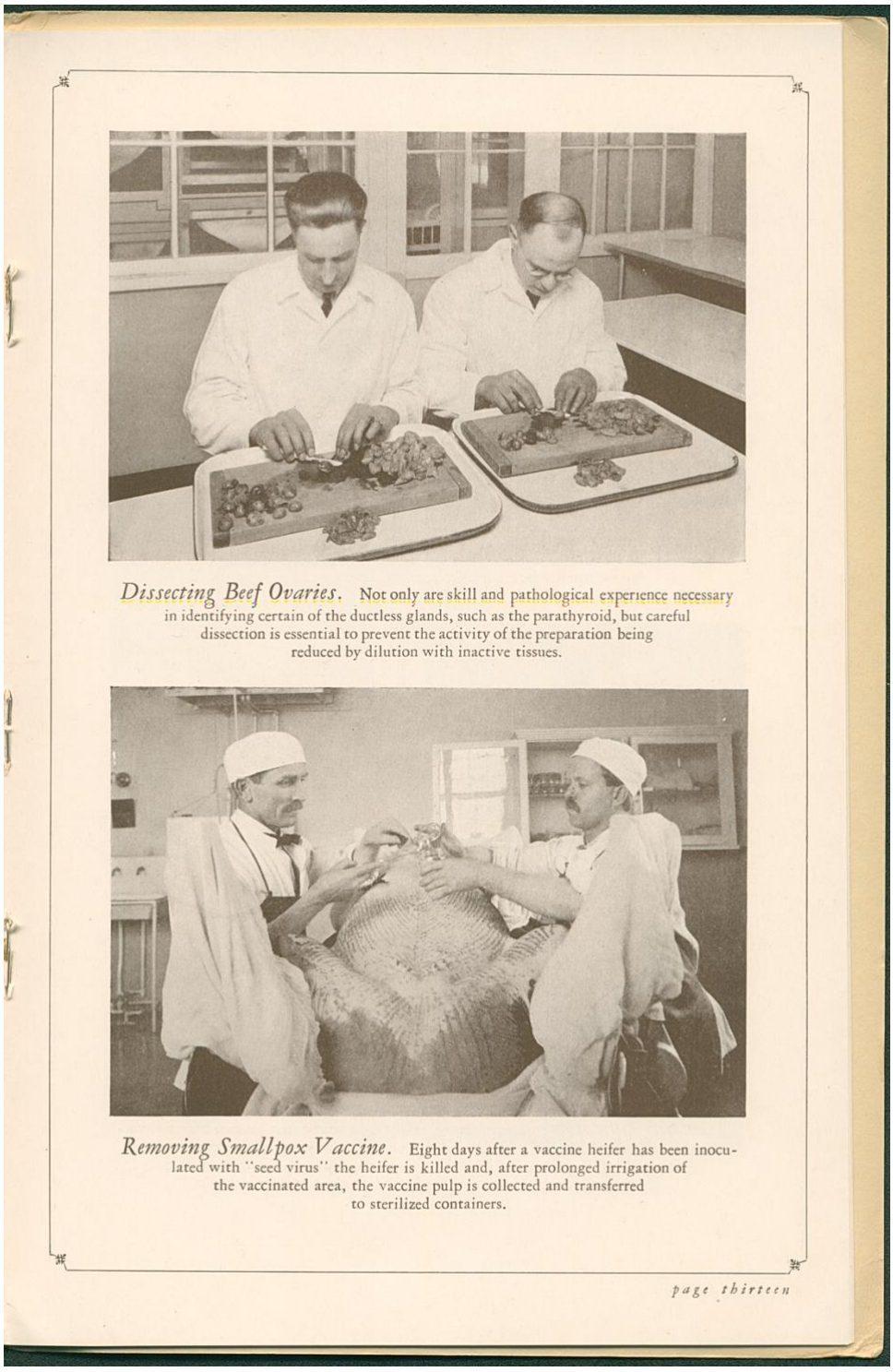
Pathological Research. The rabbit has been inoculated with cultures of *spirocheta pallida*. Injections are then made to determine the efficacy of various substances in destroying the organisms and rendering the animal "Spirochete free."

Endocrinology. The outstanding need in glandular therapeutics is more accurate knowledge of the physiological action of endocrine preparations. Much remains to be learned about many of the ductless glands, which are known to elaborate important internal secretions.

page ten

Figure 1: Endocrinology at Parke, Davis & Co.[476]

[476] *The Scientific and Research Work of Parke, Davis & Company* (Parke, Davis & Company, n. d.).



Dissecting Beef Ovaries. Not only are skill and pathological experience necessary in identifying certain of the ductless glands, such as the parathyroid, but careful dissection is essential to prevent the activity of the preparation being reduced by dilution with inactive tissues.

Removing Smallpox Vaccine. Eight days after a vaccine heifer has been inoculated with "seed virus" the heifer is killed and, after prolonged irrigation of the vaccinated area, the vaccine pulp is collected and transferred to sterilized containers.

page thirteen

Figure 2: Dissecting Beef Ovaries at Parke, Davis & Co.[477]

[477] *The Scientific and Research Work of Parke, Davis & Company*.

Some company literature featured short and persuasive text, including one pamphlet from 1898, entitled "Recent Changes in Pharmaceutical Manufacturing," which stated that producing biological products "required the education and skill of specialists as well as capital of no mean proportions."[478] It continued to state that "it was out of the question to prepare these remedies in the small laboratories attached to retail pharmacies," and that "they had to be made in specially constructed and equipped laboratories of the pharmaceutical manufacturer."[479] Another pamphlet from 1897 characterized physicians as naturally and necessarily "dependent" on drug manufacturers to create for them "potent" and reliable products. They explained that "ignorance or carelessness" would produce sub-par and even dangerous products:

> In no other field is the physician so dependent on the skill and reliability of the manufacturer as in the recent biological therapy. In the gland preparations, in the nucleins,[480] the serums and the toxins, we have most potent therapeutic agents. When well prepared and skillfully administered, the results obtained are most gratifying. On the other hand, when through ignorance or carelessness these preparations are not properly made, preserved and administered, very serious results may follow. Our aim is to give to the preparation of these biological products the greatest obtainable skill and care. Every precaution known to the science is taken to insure their reliability. We invite inspection of our laboratories and methods."[481]

Internal company memoranda give testament to the fact that Parke, Davis & Co. was keenly aware of its own self-image, and especially its appearance as a serious scientific actor in the eyes of the American medical community. A 1901 memorandum, as just one example, emphasized that the new scientific laboratory, which would be built that year, was as much

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[478] "Recent Changes in Pharmaceutical Manufacturing" (Parke, Davis & Company, n. d. (ca 1898), Kremers Reference Files.

[479] The quote continued: "The truth of the recent assertion by Mylius, that pharmacy continues to live in the laboratories of the pharmaceutical manufacturer, etc., rather than in the average drug store, was drastically demonstrated in connection with the manufacture of this new class of preparations". See:"Recent Changes in Pharmaceutical Manufacturing."

[480] Nucleins were a form of "antitoxic" therapy developed at Parke, Davis & Co. in conjunction with Vaughan and Novy at the University of Michigan. It involved taking the "serum" produced from yeast and injecting this as immunological treatment. See explanation in "Price List" (Parke, Davis & Company, 1900), 254, C 38 (a) I: Pabst Brewing Co. (Parke, Davis & Co. 1899-1900), Kremers Reference Files.

[481] "Bacteriological Products from the Biological Department of Parke, Davis & Co." (Parke, Davis & Company, 1897), 3, C 38 (a) I: Pabst Brewing Co. (Parke, Davis & Co. 1887-1896), Kremers Reference Files.

about creating a space to do good science as it was about shoring up the reputation of the company. It was authored by either Houghton or McClintock, and it read:

> Reputation is the best asset with Parke, Davis & Co. has and, as it appears to me at least, the work done in its scientific department has and perhaps will add more to that reputation than any other work undertaken by the Firm. Could we have a laboratory dignified in appearance and in appointments, the favorable impression produced on our many visitors would, I think, be of great value. If we can show people that we have better facilities for developing work, for testing drugs, for finding out in advance as to whether a given remedy is or is not of value, it will place us in a unique position among manufacturing pharmacists.[482]

For a model upon which this new laboratory might be built, the author of the letter suggested the company look to the "foremost laboratories of the country" and in particular to the University of Chicago. The author even suggested using the same architects that built labs at the University of Chicago, so that Parke, Davis & Co. would be recognizable as a peer institution. Parke, Davis & Co.'s ardent desire to create a scientific aesthetic is further reiterated in a 1903 memorandum authored by McClintock to employees of the Biological Department, in which he reprimanded them for not keeping neat enough records and neat enough workspaces. He wrote: "A part of the purpose of the new laboratory building is show—legitimate advertising. With this in mind, it is necessary that the various rooms should be kept in as neat a condition as the work will allow; further that all coats and hats, umbrellas, over-shoes, etc., should be kept in the place appointed for them…"[483]

Parke, Davis & Co's biggest cause for concern was not their capacity to do good scientific work, for the company knew it was outstripping the capabilities of government and university laboratories, both in the U.S. and Europe.[484] It was rather more concerned about

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[482] Houghton or McClintock? to Mr. Wm. M. Warren, "Memo Re: Providing Laboratory for Research," January 4, 1901, NMAH.AC.0001_B398F24, SI, Parke Davis Collections.
[483] "McClintock, Charles T., Memo to Workers of Biological Department Re: Keeping Complete, Exact Records and Keeping Labs Orderly," January 6, 1903, NMAH.AC.0001_B396F62, SI, Parke Davis Collections.
[484] Correspondence between Houghton and McClintock ca. 1900 reveals that these scientists felt they had little left to learn from Europe's serum production, and that they had surpassed the capabilities of the New York Board of Health. See: "Houghton, E. M. – McClintock. Letter Re: Vaccine Production and Printing of Articles and Reports," May 10, 1897, Box 400, Folder 17, SI, Parke Davis Collections; "Houghton, E.M. – McClintock

convincing orthodox physicians to buy its products, which was a hard task indeed, especially in the 1890s, when the new therapeutic field still existed on very shaky ground. This necessitated the always-delicate act of camouflaging its business model, spotlighting its scientific prowess, and aggressively ingratiating itself—although not too obviously—with the American medical establishment.

A Physician-Led Market

If our investigation of physicians' transition to commercial preparations stopped here, we might conclude that it was likely the "ethical" manufacturer who convinced physicians to "go corporate," and that this was achieved through a multifaceted and inspired campaign to get physicians onside. Yet, comparing this promotional material with the medical periodical literature reveals that physicians' decision to buy "P. D. & Co." were more complicated, more nuanced, and more engaged than simply being a case of doctors giving in to the charm of corporate suitors. Indeed, medical periodical literature suggests that physicians had far more control of the direction of the glandular drug industry than we otherwise might assume.

Let us consider, to begin, the timeline of Parke, Davis & Co.'s drug releases next to the prescription and experimentation practices of physicians, as outlined in the preceding chapter. It becomes quickly apparent that Parke, Davis & Co. only invested in making a pharmaceutical drug from a glandular extract if (and only if) that extract was already in common use in the medical community.[485] Their first glandular drug, the desiccated thyroid gland drug, was released in 1893, well after George Murray's famous experiments in 1891 (as detailed in the preceding chapter),[486] and once it was abundantly clear that thyroid gland

– Report on Vaccine Work in Pasteur Institute," May 17, 1897, NMAH.AC.0001_B406F13, SI, Parke Davis Collections.

[485] A similar observation has been made in Gabriel, "A Thing Patented Is a Thing Divulged," 136. While not focussed on endocrinology, Gabriel explained that ethical companies had difficulty getting new products on the market without first generating backing from doctors.

[486] For context about why glandular products were desiccated, see "Price List," 254. This source states that "sheep's thyroid and suprarenal glands [are] desiccated and otherwise guarded against deterioration."

therapies were both effective in treating patients with thyroid-related disorders and, most importantly for Parke, Davis & Co., that orthodox physicians regarded this as a legitimate and respectable therapy. This same pattern can be observed with the company's release of suprarenal gland preparations in 1895 and thymus preparations in 1896; American physicians were already using these products as raw extracts, following convincing studies that were well-circulated in the medical community. The same trend can be observed with Parke, Davis & Co.'s release of Adrenalin, which was a purified and improved version of suprarenal gland extract; Pituitrin, its trademarked preparation of pituitary gland extracts; and with desiccated corpora lutea, the company's refined version of ovarian extract, which had been used by gynecologists in the clinic since the late 1890s.

Parke, Davis & Co. offer hints about why it was reluctant to release a drug that was not already prescribed by a critical mass of physicians. It began with Brown-Séquard's testicular injections, which the company investigated in its laboratories but never produced or marketed. We can learn about the company's position on this controversial drug through the testimony of a Detroit-based physician, G. Archie Stockwell, who approached Parke, Davis & Co. in 1889 to get help in determining if there were active chemical properties contained within the famous injection. Stockwell, writing in the *Therapeutic Gazette*, noted that he conducted experiments which were "materially aided and furthered by the enterprise of Messrs. Parke, Davis & Co., of Detroit, who were induced to take up the matter and place it in the hands of the expert chemists of their scientific department."[487] After rounds of experiments, Stockwell and Parke, Davis & Co. concluded that probably there was something of therapeutic value in the spermatic tissue—perhaps "a vital principle in the form of a luecomaine or physiological alkaloid"—that could explain the sometimes stunning effects of

[487] G. Archie Stockwell, "Historical, Critical, and Scientific Aspects of Brown-Séquard's Discovery--The So-Called 'Elixir,'" *The Therapeutic Gazette* 5, no. 12 (December 16, 1889): 816.

Brown-Séquard's injections. Attached to this conclusion, however, Stockwell added a carefully worded and important footnote:

> Messrs. Parke, Davis & Co. wish it to be distinctly understood that they are not manufacturing this alkaloid, and have no intention of so doing, unless (perhaps) forced to do so in the future by reason of accumulated evidence of value in the product, such as shall place it in the foremost rank of remedies. They undertook to examine genital products simply to discover if an alkaloidal and vital principle existed therein, and not with any view to pecuniary or trade benefits.[488]

Stockwell explained that he felt obliged to make this note because "numerous individuals…suppose[d] this product had been, or was about to be, put upon the market by this house." Stockwell, who I strongly suspect of covertly working for Parke, Davis & Co.,[489] continued to elaborate:

> Even if it seemed desirable to manufacture, further investigations would be necessitated in order to determine, if possible, a mode of obtaining that will secure the best results, and afford the article at a price within the reach of the medical profession and consumer. Unless it can be obtained by synthesis, it would probably require to be isolated from the brains and spinal cords of mammals, and flesh and roe of fishes, procedures necessitating extraordinary trouble and waste.[490]

It seems, then, that the company was treading lightly around the controversy of Brown-Séquard's injections and was not willing to fully involve themselves in a therapy that was still under fire in the medical community. To do so would have been professionally damaging and would have isolated the company from its customer base: orthodox physicians. Even if there was some "active principle" resident within spermatic tissue, which could have merited

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[488] Stockwell, 816.

[489] Who was Dr. G. Archie Stockwell? According to the *Albany Medical Annals* (1898, p. 181), he was for ten years a "a confidential medical adviser of Parke, Davis & Co., Detroit," and "severed his connection" with them in 1898. See also "William A. Hammond Again," *The Medical Age*, December 11, 1893, 717–18. This editorial states that the Columbia Chemical Co. "allude" to Stockwell "as an employé" of Parke, Davis & Co, which Hammonds took as further fodder for foul play between these two parties. Bonnie Bluestein describes Stockwell as someone who conducted tests on Brown-Séquard's mixture "with the support of the Parke-Davis pharmaceutical firm." See: Blustein, *Preserve Your Love for Science*, 209.

[490] Stockwell, "Historical, Critical, and Scientific Aspects of Brown-Séquard's Discovery--The So-Called 'Elixir,'" 816–17.

further investigation, Parke, Davis & Co. decided to be guided by the climate of medical opinion and declined to produce the material.

