Cyborg Butterflies, Liminal Medicine: Thyroid Hormone Treatment, 1890-1970

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ABSTRACT

In this thesis, I develop a history of thyroid hormone treatment (THT) that centers on the bodies of animals and women between 1890 and 1970. This history contextualizes the current debate between two forms of THT, desiccated and synthetic. Drawing on the discourses present in biomedical journals, I trace how medical practitioners used the animals and women to demonstrate and make sense of THT's effectiveness over time. As such, I study what Catherine Waldby terms the "biomedical imaginary," or the speculative fabric of scientific thought, to demonstrate how an "ordinary" medical technology crosses and reinforces the conceptions of gender and animality.

THT emerged in the 1890s as an organotherapy, or a medicine made from animal organs. Like other organotherapies, general physicians used THT for a wide variety of ailments that had not been scientifically proven through the practices of vivisection or animal experimentation. From its emergence, THT served as a site of tension between scientific researchers and general practitioners. This tension only increased when a synthetic form of THT was invented in the 1920s, when scientific researchers embraced synthetic THT and general practitioners continued using desiccated THT. At the center of the controversy were the productive and subversive relationships of animals and women to biomedical meaning-making. Over the twentieth century, methods of defining THT's effectiveness and purity were defined in opposition to these bodies. These chemical measures combined the specialist and physician's measurement of THT's clinical effectiveness, which led to a preference for synthetic THT.

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THT	Thyroid Hormone Treatment
T4	Thyroxine
T3	Triodothyronine
TSH	Thyroid Stimulating Hormone
JAMA	Journal of the American Medical Association
BMJ	British Medical Journal
JBC	Journal of Biological Chemistry
JCEM	Journal of Clinical Endocrinology and Metabolism
AMA	American Medical Association
FDA	Food and Drug Administration
FTC	Federal Trade Commission

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Introduction

In mid-summer of 2009, Armour Thyroid, a desiccated thyroid medication, ran short. Patients picking up their prescriptions received irregular doses, alternative brands or other forms of thyroid, upsetting the delicate hormonal balance that thyroid patients struggle to achieve. All this occurred without warning to either patients or pharmacists. Armour's website stayed silent for months, not acknowledging the growing crisis.[1]

Over the spring of 2009, a rumor had circulated that the Food and Drug Administration (FDA) was beginning to shut down Armour production. This shortage seemed to confirm that rumor. Patients reported driving around to every pharmacy in their towns and cities, looking for supplies of Armour. Soon, pharmacies had run out of not only Armour thyroid, but another popular desiccated thyroid products (Naturethroid) as well. The crisis soon reached a feverish pitch. Patients flooded listservs and Facebook walls, attempting to find *any* desiccated product by mail, internet or pick-up.

Mary Shomon, author of *about.com* Thyroid Disease Guide and pro-desiccated thyroid sourcebooks, and other patients contended that the FDA and manufacturer were trying to push patients towards a synthetic medication[2] --- a treatment that they found ineffective at treating all of their hypothyroid symptoms. The shortage, they argued, was just the most recent chapter in the debate between "natural" (desiccated) and "synthetic" thyroid.

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[1] For an archive of materials around the Armour Shortage, see Mary Shomon, "Armour Thyroid and Nature-Throid Natural Desiccated Thyroid Shortage in 2009 and 2010: A Summary of Coverage from 2009 through 2010," *about.com Thyroid Disease*, March 3, 2010, http://thyroid.about.com/od/thyroiddrugstreatments/tp/desiccated-thyroid-2009.htm.

[2] Mary Shomon, "Forest Pharmaceuticals: Armour Thyroid and Thyrolar are Still Back Ordered, and the Company Couldn't Care Less," *Thyroid Disease Blog*, July 1, 2009, http://thyroid.about.com/b/2009/07/01/forest-pharmaceuticals-armour-thyroid-and-thyrolar-are-still-back-ordered-and-the-company-couldnt-care-less.htm.

At first glance, the controversy is a battle between "mainstream" and "alternative" treatment options. "Natural" thyroid is purported to treat a larger variety of symptoms, including fatigue, weight gain, concentration and libido. "Synthetic" thyroid is purported to be more specific to the physiological functions of the body and based on more scientific research. Mainstream medical editorials call desiccated THT "crude" and the patients who consume it "crazy"; reciprocally, patients call those who prescribe only synthetic THT "ignorant." Specialized physicians who treat endocrine disorders, endocrinologists, largely support synthetic; holistic practitioners (e.g. Total Functional Medical Practitioners, Doctors of Osteopathic Medicine) are more likely to support desiccated.