Parke, Davis & Co.'s close observance of physician norms, and the advisability of doing so, was clearly expressed during the Hammond affair in 1893, when the company found itself in hot water. As the preceding chapter outlined, Hammond was a prominent physician who was publicly shamed for his attempt to manufacture and sell worthless glandular products. Parke, Davis & Co. became unwittingly implicated in this drama. The company had already put a desiccated thyroid extract on the market, which was produced by chemical methods and seemed popular with physicians.[491] Yet, before the downfall of Hammond, the company began a small-scale production of another thyroid extract prepared with the Hammond formular. During the heat of the Hammond affair, Parke, Davis & Co.'s Hammond-inspired product attracted the attention of the prominent Dr. Abraham Jacobi of New York, who promptly hauled the company over the coals for engaging in fraudulent medical practice. Jacobi, writing in the *New York Medical Journal*, claimed that he had found a letter authored by the company admitting that its Hammond product had no therapeutic value, and yet the company had still palmed it off to unsuspecting physicians.[492]

Parke, Davis & Co., which strongly suspected that Jacobi had been tipped off by their rival company, H. K. Mulford, issued a fierce and almost panicked response to rescue its reputation. According to the company, this letter had been read completely out of context. What had happened, the company insisted, is that it had made thyroid extract following Hammond's formular following "the demands made upon us" by doctors who had requested the substance. Parke, Davis claimed that it had always known this product to be faulty— (the

[491] There is ample evidence that physicians bought this thyroid extract starting in 1893. See physician reports and testimonials in *JAMA, American Medicine, Medical Age, Therapeutic Gazette, American Practitioner & News, Boston Medical & Surgical Journal, Philadelphia Polyclinic, New York Journal of Medicine, The Medical Record*, etc.
[492] See "Malice," *Therapeutic Notes*, March 1895, 9.

company had indeed written about it, in the letter that Jacobi had somehow obtained and misread)—and that it had issued the product to the doctors "under protest and warning." Parke, Davis claimed:

> We have not now, and never had, any interest in the marketing of Thyroid Extract. The small quantities sold by us were furnished as an accommodation to our friends and patrons. We never recommended the product for administration, and indeed repeatedly expressed without reserve our opinion of its worthlessness. The insinuation that we sought to exploit a worthless product, we repel with the utmost contempt.[493]

Regardless of whether Parke, Davis & Co.'s account of events is true, we can read here evidence that informal relationships existed between doctors and drug companies—where doctors could ask a drug manufacturer to prepare an extract for them individually. This was not an isolated event; I have found evidence that several American physicians approached the company (and other companies) throughout the 1890s with requests for the production of bespoke drugs for use in clinical experimentation—requests that the company was only too happy to oblige.[494]

Parke, Davis & Co. was clearly jumpy following the Hammond affair, but it had a reason to be: physicians were on the lookout for fraud, and Parke, Davis & Co. was keenly aware that only the most conservative approach would win the day with prescribing physicians. This not only affected the kinds of drugs it made, but also the timing of its production and marketing schedule. It would not do well for Parke, Davis & Co. to produce and market a product if the jury was still out in the medical community about whether that product was worth prescribing. The safest bet was to create a convenient pharmaceutical alternative to a raw extract that was already in wide circulation, such as suprarenal gland extract or thymus extract. To create a market for an entirely new drug, or to back a

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[493] "Malice."

[494] Some doctors made direct contact with the company, engaged in correspondence, formed alliances, and then submitted specific requests for the manufacturing of new drugs. Relationships between Parke, Davis & Co. and American physicians will be discussed at length in the following chapter.

controversial product, was simply not worth the risk. There is even evidence that Parke, Davis & Co. was reluctant to endorse creative adaptations made to its existing drug range: as I will further detail in the next chapter, it took some time for the company to approve the sale of an Adrenalin "ointment," which had been developed by an active member of the medical community, for the company was concerned that the new product would displease physicians accustomed to prescribing diluted Adrenalin solution.[495] Simply put, if market trend analyses are anything to go by, it seems Parke, Davis & Co. closely observed and followed physician demand, and were not yet in the business of creating demand by pushing new products.

In Search of a Better Drug: Physicians Go Corporate

If physicians were already accustomed to using raw extracts, either made by themselves or by other doctors, then what prompted them to make the switch to a commercial drug? Two key themes emerge from physician writings on this subject. The first was the painstaking and improbable labor that was required to produce glandular products, and the physician's ardent desire for a "convenient" drug. In the last chapter, we gained an insight into just how onerous it was for physicians to formulate glandular extracts, which involved extracting juices from raw animal tissue, among other tasks.

Perhaps physicians would not have minded going to all this trouble if the drugs they produced worked well in the clinic, but their self-prepared formulations often left them wanting. This was the case for a physician who wrote into *JAMA* in 1902 and explained that their use of Pankreatin—a commercial preparation from pancreas extract—was "even more effective than the gland substance, while far more convenient."[496] For other doctors, such as Herbert C. Moffitt, who was also frustrated with self-prepared preparations, it took some

[495] See "Houghton, E. M. – Henry G. Carleton. Correspondence Re: Adrenalin in Treatment of Neuralgia Including Testimonials. 1906-1907," July 1906, Box 400, Folder 28, SI, Parke Davis Collections.
[496] "Organotherapy of Pancreatogenic Fatty Diarrhea," *JAMA* 38 (March 1, 1902): 620.

shopping around commercial suppliers to find the right product.[497] At the meeting of the California Academy of Medicine, held in July of 1899, he shared his process of discovery with his colleagues:

> In regard to the form of administration [of thyroid extracts], I want to say a word. I have tried many methods and forms of preparation. The fresh gland is not reliable, for the butcher occasionally supplies some other gland. Parke, Davis, & Co.'s tablets I have used, but find them often unreliable. I have used them with excellent results, for a time, but when the supply ran out and a fresh lot had to be obtained, all evidence of thyroid ingestion ceased. They vary, thus, very largely. I find the tablets made by Burroughs, Welcome & Co. very much more reliable, and use them, now, altogether. The effect from them is constant, so far as my experience has gone.[498]

The second major theme in physician writings, already hinted at by Crary and Moffit, which led doctors to manufacturing firms, was their desire for standardized glandular products. Doctors working on glandular products were interminably frustrated with non-uniform preparations, which they found to be unreliable, ineffective and difficult to prescribe as an exact dose. This frustration was expressed from the very beginning of the glandular extract movement in America, and it informed doctors' decisions to shift from raw thyroid extracts to powdered extracts sourced from the market. In 1894, a Dr. G. T. Jackson told his colleagues at the American Dermatological Association that he "prefers to use the powder of desiccated thyroid in gelatine capsules, as that method allows for exact dosage, and assures the absorption of the medicament." He also added that it was "greatly cheaper than any glycerine extract" which is, surprisingly, one of the very few mentions that doctors made about the financial advantages of using commercial substances.[499] Another medical commentator, also in 1894, thought that handmade thyroid preparations were "utterly inert therapeutically," which he also said about any drug "made by maceration in glycerin, water,

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[497] Herbert C. Moffitt, "Thyroid Extract in Myxedema," *JAMA* 33 (August 12, 1899): 414–15.
[498] Moffitt.
[499] "American Dermatological Association: Thyroid Feeding in Diseases of the Skin," *Boston Medical and Surgical Journal* 131, no. 2 (July 12, 1894): 40. Jackson does not elaborate how commercial preparations were more viable—perhaps the time he saved on preparing fresh extracts could be given to (paying) patents.

and alcohol, possibly in connection with a little [boracic] acid."[500] The author added that "consequently those who desire to employ Thyroids medically have no recourse but to prescribe the desiccated powdered gland."[501] Another author, writing in 1895, stated simply and without explanations that "I have tried thyroid gland in pulverized form, and the Thyreodiin of Parke, Davis & Co., and greatly prefer the latter."[502]

But even doctors who did use powdered extracts were not saved from frustrations with accurate dosing and the effectiveness of treatment, as we learned from Moffitt. It was common for doctors to start their thyroid patients on very low doses of medications, and then to work up to higher doses, for fear of causing "irritation" to the patient.[503] For some physicians, such as Dr. T. Edes, even "capsules of dried thyroid" were ineffective for thyroid-related disorders, including exophalmic goiter, which led him to experiment with other animal extracts to help his patient, including extracts from the thymus gland and spleen.[504]

Physicians were thus aware that both doctors and drug companies struggled to create uniform biological products, especially when it came to wrangling fresh animal material and mixing it with unknown chemical properties. Yet, there was a still a vague sense amongst doctors that (some) manufacturers were more adept than doctors at achieving a standard (however flawed), especially when it came to processing large amounts of animal glands and tissue. This sentiment was expressed to the Association of American Physicians in 1897,

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[500] "Thyroid Extracts," *Medical Age* 12, no. 21 (November 10, 1894): 661.
[501] "Thyroid Extracts." The *Medical Age* was a Parke, Davis & Co. publication, and so it is not surprising to see this journal publishing accounts from doctors who derived handmade thyroid preparations and lauded powdered (commercial) products.
[502] "Therapeutic Benefits: The Treatment of Obesity," *Medical Age* 13, no. 11 (June 10, 1895): 347.
[503] For example, see S. J. Meltzer, "Myxoedema," *Medical Age* 14, no. 5 (March 10, 1896): 129–32. Meltzer wrote: "The powder was given in capsule, beginning with five grains daily for the first three days, and increasing the dose one grain every fourth day. This was, to be sure, a very conservative course, for in many reports we read even of ten grains and more being given three times a day as an initial dose. It must be borne in mind, however, that two cases of death have occurred during the course of treating with subcutaneous injections and although, so far as I know, no fatal results have as yet occurred from the administration of thyroid by the mouth, many writers speak of serious accidents from the use of large doses. I therefore preferred to advance cautiously…" (p. 131).
[504] Robert T. Edes, "Exophthalmic Goitre Treated with Animal Extracts, and Especially Extract of Thymus," *Boston Medical and Surgical Journal* 134 (January 23, 1896): 82–83.

when John J. Abel and Dr. William Osler from Johns Hopkins discussed their experiments with suprarenal products. They suspected the glands "furnished to the blood" something that made the blood-pressure rise but admitted that "the nature" of the secretion "could not be made out." Osler asked Abel if he had taken a look yet at "the commercial products on the market to see if this blood-raising product could be obtained." Osler himself had achieved no good effect from treating his Addisonian patients with "suprarenal capsules," presumably of the fresh variety.[505] Abel responded that he "had not looked for a commercial product" but he "thought it was very likely that one could be obtained, for it was a very simple matter to take the suprarenal capsules from sheep and dry them and reduce them to powder."[506]

A "Stable" Drug: The Arrival of Adrenalin

Physicians' discourse about achieving "uniform" and "standard" glandular preparations, which appeared sporadically in the medical periodical literature in the 1890s, intensified in the wake of Parke, Davis & Co.'s release of Adrenalin in 1901. It was the first glandular product to be successfully distilled to its active, chemical parts—both inside and outside of manufacturing firms—and consequently, it was easily standardized by both chemical and biological assays. It had also been produced by chemists,[507] and was characterized by Parke, Davis & Co. as a "pure" and chemical drug, which contrasted starkly with the other glandular

[505] Osler does not state whether these "suprarenal capsules" came in the desiccated or fresh form, but typically this type of phrasing referred to fresh preparations.

[506] "The Chemical Properties of the Blood-Pressure-Raising Constituent of the Suprarenal Capsule," *Boston Medical and Surgical Journal* 136 (May 20, 1897): 492–99.

[507] The isolation of the active principles of the suprarenal glands was worked on independently (and collaboratively) by three chemists: John Abel at Johns Hopkins, Aldrich at Parke, Davis & Co., and Jokichi Takamine, who was a consultant with Parke, Davis & Co. with laboratories in New York. Takamine received the most credit for discovering the "pure" and isolated active principles, and his efforts were promoted by Parke, Davis & Co. See "Historical Highlights," 4. For an insider's scoop on Takamine's relationship to Parke, Davis, Co. at time of adrenalin's isolation, see Merker, Interview with Dr. Harvey Merker. Merker described him as technically a consultant of the company, with offices in New York, but someone who was around "a great deal" (p. 12). For information on the controversy that ensued between Takamine, Abel and Aldrich, see John Parascandola, "Abel, Takamine, and the Isolation of Epinephrine," *Journal of Allergy and Clinical Immunology* 125, no. 2 (February 2010): 514–17, https://doi.org/10.1016/j.jaci.2009.11.044; Mitsuo Ishida, *Hormone Hunters: The Discovery of Adrenaline* (Kyoto University Press, 2018); Brian B Hoffman, *Adrenaline* (Cambridge, Mass.; London, England: Harvard University Press, 2013).

extracts on the market, which now looked crude by comparison. Perhaps most importantly for the company, Adrenalin was proven to have remarkably potent vasoconstrictor and hemostatic effects, and this caught the immediate attention of doctors, who prescribed it widely and generally for all manner of remedies, but especially for asthma, hay fever and for use in operations as a coagulant and anesthetic (in conjunction with cocaine).[508] Following Adrenalin's release, approximately fifty percent of entries about glandular products that appeared in medical periodicals were about the new Adrenalin chloride and like products, and this intense interest in the drug was maintained throughout its first decade on the market.[509]

What was foregrounded in this significant body of Adrenalin literature was both discussion about the effects of the drug, which almost all commentators agreed was powerful, and also its mode of production. Indeed, from some physicians' writings, we get the sense that they were just as interested in Adrenalin's status as a "stable" preparation as they were in its efficacy in treating patients. Take, for example, Dr. Albert Bulson from Fort Wayne College of Medicine, Indiana, who wrote into *The Medical Age* in 1901 about his experiments with samples of Adrenalin chloride, sent to him (and other doctors) by Parke, Davis & Co.[510] He found Adrenalin to be useful in a number of maladies, including ear infections, inflammation, hemorrhage, and found it to be a potent hemostatic in minor operations. But what impressed him most was how "stable" it was as a drug. He marveled

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[508] Some doctors conducted an extraordinary number of experiments to test its efficacy, such as Dr. Dudley S. Reynolds of Louisville Kentucky who performed 1, 222 experiments on patients suffering various eye complaints. See: Dudley S. Reynolds, "The Therapeutic Value of Adrenalin Chlorid," *American Medicine* 2 (July 6, 1901): 32–33. See also Dr. Kaplan's experiments in: "Adrenalin Chlorid in Asthmatic Attacks," *American Medicine*, May 20, 1905, 832.

[509] Articles typically concerned the use of Adrenalin as a haemostatic, such as this article: Charles A. Elsberg, "Some Remarks on the Use of Adrenalin as an Addition to Solutions for Local Anesthesia," *American Medicine* 3 (March 1, 1902): 355–56.

[510] Albert E. Bulson, "The Use of Adrenalin Solutions," *The Medical Age* 19, no. 11 (June 10, 1901): 409–13. It is unclear from the source material whether Bulson requested samples, or if Parke, Davis & Co. sent them without solicitation. I would wager that it was the latter, especially given that Bulson was based in Detroit, close to Parke, Davis & Co, likely had connections to the University of Michigan, and because he said that "these solutions were recommended to me, as to many others to whom they were sent…" Note also that *The Medical Age* is a Parke, Davis & Co. publication, and so it is not surprising to see the journal publishing positive comments by doctors about Adrenalin.

that Adrenalin was "fairly permanent for a prolonged length of time" by which he meant it did not deteriorate when unstoppered, like desiccated extract was known to do, especially when it was mixed with solution. Bulson said the "permanency" of the preparation was "a great point in [its] favor."[511]

> The fact that these solutions are uniform in strength, do not have to be freshly prepared each time, do not have to be filtered or sterilized, and are permanent for even a few weeks, is sufficient to warrant me in advocating for their use in preference to the ordinary suprarenal gland solutions that we have heretofore been accustomed to using.[512]

He continued to state that the new Adrenalin chloride meant that physicians no longer had to "deprive [themselves] of the beneficial effects of suprarenal gland solutions because of the inconvenience and time required to prepare fresh solutions each time the substance is used,"[513] suggesting that he, too, was irritated by the labor-intensive nature of using fresh preparations.

Another physician, writing into the American *Practitioner & News* in 1901, and who successfully used the drug to treat hay fever, thought Adrenalin gave physicians more "certainty." He said: "Until the chloride of adrenaline made its presence on the market, other preparations were handled with difficulty and probably with some uncertainty. The chloride, however, seems to be uniform in its action, and can be relied upon. Its power to blanch the mucous surfaces is certainly very great."[514] Dr. Emil Mayer, also writing in *American Practitioner & News*, applauded the drug. [515] Reflecting on the old suprarenal gland preparations, he wrote: "Its instability, the involved method of preparation, its unsightliness, and the inexactitude of its various strengths tend to make us welcome a preparation that is

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[511] Bulson, 411–12.
[512] Bulson, 412.
[513] Bulson, 409.
[514] Anon, "Adrenaline, The Hay-Fever Subjects' Friend," *American Practitioner & News* 31, no. 12 (June 15, 1901): 479–80.
[515] Emil Mayer, "Clinical Experience with Adrenalin," *American Practitioner & News* 31, no. 11 (June 1, 1901): 435–37.

exact, stable, and, above all, clean."[516] Beaman Douglass was still using desiccated suprarenal extract in 1903, perhaps out of habit, but he admitted that "the most reliable preparation of suprarenal gland is adrenalin chlorid[e]."[517]Another physician, Schweintiz, said that both the old suprarenal extracts and the new Adrenalin chloride gave him "equally good results" but thought that the new drug had "the advantage of being more easily sterilized," presumably because it did not contain desiccated animal tissue.[518]

With the release of Adrenalin by Parke, Davis & Co., physicians had their first real taste of a glandular product that was routinely effective and easy to use, and it left them wanting more. They even started to turn against their beloved thyroid preparations, which had spent so long as the leading product of the glandular product drug industry, evidenced by increasingly critical commentaries about the drug's lack of "uniformity" and "purity."[519] Adrenalin was so reliably uniform, so stable and so *unlike* the other glandular products on the market that it simultaneously gave doctors more confidence in what a manufacturing company could produce—how could it not, after getting one's hands on Adrenalin?—and less confidence in the drugs that were currently circulating on the market. A raw extract or even desiccated extract would no longer do. The task that remained for doctors after the 1901 launch of Adrenalin was to further understand the drug, including how it was produced and how it should be used in the clinic.

For some physicians, better understanding Adrenalin meant getting closer to Parke, Davis & Co. as the manufacturer.[520] In June 1901, over a dozen ear, nose and throat doctors

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[516] Mayer, 435.
[517] "Suprarenal Extract," *American Medicine* 5 (May 16, 1903): 799–800.
[518] "The Suprarenal Gland in Ophthalmic Practice," *American Medicine* 5 (January 3, 1903): 40.
[519] For example, see: "The Physiological Effects of Extracts of Ductless Glands," *American Practitioner & News* 32, no. 2 (July 15, 1901): 71. Heinrich Stein, "Untoward Effects of Thyroid Medication and How to Forego Them," *American Medicine* 16 (January 1910): 11.
[520] The arrival of Adrenalin was not the first time that physicians made direct contact with the higher ups at Parke, Davis & Co. See Solomon Solis-Cohen, "The Therapeutic Properties of Animal Extracts," *The Philadelphia Polyclinic*, 1893, 309–18; Edes, "Exophthalmic Goitre Treated with Animal Extracts, and Especially Extract of Thymus"; Merker, Interview with Dr. Harvey Merker, 19; "A New Thyroid Preparation,"

invited Jokichi Takamine, the celebrated co-discoverer of Adrenalin and consultant to Parke, Davis & Co., to speak at the annual meeting of the American Laryngological and Rhinological and Otological Society conference, which took place in New York.[521] Takamine clearly knew some of the doctors, and had provided at least one of them, a Dr. Stucky from Kentucky, with "powder" the year before to aid his experiments in the clinic.[522] Before he stood up to speak, Takamine listened carefully to the discussion in the room about Adrenalin, which mostly included anecdotes about some quite alarming side effects such as the "intolerable pain" experienced by one patient, and the "violent sneezing" experienced by many patients who had sniffed the drug up their noses to treat symptoms of hay fever. Some of this sneezing could last up to ten or twelve hours, reported one doctor. Another doctor, a Dr. Myles from New York, shared an unfortunate story about how Adrenalin had backfired in one of his hay fever patients who "wanted to have his nostrils clear as he expected to have a good deal of talking to do" the following day at work. After inhaling the Adrenalin, however, "[the patient's] wife had to sit up with him all night and he was unable to attend to 7 important committee meetings which he had down for the following day." According to Dr. Myles, this experience "had caused [the patient] to lose some of his faith in the drug."

In his speech, Takamine thanked those present for the opportunity to speak and said that he was "well pleased with the way in which the drug had been discussed." As for the unfortunate side effects, he stated that from a chemical point of view he was "at a loss to understand why it should have had the irritating effect it had." He then deferred to the

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The Journal of the Alumni Association of the College of Physicians and Surgeons, Baltimore 15, no. 1 (1912): 32; Augustus A. Eshner, "Progress in Organotherapy," *The Philadelphia Polyclinic* 5, no. 27 (July 1896): 261–66. Similarly, there is evidence that Parke, Davis & Co. made direct contact with physicians in this period, too, through letters of correspondence and through sending drug samples. For example, see E. Fletcher Ingals, "Notes on Adrenalin and Adrenalin Chlorid," *JAMA* 36 (April 27, 1901): 1155–57. This will be further detailed in the next chapter.

[521] Norton Wilson, "Clinical Notes on Adrenalin," *American Medicine* 1 (June 1, 1901): 382–83, 437–38. Including Wilson, fifteen physicians are mentioned in this paper. Possibly, there were more physicians in attendance at this meeting who did not get recorded in the meeting minutes.

[522] Possibly this was pre-market material, sent by Takamine to Dr. Stucky for clinical experimentation on "Dec. 1" of 1900. See Wilson.

professional expertise of the doctors present, saying that "it depended on the members of the medical profession to decide how and when the drug should be used, and in what strength." What the manufacturer could do, he suggested, was to offer a drug to the medical community "in the pure form of chemical crystals," which he reminded his audience was the first time such a feat had been achieved in the realm of organotherapy.[523]

That same year, at the section on Materia Medica, Pharmacy and Therapeutics at the Annual Meeting of the American Medical Association, Takamine again appeared as an invited guest and speaker, and so did Dr. McClintock and Dr. Houghton from Parke, Davis & Co.'s biological laboratory. It was the "Organotherapy" symposium, and McClintock was slated to open it with his paper entitled "the Mode of Manufacture of Serums and Organic Extracts." He did not attend as planned, and nor did Solis-Cohen, who had intended to present on "The Theory and Practice of Organotherapy." Nonetheless, a robust discussion still took place between Takamine and Houghton, who presented separate papers on Adrenalin, and a number of doctors, including Dr. Sydney Kuh, of Chicago, who gave a paper on pituitary glands, and Dr. John M. Dodson, also of Chicago, who gave a paper on thymus extracts. Dr. Victor Vaughan of the University of Michigan was also present, which is not surprising given his longstanding relationship with Houghton and McClintock, and he presented a paper on the advances of pharmacology which he thought "was certainly becoming a science" following the efforts of investigators such as Takamine.[524] He also shared his own results of using thyroid extract and Adrenalin in the clinic which he claimed had produced "extraordinary results."

In the discussion that followed, doctors asked each other questions about the correct dosage of Adrenalin, whether it was toxic to patients, and if it could be tolerated in the

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[523] Wilson, 437.
[524] "American Medical Association, Annual Meeting at St. Paul, Minn. June, 1901. Section on Materia Medica, Pharmacy and Therapeutics, Third Day," *JAMA*, June 1901, 540.

stomach. Houghton and Takamine were called on by the doctors to answer these questions, but the Parke, Davis & Co. representatives had little to contribute. They freely admitted that their clinical knowledge of the drug was limited to what could be uncovered through further experimentation by practicing physicians. Possibly buoyed by Takamine and Houghton's deference to physician expertise, the doctors present stepped in to offer each other insights from their own clinical investigation, including Dr. Vaughan, who gave anecdotal evidence that one of his patients had been successfully treated for hemorrhage of the bowel, and stayed with Adrenalin tablets for three months "without any apparent untoward effects."[525]

What we see in this source material is not only the physicians' ongoing quest to learn more about Adrenalin and other organic extracts and how they could be effectively deployed in the clinic, but also an emerging dialogue between them and Parke, Davis & Co. Where earlier in the glandular extract movement—especially in the early 1890s—doctors had relied on each other to build new knowledge about glandular extracts, by 1901 we can see them reaching out to the company for answers and, importantly, inviting executives into privileged professional spaces including the AMA. Takamine, Houghton and McClintock were invited to these meetings as presenters and were regarded by the doctors as experts in chemical drug production. This is a striking development in the medical community's attitudes toward druggists and speaks not only to the changing role of ethical manufacturing firms in American medical enterprise,[526] but also to the improving capabilities of high-end drug firms such as Parke, Davis & Co to provide American physicians with what they wanted. Parke, Davis & Co. executives were invited to the table for discussion because the company was adept at speaking the language of physicians—especially on matters of the sterility, stability, and purity of drugs—and had developed a glandular product that was indisputably powerful.

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[525] "American Medical Association, Annual Meeting at St. Paul, Minn. June, 1901. Section on Materia Medica, Pharmacy and Therapeutics, Third Day."
[526] This cultural transformation is closely investigated in Gabriel, *Medical Monopoly*.

Another striking theme that emerges from this source material concerns the labor of drug production and the labor of clinical testing. As participants at these meetings saw it, it was the job of Parke, Davis & Co. to produce the pure crystalline form of Adrenalin, and up to doctors "to decide how and when the drug should be used, and in what strength."[527] This partitioning of manufacturing labor from clinical testing, and its reallocation to the drug company, is a remarkable development for, as we know, in the early 1890s, doctors had performed both tasks as an integrated whole. As we saw in the last chapter, doctors would move between their workshop bench where they made drugs, and the clinic where they treated patients, making quick adjustments to drug dosage and drug design on the fly and in response to patients' clinical presentations.

Adrenalin, however, was a different kind of drug. In their discussions of Adrenalin, doctors knew that they were in the presence of the "next-gen" of glandular products: "pure" and chemical drugs that they were incapable of producing in clinic. Indeed, as Parke, Davis & Co. would later explain in promotional material, it took between 10,000 and 15,000 head of cattle to produce just one pound of Adrenalin—a manufacturing feat that was extraordinary and entirely beyond the capacity of any one individual or small organization.[528] Whether they liked it or not, physicians who wanted to work with Adrenalin were forced to give up their control over the drug production process, and to trust that Parke, Davis & Co. was as ethical and scientific as it claimed to be.

Conclusion: Less is More

As the culture of mortar-and-pestle drug manufacturing was slowly and consciously phased out of medical practice, and the company emerged as the primary producer of glandular products, there was a marked decrease in the diversity of glandular products that got

[527] Wilson, "Clinical Notes on Adrenalin," 437.
[528] "Parke, Davis & Company (History)," 6.

prescribed by doctors. In the 1890s, all manner of glandular products were being trialed and tested in the clinic, from lung tissue to brain tissue to Brown-Séquard's testicular injections. By 1910, however, this colorful and controversial range of drugs had been whittled down to just a few commonly prescribed therapies: desiccated thyroid extract, Adrenalin and, to a lesser extent, ovarian and pituitary extracts.[529]

This more limited usage of glandular products ca. 1910 makes sense if we recall the distance that had been travelled since the early 1890s and, especially, the relationship that had started to evolve between American doctors and, at the very least, Parke, Davis & Co. As physicians increasingly turned to the company for commercial preparations and gave over the responsibility of drug production to the manufacturing firm, they also gave up their capacity to creatively produce new drugs themselves, in the clinic, with their bare hands, their mortar-and-pestle, and their connection to animal industries. This meant that if they wanted to trial a new drug, they would either need to dust off their old skills as DIY manufacturers—a phenomenon that appears to happen less and less after 1900—or rely on the manufacturer to create a new drug for them.

We also know, however, that Parke, Davis & Co. made drugs conservatively, with restraint, and only with the backing of the medical community. While the company did oblige some requests for bespoke products in deference to special relationships it maintained with some doctors, its primary task, as the company saw it, was to identify existing drug markets and focus on producing high-quality pharmaceutical preparations that matched the needs and expectations of these markets. By an implicit rule, the company avoided controversial drugs. These market forces, which shaped both the company's willingness to produce only some kinds of drugs, and the doctors' *un*willingness to expend unnecessary labor in the preparation

[529] There were, of course exceptions to this rule, but for the most part, one mostly sees these four drugs in common circulation in orthodox practice.

of glandular drugs, resulted in a constriction of the available drugs on the market, and a more intense focus on the fewer drugs that had robust medical and commercial backing.

Yet, despite what might have been lost in drug diversity, and in physician control over the drug production process, something was gained in the process. Doctors seemed to prescribe fewer glandular drugs with more confidence and consensus than they ever had under the old regime of using "fresh" preparations. In this sense, we might even credit the rising influence of ethical manufacturing firms, such as Parke, Davis & Co. in the glandular product market as a much-needed stabilizing force on the still-developing field. But at the same time, we should also credit doctors too: they were the ones who demanded better and more convenient drugs, identified better products on the market than they could have made themselves, and realized that outsourcing drug manufacturing labor could be a boon for the still-developing field. We should also credit them for the oversight they continued to have over drug production and Parke, Davis & Co.'s product line. As the next chapter will fully explore, doctors remained very much involved in the drug production process in the early twentieth century, albeit in a different form to the glandular extract movement of yore.

Chapter 5: Working with the Company: Parke, Davis & Co., American Doctors, and the Co-Production of Glandular Products, 1900-1919

In the early 1890s, Charles Brown-Séquard struggled with a key question that concerned, and threatened, the future of the glandular therapeutics' movement. Who or what would produce high-quality and reliable glandular products, if not the government or capable and charitable medical scientists, such as himself and his assistant Jacques Arsène d'Arsonval? At issue for him was the relationship between "science" and "commerce." As a nineteenth-century savant with traditional values, he thought that profit-seeking in science was improper and went against a core professional principle that he abided: disinterestedness. This is why he repeatedly declined offers from invested parties, and suggestions by his own confidants, to commercialize his laboratory and to sell his products to doctors.

American doctors initially shared Brown-Séquard's aversion to commercial manufacturers and commercial drugs, as Chapter 3 showed, and preferred to make their own glandular products by hand, using raw animal tissues and organs, and slow filtrations devices. Yet, beginning around 1895, doctors slowly began to turn to the medical marketplace for their supply of glandular drugs. By 1910, almost all doctors who used glandular drugs in the clinic opted for commercial preparations over physician-prepared formulations. They wanted a more convenient and better-quality drug than they could prepare themselves, and they found that both needs were met in preparations that were produced by ethical manufacturing firms, such as Parke, Davis & Co.

As this chapter will fully detail, American doctors' support for Parke, Davis & Co. grew stronger between 1900 and 1919 and extended beyond the simple consumer act of buying "P. D. & Co." They also started to help the company with clinical testing of glandular products that had yet to be launched on the market and, in the process, provided critical feedback to the company on products-in-development. It began informally and casually in the late 1890s, when "physician friends" of Parke, Davis & Co. conducted clinical tests of drugs

on the company's behalf.[530] The company's testing process quickly grew into a formalized and institutionalized system of clinical testing, such that there were hundreds and then thousands of American doctors from around the nation who helped the company trial new and experimental products, according to Parke, Davis & Co. estimates.

In the 1900-1919 period, American physicians tested for the company various iterations of Adrenalin (solution, extract, inhalant, ointment), [531] and pituitary gland extracts (both posterior and anterior pituitary lobes, in varying combinations),[532] the latter of which entered clinical trials in the early 1910s. From 1914 and 1915, general practitioners, obstetricians and gynecologists started trialing ovarian extracts for the company, which were intended to treat diverse conditions in women including amenorrhea and dysmenorrhea, menopause, and hysteria. There were also less popular drugs put out by Parke, Davis & Co. in this period and trialed by physicians, such as "pineal gland extracts" and "desiccated and defatted lymphatic gland extracts," although these never quite found a stable market and quickly disappeared from doctors' clinics and company records.[533]

Parke, Davis & Co. executives referred to doctors who tested their products as clinical "co-workers," denoting their status as colleagues and co-producers of pharmaceutical knowledge. Many of these physician co-workers were actively recruited into this work by company executives, including Drs. Elijah Houghton and Charles McClintock—two medical scientists, introduced in the previous chapter, who had strong connections to the University of Michigan. Some physician co-workers—many of whom were based at medical schools—

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[530] "Physician friends" and "friends of the House" were terms used my company executives, as this chapter will fully detail.
[531] "Biological Board Memo, 1904," 1904, NMAH.AC.0001_B394F29, SI, Parke Davis Collections.
[532] "Historical Highlights," 6.
[533] This system of clinical testing continued after Larned's sudden death in 1923 but it seems to have been superseded by a more manageable system of clinical testing with a smaller number of medical men who were either "outstanding clinicians" in private practice, connected with "prominent" hospitals, or were teachers in "leading universities and medical schools." See Walter M. Chase to Dr. Lescohier, "Department of Experimental Medicine, Its History and Development," March 22, 1937, NMAH.AC.0001_B397F52, SI, Parke Davis Collections.

were the instigators of company-sponsored drug trials and approached Parke, Davis & Co. with requests for experimental drugs and resources for testing.

Why were American doctors so heavily involved in Parke, Davis & Co. operations in the first two decades of the twentieth century, and how did this involvement shape the emergence of endocrinology as a field of medical science? This final chapter of the dissertation reckons with these questions, which take us to the heart of two important trends that radically transformed the face of early-twentieth-century clinical endocrinology in America. The first was the pharmaceuticalization of the therapeutic field, as evidenced by the increasing popularity of commercial glandular preparations with prescribing doctors (as detailed in Chapter 4). The second and related trend, which is the central focus of this chapter, was the pharmaceuticalization of the American clinic, which manifested in hundreds and then thousands of American doctors working on behalf of the company by undertaking clinical testing of company drugs in their own clinics.[534]

These are two remarkable developments, especially when we reflect on how endocrinology began just a few decades earlier, with Brown-Séquard's and doctors' own aversion to commercial enterprise and commercial medicine. In the early 1890s, the trade in organic extracts was very much maintained by the singular initiative of doctors who wanted to experiment with the new therapeutic craze. Commercial druggists were almost entirely absent from early efforts to make new drugs and trial them in patients. By the first decade of the twentieth century, however, the ethical manufacturer had, unequivocally, become a major actor in developing glandular products, the drug trade, and the clinical field, as this chapter will fully detail. How can we make sense of this historical change, which concerns both the

[534] My thinking about the pharmaceuticalization of the American clinic through clinical trials has been inspired by Gabriel, "The Testing of Sanocrysin." See especially pp. 631-2, where Gabriel writes that "...the trial should be understood as an important turning point in the pharmaceuticalization of medical science itself, that process whereby questions of health and illness are increasingly understood through the framework of goods manufactured and sold for the pursuit of private profit."

rise of corporate infrastructure in American medicine, and the transformation of physicians' expectations about how new glandular drugs should be produced?

The transformation of physicians' general attitudes toward ethical manufacturing firms and their products, writ large, might not come as a surprise to historians of pharmacy. They have long-noted both the rising influence of such firms at the turn of the century, and American physicians' slow (and in some cases reluctant) embrace of a pharmaceutical model of drug production, as detailed in the introductory chapter.[535] That the same physicians who decried commercial preparations in the early 1890s came to patronize commercial manufacturers in the early 1900s is a compressed version of a wider transformation that was underway in the American medical community in the second half of the nineteenth century and first decades of the twentieth. This has been carefully and convincingly expounded by historian Joseph Gabriel, who tracks the American medical community's slowly changing views on the role of commerce in medicine, and especially the system of patent protection for drugs and drug processes. Gabriel shows that American doctors, who in the mid-nineteenth century rejected pharmaceutical companies as unscientific and unethical operators, had by the interwar period become fully integrated in American medical practice.[536] This was not just because ethical manufacturers got better at marketing themselves to the medical community as "scientific" actors, and improving their drug production capabilities such that they could produce effective "scientific" medicine for use by doctors. It was also occasioned by the arrival of new and effective drugs from Europe, namely diphtheria antitoxin, that were protected by patents.[537] This mounted a strong argument to American doctors that medicine produced by commercially motivated actors could be effective, scientific, and innovative.

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[535] Liebenau, *Medical Science and Medical Industry*; Gabriel, *Medical Monopoly*; Gabriel and Holman, "Clinical Trials and the Origins of Pharmaceutical Fraud."
[536] Gabriel, *Medical Monopoly*.
[537] Gabriel; See also Gabriel, "A Thing Patented Is a Thing Divulged."

What is surprising, however, and what we need to learn more about, is how very involved American doctors were in the process of commercializing scientific medicine at the turn of the century. The history of clinical endocrinology reveals that doctors were not just consumers of commercial drugs between 1900 and 1919. They were also producers of it, and actively built personal and professional relationships with ethical firms, such as Parke, Davis & Co. As I show in this chapter, doctors and Parke, Davis & Co. were jointly invested in transforming American endocrinology from the artisanal, physician-led enterprise that existed in the 1890s, into a massive pharmaceutical operation with an influence that came to be felt in every clinic across the nation.

Productive relationships between company and clinic were critical to developing clinical endocrinology as a field of medical science.[538] No American physician could practice gold standard glandular therapeutics in the early twentieth century without relying on commercially produced drugs, and no commercial glandular product could enter the American clinic without the medical community's endorsement. This co-dependency was recognized by Parke, Davis & Co. and American physicians alike, and it led to the widespread and sustained communication between them about how new glandular drugs should be developed for clinical use, and how they should be marketed.

Yet, as this chapter demonstrates, the relationship between company and clinician was complicated and needed careful management. Physician-collaborators were still customers, after all, and Parke, Davis & Co. was careful to only represent its best self to its "co-workers." Company records from Parke, Davis & Co. help reveal some of these complexities, as well as the details of how corporate drug trials were organized and operationalized in the

[538] My thinking about the collaboration between physicians and Parke, Davis & Co. has been shaped by a literature that examines such collaborations in the interwar period in America. See Swann, *Academic Scientists and the Pharmaceutical Industry*; Parascandola, "Industrial Research Comes of Age: The American Pharmaceutical Industry, 1920-1940"; Rasmussen, "The Drug Industry and Clinical Research in Interwar America."

early twentieth century.[539] It is to these company records that I now turn, to uncover how Parke, Davis & Co. first engaged physicians to help make drugs. In the section below, I describe how Parke, Davis & Co. began clinical testing with a local network of trusted friends, which broadened as the company expanded. Next, I show how Parke, Davis & Co. institutionalized the clinical trial and developed a system of seeking feedback from physicians across the nation. In the last section, I offer the physicians' perspective by showing some of the medical personnel who became involved with the company between 1900 and 1920, and detailing what led them to Parke, Davis & Co.

Soliciting Friendly Feedback: Early Drug Trials at Parke, Davis & Co, 1889-1901

"Cooperate with the Physician," instructed a page-length Parke, Davis & Co. advertisement that appeared in the June 1910 edition of the *Practical Druggist,* a New York-based periodical read by druggists, pharmacists, and those who worked in pharmaceutical manufacturing.[540] This direct and almost imperious headline, written as an instruction from the Detroit-based drug company to owners and employees of drug stores, was followed by a revealing subtitle that left little room for misunderstanding: "It will mean prestige, business, profit." In this unusually brash Parke, Davis & Co. advertisement, which was intended for druggists-retailers and not physician-customers, the company revealed the cornerstone of its business model and the secret to its success as the largest manufacturer of ethical drugs in America in the early twentieth century: physicians. Parke, Davis & Co. needed physicians to

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[539] This apparent neglect of the corporate clinical trial is true even for literature that specifically addresses the rise of the clinical trial in early twentieth-century America. For example, Harry M. Mark's *Progress of Experiment*, which is still regarded as the authoritative account on early twentieth century clinical trials in the U.S., fails to mention the work done by drug companies in this period. See Marks, *The Progress of Experiment*. Marks does come closer to the corporate drug trial in a 2006 article on "collective [clinical] investigations" conducted in turn-of-the-century Britain and America. He claims that trials were coordinated by "…local medical societies, national specialty groups and at least one drug company," but does not elaborate further on which drug company this was, and how they managed the trials. See Marks, ""Until the Sun of Science … "," 148–49.

[540] "Advertisement: Co-Operate with the Physician," *Practical Druggist and Review of Reviews*, June 1910, 3.

buy its products, and it also needed to "cooperate" with physicians to make this happen. It was a message the company reiterated again in this *Practical Druggist* ad, apparently for good measure: "Co-operate with the physician. Supply our standardized products…to do so will strengthen the faith of the physician in the value of your merchandise…it will bring business to your store. It will multiply your profits."[541]

What Parke, Davis & Co. took pains to communicate in this advertisement is that orthodox physicians, and orthodox physicians alone, kept the ethical drug trade afloat. Unlike patent manufacturers, who attempted to sell and advertise their products to both patients and doctors alike, Parke, Davis & Co. were constrained by the medical community's expectation that an "ethical" manufacturer would only advertise and sell products to doctors. It was part of an informal but quite rigidly policed code laid out by the AMA at the turn of the century that to sell or advertise to those outside the profession would be an action of "profit-seeking," which was regarded as incompatible with the production of high-quality scientific medicine.[542]

To remain in the good books of the American medical community, and to retain their status as "ethical" manufacturer, Parke, Davis & Co. thus had to resign itself to a physicians-only customer base.[543] Instead of seeing this as severely limiting to the growth of their company, Parke, Davis & Co. interpreted it as an invitation to create a medical monopoly.[544]

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[541] "Advertisement: Co-Operate with the Physician."
[542] Gabriel, *Medical Monopoly*.
[543] There is strong evidence in the Parke, Davis & Co. archives that the company routinely declined sale of their products to non-medical people. For example, Dr. A. W. Lescohier, a company executive, declined to sell pineal gland products to a military man because he was not a doctor. Lescohier explained to this person that Parke, Davis & Co. only do business with medical professionals and members of the drug trade. See A. W. Lescohier to Mr. A. F. Luedke, "Declining Sale," June 21, 1915, NMAH.AC.0001_B413F21, SI, Parke Davis Collections. A similar letter survives in the Parke, Davis & Co. collections, this time from 1915 to a Mr. Overland who wanted to self-treat with pineal gland product. Lescohier declined his request. See A. W. Lescohier to Mr. Obert Overland, February 16, 1915, NMAH.AC.0001_B413F21, SI, Parke Davis Collections. For yet another letter penned by Lescohier to decline sale of pineal gland to a non-medical person, see A. W. Lescohier to H. B. McAllister, January 26, 1915, NMAH.AC.0001_B413F21, SI, Parke Davis Collections.
[544] For more detail on the plight of the "ethical" manufactuer, see Gabriel, *Medical Monopoly*.

If it could exclusively tend to the needs of orthodox physicians, abide by their rules, and win both the recognition and favor of the medical community as top-end ethical manufacturers, then the company would be well on its way to securing a mandate, granted by doctors themselves, to produce and sell high-quality drugs.

It was in this spirit of "cooperating" with the physician—and so securing their approval and business—that Parke, Davis & Co. first developed an informal system in the 1880s of sending new and experimental drugs to physicians for testing and appraisal. In a recent and compelling piece by Joseph Gabriel and Bennett Holman, we learn that it was industry reformer Francis Stewart who was one of the first to plant the seeds for corporate-sponsored drug trials at Parke, Davis & Co.[545] To improve relations between company and clinician and "to harmonize the interests of science and commerce,"[546] to use Stewart's words, the company sent free samples of new drugs to physicians working in hospitals with an invitation to evaluate the drugs for clinical utility before they went to market. Products were sent to doctors as a gesture of transparency; doctors got to, in effect, peek behind the veil of the drug production process and shape the conversation about how the drug was made. If it was good enough, in the estimation of the clinicians who did the testing, the drug would be put on the open market and doctors could have confidence in the product. If the product was bad, then it could be sent back to the manufacturing house for development. Both positive and negative feedback was highly valuable for Parke, Davis & Co., who strove to market products that were physician-approved. It was also a boon for the clinician, who wanted clinical efficacy in a drug and a product they could trust.[547]

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[545] Gabriel and Holman, "Clinical Trials and the Origins of Pharmaceutical Fraud." See also Chase to Lescohier, "Department of Experimental Medicine, Its History and Development," March 22, 1937.
[546] Gabriel and Holman, "Clinical Trials and the Origins of Pharmaceutical Fraud," 546.
[547] Gabriel and Holman, 546. According to Gabriel and Holman, the "hospital plan" came with Parke, Davis & Co.'s promise that both good and bad results would be published in working bulletins and distributed to the medical community. For more context on the late nineteenth-century culture of seeking collective feedback from physicians, see Marks, ""Until the Sun of Science … "."

Who were the doctors that tested Parke, Davis & Co. drugs, and what feedback did they give? How were they recruited into this role, and how did the company use their feedback? A cache of company correspondence that survives from 1897-1901 suggests that local networks in Detroit, and especially personal contacts of company executives, were crucial to getting clinical testing off the ground. This correspondence was mostly generated by McClintock and Houghton, who had earlier worked as junior faculty at the University of Michigan's Medical School before taking up research and management jobs at Parke, Davis & Co. McClintock and Houghton were actively encouraged by their academic mentors to give up their university work in favor of new opportunities at the manufacturing firm, which promised an environment in which the young medical scientists could pursue their academic interests without restraint and positively influence the medical community.[548]

McClintock and Houghton kept in touch with their mentors at the University of Michigan while they worked at Parke, Davis & Co., and asked them to do clinical testing of drugs in development. In 1899, for example, Houghton asked his former mentor Professor Arthur R. Cushny, Chairman of Pharmacology, to help test Chloretone—a mild anesthetic that was suspected of having broad pain-relieving properties.[549] Houghton worked closely with Cushny before coming to Parke, Davis & Co, and collegiality and even friendship is evident in their letters. Cushny wrote: "Many thanks for your kind letters and for the Chloretone, which arrived in good order. It is such a beautiful specimen, that I am loathe to

[548] See "Biological Therapy-- Historical Sketch," 1914, NMAH.AC.0001_B397F10, SI, Parke Davis Collections; "Houghton, Smith and Others. Controversy over Dates of Research on Biologicals. Gives Other Historical Dates. 1923-1925.," May 1923, NMAH.AC.0001_B397F28, SI, Parke Davis Collections. In one of the letters in this series of correspondence, Houghton wrote about his arrival at Parke, Davis & Co. "I considered the matter carefully with Dr. Cushney [sic], Professor of Pharmacology, my chief, Dr. Dock, Dr. Novy, and Dr. Vaughan, and they advised me, if arrangements could be made, to come to Detroit, as they believed that there was an opportunity for serving the medical profession, provided Parke, Davis & Company gave Dr. McClintock and myself a free hand to conduct a biological laboratory covering both bacteriology and pharmacology…" (p. 15 and 16 of PDF).

[549] There is also evidence that Houghton and McClintock read and commented on draft scientific papers shared with them by scientists in the University of Michigan Pharmacological Laboratory. See "Wallace and Mogk – 'The Cardinal Action of Suprarenal Extract' – University of Michigan Pharmaceutical Laboratory, 1899," 1899, Box 406, Folder 26, SI, Parke Davis Collections.

break upon it. I have taken to giving five solutions, as you suggest, with excellent results."[550] Cushny also reported that it could be used in smaller quantities over a long period of time. Had Houghton tried this, Cushny wondered? Houghton, whose interest was piqued, sent back lower doses of Chloretone to Cushny so that he might conduct some more trials.

Houghton and Cushny wrote each other in tones that were warm and familiar: "Dear Houghton," Cushny wrote; "My Dear Prof. Cushny," Houghton replied.[551] A personal touch was important for getting new and experienced drugs out to trial, but so too was professional exchange. Houghton had been trying to acquire the professor some "loco weed," free of charge, to be used for experimental purposes, perhaps in thanks for Cushny agreeing to test Chloretone. When five pounds of it arrived in Cushny's lab, Cushny wrote back to Houghton with thanks and Houghton brushed it off as no bother. "Any time we can be of service to you in the way of supplying you with crude drugs, etc., we shall be very glad to do so." Houghton then offered to host him at the Parke, Davis & Co. campus. "The next time you come to the city, I shall consider it a great pleasure, if you will come out and visit the laboratory. Please let me know a little beforehand, and I will have proper arrangements made."[552]

Cushny did pay Houghton at least one visit, in August 1901, where they talked about the company's new wonder drug Adrenalin.[553] Earlier that year, Cushny had been helping Houghton work out whether Adrenalin could be ingested as a tablet for "internal use," which would be an extension from its normal use as an inhalant and topical solution.[554] Houghton, writing to his colleagues at the Parke, Davis & Co. office in Biltmore, admitted that he was

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[550] Arthur Robert Cushny to E. M. Houghton, "Experimental Work at the University of Michigan," November 30, 1899, NMAH.AC.0001_B404F28, SI, Parke Davis Collections. Underlined "Chloretone" in original.
[551] Cushny to Houghton.
[552] E. M. Houghton to Arthur Robert Cushny, "Experimental Work at the University of Michigan," December 1899, NMAH.AC.0001_B404F28, SI, Parke Davis Collections.
[553] E. M. Houghton to Arthur Robert Cushny, "Explaining Adrenalin to Doctors and Asking for Results in Its Use," August 6, 1901, NMAH.AC.0001_B406F40, SI, Parke Davis Collections.
[554] E. M. Houghton, "Explaining Adrenalin to Doctors and Asking for Results in Its Use," June 19, 1901, NMAH.AC.0001_B406F40, SI, Parke Davis Collections.

"extremely doubtful" that "internal administration [could be] followed by satisfactory results," and reported that Cushny was of the same opinion. Houghton added that Dr. Bates from New York did feel, however, that there was some potential in Adrenalin tablets which, in Houghton's mind, justified further experimentation and clinical testing.[555]

Dr. Victor C. Vaughan, the dean of the University of Michigan's Medical School and former supervisor of Houghton and McClintock, was another close and long-term informant of the company and conducted tests on their behalf.[556] In 1901 and early 1902, Vaughan had also been testing Adrenalin, like Cushny, and he found it quite effective in treating hemorrhoids. Houghton interpreted these results as evidence in favor of Adrenalin's efficacy in internal administration, but he remained cautious, given Cushny's bad results.[557] In a memo to his colleagues in February 1902, Houghton wrote that "at the present time there is considerable different of opinion among medical men" and that "more clinical experience is needed on this particular point." The company was certainly not yet in a position to "recommend" to doctors the subcutaneous injections of Adrenalin, wrote Houghton.[558]

Houghton was hyper responsive to his informants' opinions, which is why he was reluctant to recommend the internal use of Adrenalin to doctors when there was still uncertainty about its effect. This is also why he became very irritated when he learned through his network of local physicians that Vaughan was bad-mouthing another experiment drug and biologic, Nuclein, to local doctors.[559] Houghton complained about Vaughan in a

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[555] Houghton.
[556] I have evidence that Dr. Vaughan was still involved with the company in 1917, and even sent his son, who was an epidemiologist with the Detroit Board of Health, to advise the company. See Dr. W. E. King to E. M. Houghton, "Report on Progress in Biological Preparations. Oct. 9, 1917," 1917, Box 400, Folder 40, SI, Parke Davis Collections.
[557] E. M. Houghton to Parke, Davis & Co. (London), "Correspondence Re. Adrenalin Used for Typhoid Fever and Gastric Hemorrhages," February 6, 1902, NMAH.AC.0001_B400F24, SI, Parke Davis Collections.
[558] Houghton to Parke, Davis & Co. (London). Vaughan also tested "Nuclein" for the company in 1897.
[559] Nuclein was a pioneering immunotherapy developed mainly from yeast cultures. It was considered a biological, but its time in the sun was brief and was rarely used beyond 1900. See E. M. Houghton to Charles McClintock, "Re. Vaccine Production and Printing of Articles and Reports," May 10, 1897, NMAH.AC.0001_B400F17, SI, Parke Davis Collections.

letter to McClintock,[560] worrying about the effect it might have on the company's "physician friends" who might be turned off the drug before they had given it a chance in the clinic.[561]

Local physicians were critical stakeholders in Parke, Davis & Co.'s early clinical trials, which is why Houghton was so angry at Vaughan. Much more than individual faculty members at the University of Michigan,[562] it was Michigan-based doctors who did the most to provide feedback on new and experimental drugs that were produced by Parke, Davis & Co. The doctors to whom Vaughan was bad-mouthing Nuclein might have been Dr. Collins H. Johnston or Dr. Herbert Maxon King of Grand Rapids, who had been recently using the drug with "satisfaction." They along with "a number of physicians" were also testing Nuclein at the same time as Vaughan.[563] In fact, between twenty-five and thirty pounds of it had been

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[560] Houghton wrote: "Will say that I do not know just what purpose Dr. Vaughan has in stating to one or two of our physician friends that the new Nuclein would not prove satisfactory. When I talked to him he said he had only tried it on one patient and had then only given it to her for three or four days…" See E. M. Houghton to Charles McClintock, "McClintock's Article, Nuclein Exhibits," May 19, 1897, NMAH.AC.0001_B396F57, SI, Parke Davis Collections. This letter can also be found in Box 400, Folder 18 in the same collections.

[561] Houghton also objected to Vaughan's method of treating just one patient, which he found to be very unscientific. Clearly Vaughan did not realize the purpose of a trial in determining a drug's utility, wrote Houghton to McClintock. "I told him we did not propose to put this preparation on the market at present." See: Houghton to McClintock.

[562] I have evidence that at least four faculty members did testing for Parke, Davis & Co: Prof. Cushny, Prof. Vaughan, Dr. Novy and Prof. J. N. Martin. For details on Dr. Novy, see Charles McClintock to Mr. Swift, "The Work of the Department of Experimental Medicine," August 15, 1904, C38(a), Kremers Reference Files. For Prof. Martin, see E. M. Houghton to Prof. J. N. Martin, May 15, 1899, NMAH.AC.0001_B400F22, SI, Parke Davis Collections. In 1905, Dr. Cushny and Dr. Novy helped found the Council of Pharmacy and Chemistry at the American Medical Association, whose role it was to test "ethical" drugs for their chemical composition and strength. See "American Medical Association. Council on Pharmacy and Chemistry," *California State Journal of Medicine* 3, no. 4 (1905): 103–4." I also have evidence that Dr. Paul DeKruif advised the company in 1917 on serum production when he was in Ann Arbor. See King to Houghton, "Report on Progress in Biological Preparations. Oct. 9, 1917," 1917. Parke, Davis & Co. also worked with professors from the Michigan Agricultural College at Lansing. See "Additions to the List – Suggestions and Actions Taken, 1904-1927," multiple dates, NMAH.AC.0001_B396F67, SI, Parke Davis Collections. Doctors were prominent in company correspondence, but there is evidence that local public health officials, too, had a stake in Parke, Davis & Co.'s drug production. In a letter to McClintock in April 1897, Houghton reported, among other things, that "the Chairman of the Public Health Committee of the House of Representatives of Michigan is in town this afternoon and will visit our Laboratory tonight. The other members of the Committee will be here tomorrow." See Charles McClintock to E. M. Houghton, "Re. Progress Made on Vaccines and Business Company and Personnel," April 30, 1897, NMAH.AC.0001_B400F16, SI, Parke Davis Collections. See also correspondence between McClintock and William K. Jacques, who was the director of the diphtheria antitoxin staff within the Chicago Department of Health. See: "William K. Jacques. Letters to Dr. McClintock Re: Better Type Injection Mechanisms for Serums. October 1897," 1897, NMAH.AC.0001_B398F44, SI, Parke Davis Collections.

[563] Houghton to McClintock, "McClintock's Article, Nuclein Exhibits," May 19, 1897. This letter can also be found in Box 400, Folder 18 of the same collections.

sent out to local physicians in late April and early May of that year which, given the small weight of a liquid solution of a drug, might have amounted to dozens of doctors.[564]

We can glean insights into Parke, Davis & Co.'s early testing practices from surviving documents that record the names and addresses of doctors who received drugs around 1900.[565] One surviving list includes the names of approximately forty-five doctors and dentists who received Chloretone, most of whom came from Ann Arbor and Detroit, but with others based in Flint and Pontiac. About one third of the list comprised doctors from neighboring states and cities, including Chicago, Philadelphia, New York, and Madison, Iowa. Only one contact, a Dr. Chas W. Hoare, came from Canada, but he lived and worked just across the Detroit River in Walkerville, Ontario.

Physicians from the city of Detroit are overrepresented in the Chloretone list, and indeed in company correspondence generally, owing, no doubt, to McClintock and Houghton's strong ties to the local area. Not only was the Parke, Davis & Co. campus based in the outskirts of Detroit, but Houghton maintained an ongoing adjunct appointment at the Detroit College of Medicine, which was useful for making connections with medical professors and soon-to-be physicians.[566] Two of these Detroit-based physicians were Dr. W. N. Donald of Jefferson Ave who tested Chloretone for Houghton in 1889, and Dr. Mantaon who wrote to Houghton the same year requesting more information on the drug before running trials in his clinic. [567] Dr. Andrew Biddle was another of these Detroit physicians,

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[564] Houghton to McClintock, "Re. Vaccine Production and Printing of Articles and Reports," May 10, 1897.
[565] "Sample Chloretone Tablets--List of Names," 1899, NMAH.AC.0001_B404F27, SI, Parke Davis Collections.
[566] McClintock had been pressing Houghton to use his appointment at the Detroit College of Medicine to further the agenda of Parke, Davis & Co. In a letter to McClintock dated April 30, 1897, Houghton writes that "I have done all possible to further your cause in connection with the College," which seemed to relate to installing a "Professorship in Hygiene of Physiological Chemistry." See McClintock to Houghton, "Re. Progress Made on Vaccines and Business Company and Personnel," April 30, 1897.
[567] E. M. Houghton to Dr. W. N. Donald, "Re. Successful Use of Chloretone as a Hypnotic," July 12, 1899, NMAH.AC.0001_B404F20, SI, Parke Davis Collections. E. M. Houghton to Dr. W. P. Manton, "Detailed Information of Using Chloretone," December 15, 1899, NMAH.AC.0001_B404F29, SI, Parke Davis Collections. This apparently strong network of Detroit physicians, who were the first to receive experimental medicine from Parke, Davis & Co. were good for more than just experimental data and discretion. There is

who was asked by McClintock in 1901 to trial Adrenalin ointment for the treatment of skin conditions including rosacea. "Apparently this works on the skin in some such way as the aqueous solution does on the eye and mucous membranes." McClintock signed off with the usual line: "Please give it a trial, and let me know what you think of it."[568]

In addition to the obvious practical benefits of having drug samples sent locally to Detroit clinics rather than faraway locations, it was highly strategic for Parke, Davis & Co. to run drug trials close to home. It facilitated a system of quick medical feedback on experimental drugs, which allowed for new products to be revised and returned for testing, as we saw in the Houghton-Cushny correspondence. It also contained negative feedback about drugs to the local level. Parke, Davis & Co. could keep its finger on the pulse of these trials and quickly identify when things were going wrong. Local physicians were presumed to be more loyal to the company than others outside their network or, at the very least, sympathetic to the mission of Houghton and McClintock as hardworking individuals with local ties who were trying to create high-quality and reliable drugs.

What company documents also make clear is that Houghton and McClintock gave their "physician friends" wide latitude for experimentation and feedback about their drugs. In case of Adrenalin, they took physicians' lead on how it should be used in the clinic, what diseases it should be used to treat, appropriate dosing, and even on matters as trivial as the expiry date of the product. In a letter to Dr. Elwood, an ear, nose and throat doctor from Menominee, Michigan, who had been in touch with the company about Adrenalin, McClintock admitted that "Adrenalin is comparatively new and its limitations not made out. Those who have reported on it say that as long as it has not become pinkish in color it is

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evidence that they also supplied the House with contacts and experimental materials, including cultures of Hodgkin's Disease "baccilus" that was extracted from the "enlarged glands" of a small boy suffering from the disease in Detroit. See E. M. Houghton to H. M. Letton, "Correspondence Re: Experimental Vaccine for Hodgkin's Disease," August 9, 1915, NMAH.AC.0001_B407F25, SI, Parke Davis Collections.

[568] Charles McClintock to Dr. Andrew Biddle, "Explaining Adrenalin to Doctors and Asking for Results in Its Use," April 24, 1901, NMAH.AC.0001_B406F40, SI, Parke Davis Collections.

perfectly good…"[569] This letter came after earlier correspondence between Elwood and Houghton and McClintock,[570] in which Ellwood requested samples of Adrenalin chlorid solutions at two specific concentrations—1-1000 and 1-5000.[571] In a reply, Houghton informed Elwood that he did not have the 1-5000 solution available, and that Parke, Davis & Co. did not even "market" this strength, but he was curious enough about its effects to instruct Elwood how to make up this concentration and to encourage him with his experiments.[572]

Feedback about experimental drugs was solicited by Parke, Davis & Co. and provided by "physician friends" in letters that transitioned seamlessly between personal and professional content. Dr. Ellwood, for example, finished his letter to McClintock by asking if he wanted to come fishing with him in Michigan.[573] McClintock's reply, which confirmed that he would send Elwood Adrenalin as requested, included this friendly closing line: "Let me know in the Spring what you can offer in the way of fishing."[574] Similarly, Houghton wrote a long note to Dr. J. Z. Hunt of Lowville, of New York, about the chemical preparation and pharmacological effects of Chloretone, its popularity with "several physicians in Detroit," and a request that Hunt himself test the samples that Houghton had sent along with his letter. This otherwise professional and formal note began with an intimate salutation—"Dear Brother"—and concluded with details about Houghton's family life: "We are all well at home. Jennie and Ruth are preparing to go East about the middle of May. Hoping this will

[569] Charles McClintock to Dr. Calvin R. Elwood, "Explaining Adrenalin to Doctors and Asking for Results in Its Use," June 20, 1901, NMAH.AC.0001_B406F40, SI, Parke Davis Collections.
[570] The recipient of Ellwood's letters is not disclosed.
[571] Dr. Calvin R. Elwood to Charles McClintock, "Explaining Adrenalin to Doctors and Asking for Results in Its Use," February 22, 1901, NMAH.AC.0001_B406F40, SI, Parke Davis Collections.
[572] E. M. Houghton to Calvin Elwood, "Explaining Adrenalin to Doctors and Asking for Results in Its Use," March 16, 1901, NMAH.AC.0001_B406F40, Parke, Davis & Company Collections, Smithsonian Institution.
[573] Elwood to McClintock, "Explaining Adrenalin to Doctors," February 22, 1901.
[574] Charles McClintock to Dr. Calvin R. Elwood, "Explaining Adrenalin to Doctors and Asking for Results in Its Use," February 25, 1901, NMAH.AC.0001_B406F40, SI, Parke Davis Collections.

find you and Burton both well."[575] Houghton and McClintock's "physician friends" who provided critical and timely feedback on experimental drug were clearly real friends of the two men, and their correspondence reveals that their personal ties to physicians in the local area were expertly mobilized to get professional work done.

Houghton and McClintock's correspondence also reveals that they really did listen to physicians' feedback, and physicians really did have a hand in shaping drug development at Parke, Davis & Co. Negative feedback was enough to direct the course of the development and marketing of a new drug, as we saw with Houghton's investigation of Adrenalin. Positive feedback was received both as a green light for forging ahead with the drug as a commercial product, and excellent fodder for drug advertising. If enough positive reports were generated about a drug, then Houghton and McClintock could use them as evidence of the drug's merit as determined by the investigations of "selected physicians." [576] In some cases, specific physicians' names were cited to advertise a new product. One of these physicians was Dr. George F. Butler, who in 1899 was a professor of materia medica, therapeutics, and clinical medicine at the College of Physicians and Surgeons in Chicago.[577] Butler's positive experience with Chloretone led Houghton and McClintock to write him directly with a request that they use excerpts from his report to advertise Chloretone. Butler accepted with

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[575] E. M. Houghton to Dr. J. Z. Hunt, April 5, 1899, NMAH.AC.0001_B400F21, SI, Parke Davis Collections.

[576] In October 1889, after "some 30, 000 tablets" of Chloretone were successfully trialed by "selected physicians," Houghton contacted Mr. Warren, the General Manager of Parke, Davis & Co. to get the green light on marketing. When Warren signed off, Houghton then contacted J. C. Spratt, who oversaw the company's travelling salesman. Houghton said to Spratt: "We trust that you will rapidly get [Chloretone] before the profession," and urged him to use language surrounding the quantity of experiences and clinical trials that had been conducted by "selected physicians." E. M. Houghton to Mr. J. C. Spratt, "Campaign for Chloretone," October 24, 1899, NMAH.AC.0001_B404F24, SI, Parke Davis Collections. Houghton wanted Spratt to keep offering free samples to "wide-awake physicians who will properly use them and report their results," showing that even when a product was being marketed, Houghton was still keen to expand his network of testing physicians. I have been unable to identify Spratt's exact position within the company in the year 1899, but in 1907 he was the Manager of the Travelling Service of Parke, Davis & Co. and had 356 men under his "direct supervision." See "Greater New York," *The American Druggist and Pharmaceutical Record*, April 8, 1907, 210. Judging by the tone of Houghton's letter to Spratt in 1899, we can assume that Spratt held some managerial role of the traveling service around 1900.

[577] "Deaths," *Illinois Medical Journal* 40 (July 1921): 80.

reservations that his writing was not smooth enough for publication. But no matter, he said, because "I consider the substance a very good hypnotic indeed."[578]

Other times the company would simply allude to the thorough clinical testing that had been conducted by physicians, communicating both the trustworthiness of the product, and the support it had from "prominent" members of the medical community. For example, in a 1901 page-length advertisement in the *Therapeutic Gazette* for a new adrenal gland product that was mixed with Chloretone, the company stated that "many reports from prominent rhinologists and others claim immediate relief in the treatment of Hay Fever with this remedy."[579] It went on to say that it could be "used practically on every mucous membrane" but that it is "especially recommended [by doctors] in inflammation of the nose, throat, eye, and ear." A different section of the same advertisement discussed the strong clinical performance of Chloretone— "we have hundreds of favorable reports of its use"—which added confidence to its pairing with adrenal gland extracts. At the bottom of the advertisement about Chloretone and "Suprarenal Liquid with Chloretone" was the line "LITERATURE FURNISHED ON APPLICATION," suggesting that medical reports, and an abundance of them, could be supplied on doctors' request.[580] This kind of reference to medical literature was typical of company advertisements.

Product advertisements were also accompanied by reminders to doctors that Parke, Davis & Co. was a pioneer in the chemical and physiological standardization of drugs. One 1902 advertisement, also published in the *Therapeutic Gazette*, was entitled "Why Experiment?" and it began by striking fear in the reader:

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[578] Dr. George F. Butler to Parke, Davis & Co., October 2, 1899, NMAH.AC.0001_B404F22, SI, Parke Davis Collections.

[579] "Advertisement: Chloretone," *The Therapeutic Gazette* 25 (1901). This ad can be found in the advertising section of the journal (no page number is listed). See Medical advertisement collections at Ebling Library, UW-Madison.

[580] This marketing strategy was not limited to glandular products. Parke, Davis & Co. adopted very similar language when marketing many of their products around 1900 (and beyond). See especially advertisements for diphtheria antitoxin.

> There is a vast difference in the therapeutic activity of the drug extracts with which the market abounds. Some are weak, inert, unreliable. Others possess an unusual and dangerous potency. The physician who prescribes them at haphazard is walking in the dark—his is forced to experiment.[581]

And then in bold type, immediately following this passage, came another:

> There is one way by which the medicinal worth of drug extracts can be determined before administration. There is one way of preparing them which will render them always of uniform strength and efficacy—the same to-day, to-morrow, next week, next year. That way is our way."

The "way" of Parke, Davis's & Co., the advertisement continued to explain, was to "employ scientific methods to correct natural discrepancies" in manufactured drugs, which was achieved through physiological and chemical assays. "Why order or prescribe a preparation of unknown strength? Why experiment?" the ad concluded.[582]

In this curious advertisement, we see the company making negative connotations around the word "experiment," which was a term that was commonly employed by doctors who discussed their clinical investigations with glandular products circa 1900 (as Chapter 3 detailed). Parke, Davis & Co. seemed to be suggesting that experimentation with new drugs in the clinic was inherently risky, for it involved rolling the die on commercial products of unknown strength and reliability. If doctors used P. D. & Co. products, however, this advertisement seemed to say, they would not have to "experiment," for the company's products were standardized, reliable, and would deliver good results. Leave the risky experimentation to us, the company seemed to tell doctors, and we will give you a product that works.

Yet, Parke, Davis & Co. really did need doctors to experiment in the haphazard sense of the word. Clinical testing with experimental drugs was the only way that the company could determine if and how a drug could be successfully marketed to the medical community.

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[581] "Advertisement: Why Experiment?," *The Therapeutic Gazette* 26 (1902): 47.Medical advertisement collections at Ebling Library, UW-Madison.
[582] "Advertisement: Why Experiment?"

The company did not have the capability to do clinical testing itself, beyond the experiments that were performed on all manner of laboratory animals at the laboratory in Detroit. Getting experimental products in the hands doctors was critical. The next section will show that the company executives thought very carefully about whom they trusted to do true experimental work with new and experimental glandular products, and which doctors were kept at an arms distance and treated more strictly as customers.

"Co-Workers" & "Friends of the House": How Parke, Davis & Co. Operationalized Clinical Testing

Informal and ad-hoc clinical testing existed at Parke, Davis & Co. since at least the 1880s and perhaps even earlier,[583] but it was not until Dr. Ezra R. Larned arrived at the company in 1901 that it was formalized and institutionalized as standard company practice. Larned was a recent graduate from Rush Medical College and, when he started working at the Chicago Branch, he was quick to notice that the company could be doing more to closely engage physicians.[584] He argued that the company should be "systematically enlisting help" from "prominent physicians throughout the country" for the development and testing of Parke, Davis & Co. products.[585] He meant to extend Houghton and McClintock's informal system of local testing to "prominent" physicians in each state. If they found the drugs favorable and submitted clinical reports and testimonials stating as such, then it could do wonders for marketing. It would also grow the market and increase the company's market share, for as drugs were shipped out to the states for clinical testing new clinics would be added to the company's network.[586]

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[583] Gabriel and Holman, "Clinical Trials and the Origins of Pharmaceutical Fraud." See also Chase to Lescohier, "Department of Experimental Medicine, Its History and Development," March 22, 1937.
[584] Chase to Lescohier, "Department of Experimental Medicine, Its History and Development," March 22, 1937.
[585] Chase to Lescohier, 2.
[586] Chase to Lescohier, 2.

After a successful pilot program of physician-run trials in the Chicago area that started in 1901, Larned was brought to Detroit to set up the Department of Experimental Medicine, which was singularly charged with the task of administering these trials.[587] From there, he slowly recruited and managed a national network of physicians that, by the 1930s, had grown to a staggering 2,400 practitioners.[588] Larned needed help to create this vast network of doctors. His winning strategy was to employ thirty company men who were each stationed in different cities in the country, and from there they would "get in touch with and to enlist the interest of prominent clinicians" in their local areas in fields as diverse as "pediatrics, obstetrics, gynecology, laryngology, surgery, ophthalmology."[589]

This group of thirty was given the formal designation of Department of Experimental Medicine Representatives and the casual designation of "attachés," and became the first port of call for physician co-workers in these territories.[590] If Larned's role was to coordinate the company's clinical efforts from the Detroit headquarters, then the attachés were the hands and feet on the ground, keeping "in frequent touch with the physicians, collecting their reports and assembling other findings on which could be based the decision as to whether or

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[587] In 1901, Parke, Davis & Co. launched the Department of Experimental Medicine. According to the company, it was the "the first organized, systematic method of clinically proving medicinal agents before marketing them." See "Historical Highlights," 4. This source continues to claim that Parke, Davis & Co. were the first pharmaceutical company to test their products in the clinic before releasing them on the market.

[588] A complete database of doctors who were engaged in trials at Parke, Davis & Co. has not been located, and perhaps does not exist, but an internal company memorandum authored in 1937 claimed that Larned's group of co-workers grew to "some twenty-four hundred physicians selected from among the ablest specialists and general practitioners in the medical profession of America." See Chase to Lescohier, "Department of Experimental Medicine, Its History and Development," March 22, 1937. A company advertisement from the 1920s corroborates the very large number of doctors who were involved with the company in the first two decades of the twentieth century, stating that the Department of Experimental Medicine had "secured the willing co-operation of over two thousand specialists and general practitioners throughout the country." See *The Scientific and Research Work of Parke, Davis & Company*.

[589] Chase to Lescohier, "Department of Experimental Medicine, Its History and Development," March 22, 1937.

[590] See Dr. Martin Crook's letter to Larned re. Dr. Tom Williams in E. R. Larned to Dr. Francis et al., "Addition to the List of Pineal Gland Extract," June 11, 1915, NMAH.AC.0001_B407F21, SI, Parke Davis Collections. See also Letton's letter which gives further evidence of his work liaising on the ground in Chicago with his doctor contact, O. S. Ormsby. "I will personally see that we obtain the benefit of his observations." See H. M. Letton to E. M. Houghton and Biological & Research Dept., "Correspondence Re: Experimental Vaccine for Hodgkin's Disease," August 13, 1915, NMAH.AC.0001_B407F25, SI, Parke Davis Collections.

not a certain product should be added to our list."[591] The attachés were also charged with the task of "delivering lectures to medical associations, medical schools, pharmacy schools, hospital staffs, and similar groups."[592] To manage the company's increasing regionalization, the attachés and medical representatives were periodically brought to the Detroit campus to become "house educated."[593] This meant engaging in professional development and training, being schooled in the principles of scientific medicine, and learning about new products.[594]

Communication with physicians, and physician feedback, was essential to Parke, Davis & Co.'s business model, and it became codified under Larned's direction, as evidenced by a 1904 internal company document that detailed a list of twenty-two crucial steps of drug production.[595] The first steps began with research and discovery, which involved company men scouring the scientific and medical literature for new ideas and investigating original suggestions sent in by physicians. Next came the development of the drug in the biological and chemical laboratories, followed by in-house clinical experimentation with lab animals. If the first round of experimentation indicated clinical utility, it was time to send the product out for testing to physicians and, most importantly, to request reports on how the drug fared in

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[591] Chase to Lescohier, "Department of Experimental Medicine, Its History and Development," March 22, 1937.
[592] Chase to Lescohier. Lecturing to the medical community had long been a practice at Parke, Davis & Co. See, for example, the various sources in the SI collections that detail Parke, Davis & Co.'s "Lab Week," which was a week-long education conference put on for hundreds of physicians at a time. "Section Programs, Laboratory Week," 1915, NMAH.AC.0001_B398F26, SI, Parke Davis Collections; E. M. Houghton and Mr. Bartlett, "Programs, Memos and Papers Re. Laboratory Week," April 15, 1915, NMAH.AC.0001_B398F27, SI, Parke Davis Collections; "Program of Laboratory Week for Visiting Physicians," June 1917, NMAH.AC.0001_B398F28, SI, Parke Davis Collections; Mr. Bartlett to E. M. Houghton, "Letter to Physician Re. Invitation to Lab Week Program," April 17, 1915, NMAH.AC.0001_B398F25, SI, Parke Davis Collections.
[593] John C. Spratt, "The Art of Salesmanship," *Practical Druggist and Review of Reviews*, April 1910, 372–73.
[594] "A Notable Conference: Twenty-Nine Attachés of Our Department of Experimental Medicine Discuss Problems in the Therapy of Infectious Diseases," *Therapeutic Notes*, November 1913, 144–45. Another source describes these men more as travelling salesmen who were brought to labs in Detroit in batches to receive "postgraduate education" in company research and products. See: "Parke, Davis & Co.'s Post-Graduate School," *The Practical Druggist*, November 1913, 72. A photograph taken in 1913 from one of these "educational conferences" in Detroit reveals that most attachés were medical doctors and constituted "but one coterie" of hundreds more company representatives that were stationed around the country, often as traveling salesmen. See also E. R. Larned to Dr. Francis et al., "Additions to the List-- Suggestions and Actions Taken," February 19, 1917, NMAH.AC.0001_B396F67, SI, Parke Davis Collections.
[595] "McClintock-Swift Memos: Method Outline for Recording and Reporting Experimental Work," July 1904, NMAH.AC.0001_B396F65, SI, Parke Davis Collections.

the patients. Company employees were instructed to send follow up letters to physicians who had yet to report within a month of receiving samples, and to continue waiting for slow physicians to report—but for no more than two months. After evaluating the cumulative data, it was decision time: could this product be safely and profitably marketed?

Physician feedback generated from these trials was published in *Therapeutic Notes*, a Parke, Davis & Co. publication that collected and collated (mostly favorable) clinical reports written by doctors about their drugs. Judging by the number of clinical reports authored by doctors that appear in each issue of the journal—and acknowledging the possible existence of more reports, both positive and negative, that were not printed—there could have been as many as one hundred doctors serving as "co-workers" each and every year. The twenty-odd physician reports that appear in each quarterly issue of *Therapeutic Notes* were likely just a sample of the doctors who reported to the company, for Parke, Davis & Co. often presented feedback in abbreviated form. This was the case in reporting about Pituitrin in 1910, which appeared in short excerpts that had been clipped from physician letters.[596] Other times, Parke, Davis & Co. gave full-length editorial space to "original communications" from doctors who gave detailed testimony of their (usually long-term) testing of a Parke, Davis & Co. drug. This was the case with Dr. E. A. Downéy from Huntland, Tennessee, who spent eighteen months in 1914 and 1915 using Pituitrin, which yielded "startling and gratifying results" in obstetric practice.[597]

Some of the reports in *Therapeutic Notes* appeared in the form of unsolicited feedback sent in (often anonymously) by doctors who had positive experiences with Parke, Davis & Co. drugs and felt inspired to make contact.[598] One physician "of wide repute" from

[596] "Pituitrin in Asthma and Hay-Fever," *Therapeutic Notes* 17 (1910): 70.
[597] E. A. Downéy, "Pituitrin in Obstetrics," *Therapeutic Notes*, 1915, 126.
[598] Most of the feedback featured in *Therapeutic Notes* was positive. Parke, Davis & Co. never published wholly negative feedback on their drugs, but they did include reports about unpleasant side effects, inefficacious uses of their drugs, and tried and true methods for achieving results.

one of the "central states" was so impressed with his use of Adrenalin in 1910 that he felt compelled to write to the company. The patient in question was his wife, whose asthmatic affliction was so great that sometimes she could not breathe. After spraying her nostrils with twenty drops of Adrenalin, the doctor-husband noticed that her paroxysms were cured and did not return. "I am not in the habit of writing this kind of letter," he penned to the company, "but this experience is *bona fide*, and I think it should be known."[599]

Other clinical reports that appeared in *Therapeutic Notes* were extracted and reprinted from medical journals from around the country, ranging from the big national periodicals including *JAMA* and *American Medicine*, to specialist journals, such as the *American Journal of Obstetrics*, to state-based and regional medical journals, such as *Gulf States Journal of Medicine and Surgery*. The physicians who wrote these articles did not necessarily have a connection to Parke, Davis & Co.—the company had merely identified their article in a journal and reprinted it for advertising purposes—but some of these authors hinted at their use of Parke, Davis & Co. products and sometimes their collaboration with the company. For example, a Dr. R. A. Bate from Louisville, Kentucky, who published an article about the pituitary gland product in the *Alabama Medical Journal*, stated that he was supplied by "The Department of Experimental Medicine of Parke, Davis & Co."[600] This casual attribution to the company was relatively common in clinical reports published in both small and big journals, for it served the practical purpose of informing a skeptical medical community which commercial products worked and which did not. It was usually always brief: "The preparation used was made by Parke, Davis & Company," reported Drs. Harvey G. Beck and

[599] "Adrenalin in Asthma," *Therapeutic Notes*, 1910, 6. Emphasis in original.
[600] R. A. Bate, "The Therapeutic Application of the Pituitary Gland," *Therapeutic Notes* 17 (1910): 33–34. Originally published in the *Alabama Medical Journal*, July, 1909. This was the department that distributed free drug samples to physicians, as the final section of this chapter will detail.

John J. O'Malley from Baltimore, who presented their paper on pituitary gland extract to the College Medical Society in 1909 and later published it in *American Medicine*.[601]

What was less common in medical periodical literature were open recommendations and praises of the company, such as those made by Dr. S. Krumholz, who published a report on thyroid serum in the *Illinois Medical Journal* in 1910, and wanted to "commend Parke, Davis & Co. for their cooperation" in supplying him a new drug for "experimental purposes."[602] The lack of open praise suggests perhaps an ongoing reluctance in physicians to advertise to their colleagues their close contact with pharmaceutical companies. Yet we can still read company involvement in some of these publications. For example, ophthalmologist Dr. Dudley S. Reynolds published a piece in *American Medicine* in 1901 which described the results of "1, 222 experiments" that he performed with Adrenalin at the Hospital College of Medicine (presumably at the Central University of Kentucky, where he was based).[603] He does not admit working with Parke, Davis & Co., but given the very large scale of his clinical trials, its temporal proximity to the launch of Adrenalin in 1901, and his praise of "Takamine," the developer and booster of Adrenalin at Parke, Davis & Co., it is very likely that Dudley was talking to the company and being supplied with products that were not yet on the market.[604] His ophthalmologist colleague and fellow Kentucky resident, Dr. J. A. Stucky, had been supplied with Adrenalin powder that same year by Takamine himself,[605] so

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[601] Harvey G. Beck and John J. O'Malley, "Recent Investigations of the Pituitary Gland," *Therapeutic Notes*, September 1910, 95. Originally published in *American Medicine*, October, 1909.
[602] S. Krumholz, "Treatment of Exophthalmic Goitre with Serum of Thyroidectomized Animals," *Therapeutic Notes*, July 1910, 71. Originally published in the *Illinois Medical Journal*, March, 1910.
[603] Reynolds, "The Therapeutic Value of Adrenalin Chlorid." For bibliographical details, see: http://www.mygenealogyhound.com/kentucky-biographies/ky-jefferson-county-biographies/dudley-sharpe-reynolds-genealogy-jefferson-county-kentucky-louisville-ky.html
[604] Reynolds, 32.
[605] Wilson, "Clinical Notes on Adrenalin."

it is plausible that Dudley had been plugged into Adrenalin testing through Stucky, or Stucky through him.[606]

Despite the thousands of physicians who worked for the company between 1900 and 1919, surviving records of specific drug trials suggest that, typically, only a few dozen doctors were engaged in any one trial. The size of a trial was determined by its cost and, sometimes, the availability of the raw materials used to create the new drug. For example, in 1915, Dr. Larned reported to his colleague Dr. W. E. King that the first forty samples of an experimental pituitary gland product were sent out to only "a selected list of co-workers," but "this supply was soon exhausted" and could not be replenished due to a shortage of the raw product.[607] According to Larned, the physicians in this trial were clamoring for more drugs and it was an awkward matter for him to prematurely end the trial because of supply-chain problems. No such supply problems existed with "Corpora Lutea," an ovarian product that was sent out for testing to Larned's co-workers in 1915. The doctors also quickly exhausted the first batch of the drug, but they were supplied with more by the company who were only too happy to ramp up production to meet demand. In the same year, Larned was working to get out to trial a new glandular product —desiccated and defatted "Lymphatic Gland"—and suggested that at least 200 bottles of one hundred tablets each ought to be distributed between

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[606] Even if physicians were unwilling to explicitly declare their allegiance with Parke, Davis & Co. in medical periodical literature, doctors commonly made pro-market statements in their writing about the company's endocrine drugs. "Adrenalin chlorid solutions are now on the market," wrote Dr. Charles A. Elsberg, an attending surgeon at Mt. Sinai Hospital, who had made it his habit to use Adrenalin as an anesthetic in minor operations. See Elsberg, "Some Remarks on the Use of Adrenalin as an Addition to Solutions for Local Anesthesia." "I find that the best solution to use…is already on the market (Parke, Davis & Co.'s Adrenalin)," wrote Dr. Charles L. Nassau, Assistant Professor of Surgery at Jefferson Medical College, who also used Adrenalin as an anesthetic. See Charles L. Nassau, "Infiltration Anesthesia," *Therapeutic Notes,* 1914, 18. Originally published in International Clinics, vol. II, series 22. Even the authorial act of repeatedly writing about, and advertising, a trademarked name, such as Parke, Davis & Co.'s "Adrenalin" or "Pituitrin," was as an act of endorsing the commercial endocrine-drug market, and Parke, Davis & Co. by extension. Dr. H. R. M. Landis, for example, did not mention Parke, Davis & Co. in his article about Pituitrin usage in obstetrics, but he did argue that there was, rightfully, a "world-wide acceptance of Pituitrin." See H. R. M. Landis, "The World-Wide Acceptance of Pituitrin," *Therapeutics Notes,* 1915, 123. Originally published in *Progressive Medicine,* vol. 16, no. 4.

[607] W. E. King to Dr. Miller and E. M. Houghton, "Experimental (Clinical) Work to Be Considered: Bacterial and Gonococcus Vaccines, Pituitrin, and Lymphatic Glands," November 24, 1915, NMAH.AC.0001_B407F28, SI, Parke Davis Collections.

approximately twenty physicians.[608] Any fewer bottles would not generate enough meaningful data, for assessing the "question of therapeutic value" required the treatment of "quite a series of cases before these physicians would attempt to give us anything like an intelligent report."[609] On the flip side, producing too much desiccated lymphatic gland could be a wasted cost for the company should the new drug be quickly proven ineffective. When the company did run very large trials, such as a 1912-1914 trial of "anterior lobe" pituitary gland with 118 physicians, it signaled the company's confidence in the product and its readiness for the market.[610]

The size of the trial also depended on whether the company was seeking genuine feedback from physicians about a product, or whether they were using clinical testing predominantly as a vehicle for product advertising. That is, drug testing at Parke, Davis & Co. was both a mechanism for true preliminary trials in the human patients, *and* a mechanism for marketing new drugs to physician "co-workers." The larger the trial, the more likely it was downstream of genuine preliminary trials and serving the function of pushing a new but already refined product into American clinics.

McClintock explained this system in a private letter to Mr. Swift, the General Manager of the company.[611] He wrote that after a new drug had been trialed in experimental models at the Parke, Davis & Co. labs, "it may then be promising enough to ask one, two or a half dozen men, who are friends of the House and usually friends of the head of the department, to try it out on a few cases and see what results they get." He continued: "If all

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[608] "Larned, E. R. King Memos. Re: Experimental (Clinical) Work to Be Considered Bacterial and Gonococcus Vaccines, Pituitrin, and Lymphatic Glands. October – November 1915.," 1915, NMAH.AC.0001_B407F28, SI, Parke Davis Collections.
[609] "Larned, E. R. King Memos. Re: Experimental (Clinical) Work to Be Considered Bacterial and Gonococcus Vaccines, Pituitrin, and Lymphatic Glands. October – November 1915."
[610] "The Anterior Lobe of the Pituitary Body," *Therapeutic Notes*, 1914, 116. According to this piece, testing happened in the two years leading up to the publication of this article (1912-1914).
[611] Charles McClintock to Mr. Swift, "Report to Mr. Swift Re: Project Work by Experimental Department, Cost Estimate, Suggested Policy for Assigning and Determining Project to Undertake," July 2, 1910, NMAH.AC.0001_B396F63, SI, Parke Davis Collections.

these reports are favorable, it then should go to the Management with the recommendation that it be submitted to our co-workers for an extensive clinical trial."[612] The reason for this, McClintock explained, is because most co-workers—as distinguished from "friends" of the House—expected a drug to work upon its arrival in the clinic, even if it was explicitly branded by the company as "experimental." Sending a truly experimental and untested drug to these co-workers would risk getting them offside should the drug perform poorly. It could even generate negative reports from prominent physicians that might be published in the medical press, which was a worst-case scenario for Parke, Davis & Co. This necessitated a round of clinical testing before the "co-worker" trials even took place. McClintock explained:

> I repeat what I said once before, that in the majority of cases we should know pretty well in advance before we offer the co-workers a thing to test, as to just what it is going to do, and our principal reason for sending it to them is not our normal one. We tell him that it is because we want his opinion as to the value of the preparation; in reality as a rule our mind is already made up to that. What we want to do is to influence him to use our products, to approve our methods, etc. The Department of Experimental Medicine, as now operated, is essentially a high-class method of advertising far more than it is a department of experimental medicine. [613]

McClintock continued to write to Mr. Swift that he "did not want to quarrel" about his frank characterization of co-worker testing, and that his main purpose was simply to emphasize that "the major part of the experimental work must be done before the thing is ready for the Department of Experimental Medicine." [614]

By making a distinction between "friends of the house" and "co-workers," McClintock identified "insiders" and "outsiders" of the company and assigned different roles

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[612] McClintock to Swift.
[613] McClintock to Swift, 2.
[614] The company broadcasted their rigorous experimental approach in company advertisements but, not surprisingly, they kept details of the real preliminary tests with "friends of the House" strictly out of company literature. They instead published assurances to their physician customer-base that their clinical testing was objective and without bias. Of Adrenalin testing, they wrote that "the samples of Adrenalin and Adrenalin Solution were placed with physicians having no connection with our laboratory whatever, who carefully tested them clinically and submitted reports which warranted us in directing Adrenalin to the attention of the medical professional generally with assurance that the long sought active principle had been found." See: C. M. W., "Letter to Salesmen Re. Claims about Adrenalin," August 12, 1904, NMAH.AC.0001_B406F53, SI, Parke Davis Collections.

to them. There were those physicians who could be trusted to provide genuine feedback on new and experimental drugs and to remain discreet about trials that did not go so well. These were the "friends of the House," and they were the first to receive a drug for clinical testing. Then there were the physicians who were less well-known to Houghton and McClintock, less familiar with the company, usually located across the country, and had higher expectations of how an experimental company drug should perform in the clinic. This latter group of physicians made up their wider national network of co-workers, and they were regarded by the company more as customers than real collaborators. As Houghton and McClintock reveal in their correspondence, the clinical testing that was done by these doctors was about product placement in clinics across the nation, and about encouraging not-yet-convinced physicians to use Parke, Davis & Co. products.[615]

There was no hard and fast definition about who constituted a "friend" of the House, but it is easily discernible in company correspondence, which is interleaved with letters that include friendly and affectionate banter between clinician and company executive—mostly Houghton and McClintock—as I showed at the beginning of the chapter. This points to the very important function of Houghton and McClintock's personal network in the medical community and their indefatigable correspondence with doctors. It also points to the critical

[615] Of course, these "co-workers" still returned real feedback to the company, and the company still listened. I have found evidence that Parke, Davis & Co. were open to pulling a product from development even after it had gone out for testing to dozens of co-workers from around the country. In 1917, samples of Iodine Compound—a powder that was used to treat topical wounds—were sent out to sixty-six co-workers in sixteen cities. Larned reported that while some doctors found merit to the new drug, "some very prominent co-workers protested against the use of Iodine Compound," claiming that it "invited infection" in the wound and was sometimes accompanied by "considerable pain on the part of the patient for an unusual period of time." Larned closed his memo by stating that "after carefully reviewing all the evidence submitted in the final reports on this problem, together with the final summary of case histories submitted, we feel warranted in advising against adding Iodine Compound to the list. See Larned to Francis et al., "Additions to the List-- Suggestions and Actions Taken," February 19, 1917. But the company's priority, as McClintock outlined to Swift, was to distribute drugs to co-workers that already worked in the clinic. See Charles McClintock to Mr. Swift, August 15, 1904, C 38 (a) I : Parke, Davis & Co (General), Kremers Reference Files. It was not only a risk to the company's reputation to send truly experimental drugs, but it was also bad for the company's bottom line when one considered the resources that were directed to product design and development. Company documents thus reveal a strategy of progressively scaling up the production of a new drug, from just a few samples for testing in animal models, to slightly more samples for testing by friends of the house, to a medium sized batch for co-worker testing, and finally to large-scale production for marketing and sale.

role of selected American doctors who agreed to work with the company, to develop new glandular products, and to guide them onto the medical marketplace.

A Company for Physicians

Houghton and McClintock's "physician friends" and "co-workers" had made room in their clinics for the company's new glandular products, and the company gained a great deal from this relationship. But so did physicians. They approached clinical testing not as an obligation to be fulfilled, but as an opportunity to shape the kind of glandular products they wanted to see on the market and in their clinics. When Parke, Davis & Co. sent them new products for testing, doctors experimented with creativity and initiative. It was common for doctors to adjust dose, duration of treatment, and even administration of the drug, and to send back notes of these adjustments to the Houghton and McClintock. Often, they listened, and adjusted their product listing in accordance with physician demand. For example, Adrenalin became a popular hay fever inhalant because doctors happened upon this usage, figuring that a vasoconstrictor that effectively controlled hemorrhages might be helpful in tightening up the nasal passages. It came to be used as a treatment for hemorrhoids, which led to the company adding "Adrenalin Suppositories" to its list.[616] Similarly, Pituitrin, which was initially marketed as another line of defense against asthma and laryngological complaints, became a powerful drug in obstetrics to hasten labor contractions because gynecologists hypothesized that there might be a clinically significant connection between the ovaries and the pituitary glands.[617]

We can also see from company records that physicians were not shy in making requests of the company, who they saw as a resource for developing their own ideas about

[616] "Advertisement: Adrenalin Suppositories," *Therapeutic Notes* 15 (November 1908): 106.
[617] See"Pituitrin in Asthma and Hay-Fever"; Bate, "The Therapeutic Application of the Pituitary Gland"; Rudolf Klotz, "On the Therapeutic Use of Pituitrin," *Therapeutic Notes* 18, no. 5 (1911): 96.

promising new drug candidates. For example, in 1898, a Dr. A. M. Smith of Tacoma Washington wrote directly to McClintock and requested that the House begin manufacturing a diabetes serum from pancreatic extracts.[618] In 1915, Dr. Tom A. Williams, a well-known neurologist in the D.C. area, suggested that the House should put on the market a 5-grain pineal gland tablet, which he thought could be exceedingly helpful in treating mental disorders.[619] In the same year, Dr. Ormsby of Chicago approached Parke, Davis & Co. to request it develop, from scratch, an experimental vaccine for Hodgkin's disease for testing in his clinic.[620] Dr. George W. Michell, who worked at the Peoria Sanatorium, Illinois, wrote the company, also in 1915, to express his sincere interest in glandular products, and suggested that he would be willing to try many different products. "In our work here we are willing to try anything in the form of ductless gland treatment."[621]

Doctors also requested from the company scientific information about drugs. This was the case with a Dr. John Rhodes from Chicago who was preparing a paper on Adrenalin for an upcoming conference of the American Laryngological Association and wanted more details from the company about how the drug affected tissues and blood vessels.[622] He had

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[618] McClintock wrote back with thanks and regret at how intractable the disease was, and how far off the company was in formulating a treatment.

[619] Larned to Francis et al., "Addition to the List of Pineal Gland Extract," June 11, 1915. His request was received by Dr. Martin Crook, a company representative in Baltimore, who forwarded his suggestion to Detroit for consideration by the "Committee on Additions to the List."

[620] H. M. Letton to E. M. Houghton and Biological & Research Dept., "Correspondence Re: Experimental Vaccine for Hodgkin's Disease," August 7, 1915, NMAH.AC.0001_B407F25, SI, Parke Davis Collections; Houghton to Letton, "Correspondence Re: Experimental Vaccine for Hodgkin's Disease," August 9, 1915; Letton to Houghton and Biological & Research Dept., "Correspondence Re: Experimental Vaccine for Hodgkin's Disease," August 13, 1915. The company obliged the request, but not without the help of a local physician in Detroit who had a patient with the same disease and offered the company some serum from an "enlarged gland" so that they might manufacture the vaccine.

[621] See: "Houghton, E. M. – Francis – Lescohier – et. Al. Correspondence Re: Mixing Adrenalin with Other Substances. 1915," 1915, Box 400, Folder 31, SI, Parke Davis Collections.

[622] "Houghton Correspondence. Adrenalin. From Doctor John Rhodes, Chicago, Treating Sarcoma with Adrenalin.," October 10, 1904, NMAH.AC.0001_B406F55, SI, Parke Davis Collections. Dr. Louis Simonson from Middletown, Connecticut, also wanted more information from Parke, Davis & Co. He had been using an Adrenalin cream as a topical anesthetic and wrote the company with queries about whether the "toxicity" he noticed could possibly be linked to the drug. The company carefully considered his claims and deemed that in this instance the toxicity was coincident with, and not caused by, drug administration. See "Houghton, E. M. – Francis – Lescohier – et. Al. Correspondence Re: Mixing Adrenalin with Other Substances. 1915."

been successfully using Adrenalin to treat sarcoma, which was a new use for the drug not yet on the company's radar. Houghton replied with keen interest, a helpful list of citations, along with a commentary on how Adrenalin affected the circulation.[623] He even offered Rhodes his personal copy of a relevant article authored by Michael Foster that had recently been published in the *Journal of Physiology*.

Dr. Richmond McKinney from Memphis, Tennessee, also wanted specialized information about the physiological action of Adrenalin in the treatment of asthma, which he had been experimenting with in his own clinic. He wrote Houghton directly, reminding him of the prevailing theory that asthma was caused by the contraction of the bronchioles, and yet here was Adrenalin, a vasomotor constrictor, apparently working "like magic" to relieve asthmatic paroxysms. How could this be, wondered McKinney? Houghton replied at length, as if responding to a colleague at an academic conference, expressing his fascination in the topic, admitting his lack of specific knowledge, and referring McKinney to several articles that had recently come to his attention.[624] "I regret that I am unable to give you any further or more satisfactory explanation," Houghton signed off.

A few days later came McKinney's reply, in which he thanked Houghton and requested that he might be allowed to publish Houghton's response in the *Monthly*, a local medical periodical in Memphis, so that it might be "read with appreciation by the various physicians in this territory who have had occasion to use adrenalin in asthma." McKinney added that such a publication "no doubt will do much toward promoting the use of this preparation." This was perhaps an unnecessary post-script for someone such as Houghton, who was a keen strategist and marketer of company products. Houghton wrote back quickly

[623] E. M. Houghton to Dr. John Rhodes, "Letter Describing Action of Adrenalin," April 17, 1906, NMAH.AC.001_B400F26, SI, Parke Davis Collections.
[624] "McClintock-McKinney Correspondence. On Use of Adrenalin in Asthma. May-June 1905," 1905, NMAH.AC.0001_B404F8, SI, Parke Davis Collections.

to agree to the publication of his letter, adding bashfully: "I had no thought of such when writing you."[625]

Other doctors approached the company with requests for clinical data to advance their own research. This was the case with Dr. Tobin from Cincinnati, Ohio, who initiated contact with the company in 1903 to make an enquiry about using Adrenalin chloride to control hemorrhage in major operations, which was an extension on its normal use as a topical anesthetic in minor surgeries. Houghton advised Tobin that "we cannot give you much encouragement" on the matter, for their own experiments in the Parke, Davis & Co. laboratory had showed that while Adrenalin Chloride controlled hemorrhage in major operations, it produced "intense inflammation and irritation" and brought about "sloughing of the parts" when injected subcutaneously.[626] After some brave experimentation, Tobin wrote back to the company saying: "Gentlemen, it seems to me that there should be an excellent field for Sol. Adren. Chloride as a routine treatment in all major surgical operations where it is desirable to control loss of blood." Tobin explained that his intention was to "call on the leading surgeons in the city" about his discovery, and so he requested the company "furnish [him] with such data as [they] have and also outline once more the best method of procedure."

McKinney and Tobin were not alone in finding new uses of Adrenalin and contacting the company with inspired ideas about new products. In 1906, Henry Guy Carleton, a well-connected Adrenalin enthusiast, generated over sixty pages of correspondence in his letters to Houghton in which he insisted that an ointment form of Adrenalin was an effective treatment for neuralgia. Houghton received Carleton's advances with caution, for Carleton was not a medical doctor, although he did seem to be extraordinarily well-connected with prominent

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[625] "McClintock-McKinney Correspondence. On Use of Adrenalin in Asthma. May-June 1905."
[626] "Houghton and Tobin Correspondence – Toxicity of Adrenalin," August 17, 1903, NMAH.AC.0001_B406F49, SI, Parke Davis Collections.

east-coast physicians. He had even managed to convince many of them to conduct clinical trials with Adrenalin ointment to test his hypothesis. Carleton wrote Houghton persistently, even from his death bed, demanding that Houghton publicly list neuralgia as one of the diseases that could be treated with Adrenalin, and he mobilized his own physician friends to lobby the company on his behalf. Houghton was equal parts bemused, interested, and concerned: who was this layman booster of Adrenalin and what did he stand to gain from his lobbying efforts? Were prominent physicians really using Adrenalin in this way?[627]

Other doctors used Parke, Davis & Co. to advance their own research, including Dr. William Morley who was a local gynecologist at the University Hospital in Ann Arbor and worked with Parke, Davis & Co. on the side.[628] He helped Dr. Aldrich, a leading chemist at Parke, Davis & Co., to develop a new ovarian drug from corpus luteum, which was regarded as the most active tissue of the ovaries. Morley did both biological and clinical testing with experimental ovarian extracts for the company well before it went out for extensive clinical testing in 1915, which was helpful in advancing his own clinical work with women who had irregular menstruation.[629] Evidence suggests that Morley was not an assistant to the company's needs, but rather leading this research. "You have already noticed the following articles which Dr. Morley has called to our attention," wrote Houghton's assistant, W. E. King, to Dr. Aldrich and a colleague Mr. Beckwith. King cited two German articles about corpus luteum, with an additional note that "Dr. Houghton approves of the idea that we proceed to do some work along this line."[630] He wanted Aldrich and Beckwith to start

[627] Houghton eventually sent Adrenalin ointment out for testing to physicians in Detroit and Chicago, including to a Dr. Davis Inglis at the Detroit Medical College who did not find encouraging results."Houghton, E. M. – Henry G. Carleton. Correspondence Re: Adrenalin in Treatment of Neuralgia Including Testimonials. 1906-1907."
[628] W. E. King to Dr. Francis, "Overlapping of Biological and Chemical Research, Dr. Francis's Claim to Adrenalin," April 13, 1915, NMAH.AC.0001_B401F33, SI, Parke Davis Collections.
[629] W. E. King to Dr. Aldrich and Mr. Beckwith, "Research on Corpus Luteum," January 22, 1915, NMAH.AC.0001_B407F16, SI, Parke Davis Collections.
[630] King to Aldrich and Beckwith.

making up a preparation "to supply to Dr. Morley" to experiment with and to "make a beginning in clinical tests on local cases."[631] If all went well, King noted, then it would be "well worth trying out on an extensive clinical scale with the idea of supplying it later on as a regular product."

Morley was not alone in driving Parke, Davis & Co. research from the outside. I have found evidence that Dr. Beebe of Cornell University and Dr. R. P. Cromarty of McGill University also worked with the company on the sidelines of their university commitments. Beebe wanted help from the company in 1912 to make a more concentrated thyroid product.[632] When their collaboration yielded an effective new product, Beebe then entrusted Parke, Davis & Co. with his formula and rights to sell and manufacture the preparation under the trade name, "Thyroprotein."[633] Cromarty approached the company in 1915 on the recommendation of "some of the physicians" at Johns Hopkins, to request materials in his study of the heart and circulation. The company sent through to him five grains of crystalline Adrenalin, one ounce of Beebe's Thyroprotein, and a quarter ounce of desiccated pituitary gland. Cromarty thanked the company and promised to send back a report.

It is impossible to know how many more physician-researchers worked with Parke, Davis & Co. in this way. Surviving company records only contain fragments of conversations, and hints of projects that were launched and led by physicians. But given the eagerness of Parke, Davis & Co. to collaborate with "prominent" doctors, especially in universities, and given the drive of doctors to develop new glandular drugs for the clinic, it is

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[631] King to Aldrich and Beckwith.
[632] Merker, Interview with Dr. Harvey Merker, 19.
[633] This new product was well-received in the medical community, being advertised by the alumni association of the college of surgeons and physicians, which recommended that "physicians who are desirous of learning more of this new thyroid preparation will do well to send a request to the manufacturers, Parke, Davis & Co." See: "A New Thyroid Preparation." There is evidence that doctors approached other companies, too. For example, in 1896, a Dr. Augustus A. Eshner, also of the Philadelphia Polyclinic and physician at the Philadelphia Hospital, explained his experiments with the pituitary gland in treating acromegaly—a known pituitary related disorder—which he had sourced from Armour & Co. See Eshner, "Progress in Organotherapy."

easy to imagine that there were others who recognized the company as an appropriate vehicle for developing their own clinical capabilities.

Indeed, we get some sense for the intensity of contact between the company and doctors, and the centrality of doctors to Parke, Davis & Co.'s operations, through a letter penned in 1915 by Dr. King to an external researcher, Mr. Allee.[634] Allee, who appears to be quite junior,[635] reached out to the company for information to assist a thesis he was writing on the "social economics" of medical research. Allee's notion of "social economics" came down to raw numbers: he wanted details on how much the company spent on their laboratory per annum, how much they had invested in infrastructure, and how many doctors from Detroit used their facilities. Perhaps not surprisingly, King did not disclose any of this numerical data to Allee, but he did pen a lengthy reply which explained the "social economics" of medical research at Parke, Davis not in terms of numbers but in terms of relationships. He explained to Allee that the company was much more than just a producer and seller of drugs. It also played a critical role in working with scientists and doctors to create new medical knowledge. King explained that the company was represented in numerous scientific and medical societies, published regularly in journals, and maintained contact with physicians in hospitals, clinics, and universities all around the country. Parke, Davis also hosted hundreds of physicians at the Detroit campus each year for a week-long conference called "Lab Week," which was led by company scientists and aimed to educate practicing doctors on the principles of scientific medicine. King liked to think of the company as a kind of scientific hub for "professional men." He wrote to Allee:

> Various members of our laboratory staff are called upon, from time to time, to render opinions and to make careful laboratory diagnosis of material for physicians and

[634] W. E. King to Mr. Allee, "Transcription of Dictated History and Workings of Research Laboratory," March 25, 1915, NMAH.AC.0001_B397F11, SI, Parke Davis Collections.
[635] He was referred to as a "boy" in an internal memo appended to his original note to the company.

> laboratory men situated in various parts of the country. In this respect our laboratory is maintained in exactly the same way that any university laboratory [is run].[636]

King continued to explain that rarely a day went by without letters of correspondence fluttering in and out of the Parke, Davis lab, with company workers explaining concepts "technical in nature" to professional men throughout the country. "Through these intimate associations," King penned, "much co-operative work is done."[637]

We might take King's glib response to Allee as an advertising ploy intended to boost the company's image. But there was truth to his argument. Internal company documents reveal that the "social economy" of medical research at Parke, Davis & Co. was built in the way that King described it. American doctors and their clinics were the backbone of company operations when it came to developing new endocrine drugs and getting them tested in patients. Company documents also reveal that this social economy was maintained by both the company and doctors, and that it was highly productive. In the case of endocrinology, what it yielded was new knowledge about the glands of the body, new glandular products for the clinic, and new confidence in the future of the field.

Conclusion

Parke, Davis & Co. promotional literature between 1900 and 1920 doubled down on the message that every company product was submitted to an "expert jury of physicians,"[638] which guaranteed its safety and efficacy. The company even claimed that it was the first manufacturing house to institute a formalized system of "clinical investigation" with physicians, that this was an epoch-making event in American pharmaceutical history, and that the arrival of company-sponsored trials was of similar significance to the company's

[636] King to Allee, "Transcription of Dictated History and Workings of Research Laboratory," March 25, 1915.
[637] King to Allee.
[638] Chase to Lescohier, "Department of Experimental Medicine, Its History and Development," March 22, 1937, 3.

pioneering efforts towards chemical standardization in the 1870s and physiological standardization in the 1890s. One trade booklet even rhapsodized that "clinical standardization "joined chemical and physiological standardization" to create a "trinity" of pharmaceutical standardization at Parke, Davis & Co.[639]

While these descriptions are dramatic and hyperbolic, Parke, Davis & Co. really were extraordinarily active in their outreach to the orthodox medical community between 1900 and 1920. In addition to the personal relationships and connections company executives fostered with local physicians, and their efforts to create a nation-wide network for clinical testing (and product advertising), the company was comprehensively represented in major national professional societies in medical, chemical, physiological and veterinary fields.[640] Their publishing presence in elite journals also multiplied in this period. What began as a few well-placed articles in elite medical journals in 1900 evolved into a mighty publishing campaign that, by the 1930s, saw Parke, Davis & Co. employees regularly landing cutting-edge journal articles in elite scientific and medical periodicals.[641]

While a defining feature of Parke, Davis & Co. in this period was its unrelenting ambition to become as integrated as possible with the medical and scientific elite, let us not forget about the ambition of American physicians. As this chapter and Chapter 4 have argued, doctors were as motivated to engage with Parke, Davis & Co. as the company was with them.

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[639] *The Scientific and Research Work of Parke, Davis & Company*, 5.

[640] A letter penned in 1915 by W. E. King to a Mr. Allee offers a detailed account of how the company was connected to professional communities in America. In addition to running their own laboratory and sending out literature to dozens of societies and institutions, Parke, Davis & Co. were also a represented (through their physician and scientist employees) in the AMA, American Veterinary Medical Association, International Veterinary Congress, International Medical Congress, International Dental Congress, International Tuberculosis Congress, American Physiological Society, American Chemical Society, American Public Health Association, The United States Live Stock Association, The American Society of Bacteriologists, the American Cancer Society, and others. According to King, Parke, Davis & Co. employees had been quoted in textbooks "and some members of our staff have contributed to standard text-books." His employees were very well connected in hospitals, societies and with scientists at home and abroad. See: W. E. King, "The Work of Parke, Davis & Company in Its Relation to Scientific Progress," March 25, 1915, C 38 (a) I : Parke, Davis & Co (General), Kremers Reference Files.

[641] See *Scientific Contributions from the Laboratories of Parke-Davis, 1866-1966* (Detroit: Parke, Davis & Company, 1966).

Doctors chose to work with the company because it was the most direct route toward improving the field of clinical endocrinology. The "intimate associations" they formed with company men also helped doctors retain control over drug production in an age when they were no longer physically handling raw endocrine glands delivered straight from slaughterhouses and creating their own glandular products in the clinic. Additionally, and more generally, doctors' closeness with Parke, Davis & Co. helped them reshape the commercial marketplace—a space widely acknowledged by the profession as unruly and corruptive—into a force that worked for them and their patients. If doctors were to shelve their own mortar-and-pestles at the turn of the century, and to hand over to the drug company the responsibility of producing new endocrine therapies, then they would do it on their terms and with a company who served their needs.

Conclusion: Remembering the Origins of Clinical Endocrinology

In 1921, Dr. Harvey Cushing of Harvard Medical School, and a specialist of the pituitary gland, thought endocrinology was ascendent in America. This he announced in his presidential address to the newly established Association for the Study of Internal Secretions, later termed the Endocrine Society.[642] As evidence, he cited the sudden uptick of interest in the pituitary glands in the early 1910s: in 1907 there were thirty-four papers published on the pituitary glands and in 1913 there were 298 titles. Cushing attributed the surge of enthusiasm in the field of endocrinology to a "chance discovery" in 1909 that the internal secretion of the pituitary gland was linked to several disorders. "There followed a deluge of papers, and soon after, the endocrinologist came into being, with the establishment a few years ago of this association," surmised Cushing. He continued to reflect:

> The impulse which launched us in such amazing numbers on our several missions some future historian may have to tell. There is nothing comparable to it, for the development of a specialty is usually a very slow process, but the endocrinologist seems to have generated spontaneously everywhere.

In reflecting on the emergence of his specialty, Cushing, himself a doctor, gave little credence to contributions of clinicians and drug company workers in the 1890s and early 1900s. In fact, he thought that these therapeutic and commercial actors were to blame for thwarting the progress of the field through what he termed "therapeutic exploitation." He stated: "A good many of us, I fear, have completely lost our bearings in the therapeutic haze eagerly fostered by pharmaceutical establishments. For this, however, a credulous profession is largely responsible."[643] Cushing thought it was the role of the newly minted Endocrine Society—called the Association for the Study of Internal Secretions—which was made up of

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[642] The Association for the Study of Internal Secretions was renamed The Endocrine Society in the early 1960s, according to Hans Lisser, "The Endocrine Society: The First Forty Years (1917-1957)," *Endocrinology* 80, no. 1 (1967): 5.

[643] Harvey Cushing, "Disorders of the Pituitary Gland," *Journal of the American Medical Association* 76, no. 25 (June 18, 1921): 1722.

elite American physicians and university-based scientists, to limit the influence of "those who recklessly [and] under full sail plow through a fog bank of therapeutics, their horns tooting."[644]

In 1933, Herbert McLean Evans, a professor of anatomy at the University of California, and a prominent researcher in endocrinology, addressed the profession with a similar message to Cushing. Reading a paper before the Congress of American Physicians and Surgeons in Washington D.C., he declared that endocrinology was finally "at the inauguration of a new era" whose achievements would at last match those of the "bacteriologic epoch so gloriously inaugurated by the labors of Louis Pasteur and Robert Koch."[645] Evans was feeling confident about endocrinology's prospects, for in the last ten years several powerful hormones of medical relevance had been isolated and put to clinical use, including insulin, and stunning advancements had been made on pituitary gland research.

What had gone wrong before the 1920s? Evans wasted no time in explaining. "Endocrinology," he told a sympathetic crowd, "suffered obstetric deformation in its very birth by the extravagant claim of the septuagenarian Brown-Séquard that he had magically restored his youth with testicular substance…" He also thought that the clinical field had "continued to suffer" at the hands of the "practicing profession," who were often more liable to effect sensational therapies on their patients, such as "making fat ladies thin," than to engage in the pursuit of real scientific discovery.[646] In Evans' view, this was the reason why "no institute of any importance devoted to medical or biologic research has concerned itself wholly or even partly with the field of the endocrines, and few universities have done so."[647]

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[644] Cushing, 1726.
[645] Herbert M. Evans, "Present Position of Our Knowledge of Anterior Pituitary Function," *Journal of the American Medical Association* 101, no. 6 (1933): 425–32, https://doi.org/10.1001/jama.1933.02740310009003.
[646] Evans.
[647] Evans, 425.

More than thirty years later, in 1967, another eminent endocrinologist, Hans Lisser, Chief of Endocrinology at the University of California and former president of the Endocrine Society (1927-1928), produced another account about endocrinology's failures between 1889 and the 1920s. Writing in *Endocrinology*, the official organ of the society, and reflecting on the society's first forty years, Lisser invoked Cushing and Evans' canonical derision of the clinical endocrinologist, which Lisser admitted were rather "cheap and snide remarks" about the field's "impoverished' beginnings. But despite attempting to take the higher ground, Lisser fell into the same pattern of assigning blame to Brown-Séquard and dismissing the work done by physicians and drug companies thereafter. In reflecting on the birth of the field, Lisser described Brown-Séquard's announcement in 1889 as a "calamitous episode." He stated:

> This age-old, old age striving for the elusive Ponce de Leon fountain of youth, supposedly then achieved by a famous scientist, became a deplorable mirage. His claims were not confirmed, ridicule and abuse were heaped on him, and a drought descended upon the field of clinical endocrinology which persisted, with but a few scattered refreshing contributions, for almost 30 years. The repercussions from this fiasco caused a cynical eclipse and darkness followed.[648]

Lisser thought that until insulin was isolated in 1921, which he described as an "epoch-making discovery" with "enormous impact," there was "very little of endocrine help which clinicians could extend to their beseeching patients."[649]

The views of these endocrinologists, which have been frequently quoted by historians of endocrinology, presaged a historical literature that has cared little for the contributions of Brown-Séquard, doctors and drug companies to the development of the field, between 1889 and 1919. The medical practice of administering the glands and tissues of animals has been "dismissed as an unhappy episode in the histories of both medicine and science," to borrow

[648] Lisser, "The Endocrine Society: The First Forty Years (1917-1957)," 7.
[649] He admitted that thyroid gland substance and Adrenalin were useful products. See Lisser, 7.

Merriley Borell's words,[650] to the point where some, like Cushing, prefer to think of endocrinology as "spontaneously generating" in the 1910s or early 1920s, when research articles appeared thick and fast in scientific journals, when the Endocrine Society was established, and when "epoch-making" hormone drugs such as insulin were rolled out into clinics and onto the medical marketplace.

Together, Cushing, Evans and Lisser sought to partition early clinical and pharmaceutical actors from the more lab-based and academic endocrinologists of the interwar period in an undisguised attempt to distance themselves and their specialty from what they regarded as "irrational" therapeutics.[651] We can appreciate why they might have wanted to do this: they admit themselves that the field long struggled for legitimacy and scientific backing, and that the sensational claims of therapeutic enthusiasts were not helpful in casting their discipline as serious and scientific. But is this boundary work and historical gatekeeping helpful to us now in the twentieth-first century, and in our project of arriving at a more complete picture of how scientific medicine came to be?

"Glands on the Market" has shown that the clinical and pharmaceutical landscapes of early endocrinology in the U.S. were far more nuanced than we have previously realized. This dissertation has shown that Brown-Séquard was a serious actor and he had serious followers. This included doctors who worked with his method in a clinical setting, and druggists who tried to make new medications from animal products. Importantly, these actors saw themselves as working toward the goals of scientific medicine, not against them. They saw themselves as building a therapeutic field that, although still in a rudimentary form, had an enormous amount of promise. Rather than dismissing their methods as "unscientific" we

[650] Phrase by Borell, "Brown-Séquard's Organotherapy," 319. She was also referencing the narratives put forward by interwar endocrinologists, specifically Evans and his comment about "obstetric deformation."
[651] They were not the only endocrinologists to do this. For more context on the interwar endocrinologists view on practitioners see Diana Long Hall, "The Critic and the Advocate: Contrasting British Views on the State of Endocrinology in the Early 1920s," *Journal of the History of Biology* 9, no. 2 (1976): 269–85.

could instead appreciate their struggles—and their labor—in developing drugs and administering medicine in the absence of clear physiological and scientific principles about glands. We could also appreciate the rationality and pragmatism of their work: as doctors have shown us, patients needed to be treated, some glandular drugs, especially thyroid extracts and Adrenalin, were indisputably efficacious in some settings, and there was clearly something generally (if not specifically) valuable in Brown-Séquard's broader therapeutic ideas. It made sense to continue to experiment with glandular products, even if the rate of success was not high. Undoubtedly, doctors' innovative methods were at times employed with a brashness and an enthusiasm that might stick in the craw of endocrinologists from another time and another century. But their efforts did yield something, not least a culture of clinical experimentation with animal glands and a mainstream acceptance of (at least some) glandular therapeutics in the American medical community. Without the clinical actors that have appeared in this dissertation, there would not have been a clinical field to refine in the interwar period.

In assessing the contributions of doctors and druggists, we should also not forget about infrastructure. "Glands on the Market" has shown that "progress" in clinical endocrinology—if we are to continue using that word—amounted to the building of productive partnerships between the medical community and Parke, Davis & Co. as well as a system for the clinical testing of experimental drugs. We saw this most clearly in Parke, Davis & Co,'s Department of Experimental Medicine, which mobilized clinicians and clinics throughout the nation to test new products before they went to market. Scholars who write on the discovery of insulin remark on the powerful partnership that was formed between the University of Toronto and Eli Lilly & Company and emphasize the importance of pharmaceutical industry to rolling out a new and promising drug. This dissertation has shown that this pharmaceutical infrastructure was in development in America well before the

discovery of insulin. At least at Parke, Davis & Co., it was being built in the late 1890s and early 1900s, and it also included practicing physicians who collaborated with the company and opened the doors of their own clinics to clinical testing with experimental drugs.

One might question what we gain by traipsing through three decades of clinical experimentation, some of which was bizarre and unsuccessful. To the extant skeptics of Brown-Séquard and his disciples, I suggest that part of the value of remembering the first thirty years of clinical endocrinology lies in coming to terms with the reasons we have ignored it. Why is Brown-Séquard so little appreciated in the history of science and medicine? Why have doctors and drug companies not appeared more prominently in histories of the scientific revolution in medicine? What pre-conceived ideas about science and medicine have prevented us from engaging with the actors who did the most to develop clinical endocrinology as a practice and as an industry?

I have suggested in this dissertation that this history has been eclipsed by our preoccupation with the laboratory over the clinic, the achievements of academic institutions over corporations, and the work of scientists over practicing physicians. But there are other explanations too, such as the attempts of twentieth-century endocrinologists, including Lisser and Cushing and Evans, to tell a very specific and a one-sided account of how their specialty came to be. By arguing that what Brown-Séquard produced was not real science, that what doctors did in the clinic yielded bogus results, and that what drug companies prepared was not real medicine, endocrinologists have offered us a truncated and incomplete narrative about how a new therapy arrived in the world, where the academic laboratory was the most important and active site of knowledge production. But there is a cost to only selectively remembering scientific and medical work that was sanctioned by the elites. We lose touch with what was—and is—really happening beyond the walls of the academy. The history of clinical endocrinology specifically teaches us that not all unorthodox ideas are irrational, that

good drugs can come from humble origins, and that the right kind of commercialization can be very helpful to developing a clinical field. It also teaches us that practicing doctors are far more resourceful and willing to experiment than we give them credit for, and that effective science medicine need not be created in a lab.

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