However, desiccated THT has been in use for 120 years, and was supported by the mainstream medical community for nearly 90 of those years. The shortage could not be entirely attributed to governmental or professional intervention. After months of questioning by patients and patient advocacy groups, the FDA and Forest Labs (manufacturers of Armour Thyroid), stated that the problem was not with the production or governmental intervention, but a problem in the supply of "raw materials" or pig thyroids.[3] While some desiccated advocates challenged the supply argument, the shortage drew attention to the tacit dependence of the (mostly female) consumers of THT on the bodies of animals. Few patients or physicians acknowledged that what makes desiccated "natural" is that it is animal-derived, which informed why desiccated THT was and is called crude. Thus, these raw materials form the center of the debate around thyroid.

This thesis studies the historical conceptions of THT's effectiveness in terms of the animal bodies that make it, and the women's bodies who consume it. I argue that THT as a

[3] American Society of Health-System Pharmacists, "Bulletin : Thyroid Tablets," *Current Shortages: Bulletin*, July 8, 2010, http://www.ashp.org/Import/PRACTICEANDPOLICY/PracticeResourceCenters/DrugShortages/GettingStarted/CurrentShortages/bulletin.aspx?id=459. Currently only one agency supplies American manufacturers of desiccated THT with pig thyroids. While roughly 112 million pigs are killed each year, stringent assay mechanisms allow only a small fraction of these to be used in making desiccated THT.

successful therapeutic is based on the conditions of these material bodies, as well as their associated images within biomedical culture.

An Introduction to Thyroid, Disease and Its Treatment

Because the thyroid is a little remarked upon organ, a brief background into the history of thyroid disease and the controversy over its treatment is necessary.

The Thyroid

The thyroid sits right below the Adam's apple, wrapped around the middle of the larynx. It is often termed the "butterfly organ" because of its shape. Situated in the endocrine system, the thyroid is principally responsible for the creation of hormones associated with growth and metabolism. Other organs within the endocrine system include the pituitary, ovaries/testes, pancreas and adrenal glands. The pituitary, at the top left of *f*, sends out a hormone (thyroid stimulating hormone or TSH) to the thyroid, which then sends out a thyroid hormones (thyroxine or T4) to the be converted in the rest of the body into a more active form (triiodothyronine or T3). Thyroid sourcebooks tout that "[t]hyroid hormone is essential for our existence, affecting every single

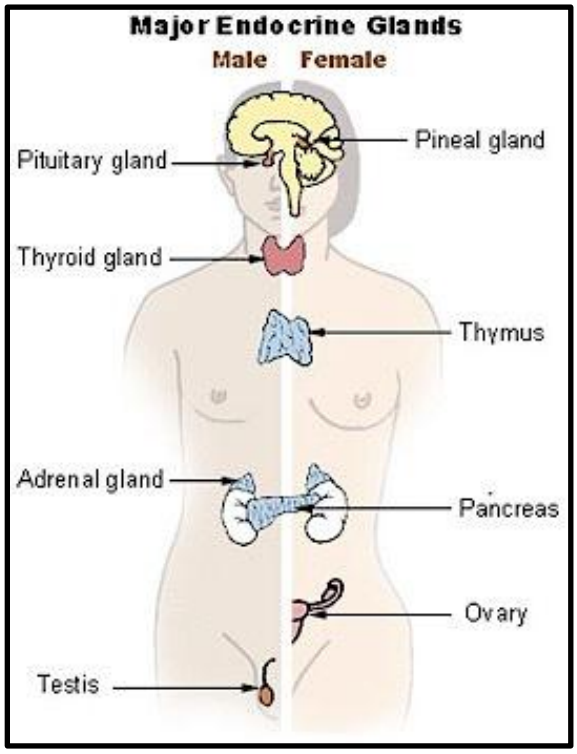

Figure I.1: The Endocrine System, http://training.seer.cancer.gov/anatomy/endocrine/glands/ (accessed Mar 2, 2011).

cell in the body."[4]

Until the latter half of the eighteenth century, physicians and medical resources offered brief and contradicting notions of the thyroid and its function within the body. Most sources connected the thyroid to its often-deadly swelling – the goiter.[5] Some resources stated that the thyroid functioned as a dam to prevent blood from rushing to the brain; others offered that it was an organ meant to beautify the neck, particularly in women, by bridging the gap between the larynx and the Adam's Apple.

The interplay between anatomical sites of gender and the thyroid is also worth noting. One eighteenth-century physician stated that the thyroid was like a "uterus around the neck" as it corresponded to the "womanly cycles," swelling and distending when under the stress of pregnancy and labor.[6] Similarly, in a review of former theories of thyroid function, editors of *Journal of the American Medical Association* (*JAMA*) cited that it expressed strong emotions "by swelling or condensing," and that "an intimate relationship between the gland and the sexual apparatus was recognized."[7] Medical researchers have codified this connection into what they called the "thyroid axis," or the interplay of the pituitary, thyroid and (particularly female) reproductive glands. Simultaneously, the thyroid inhabited both bodily and affective performances of gender.[8]

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[4] Kenneth B. Ain and M. Sara Rosenthal, *The Complete Thyroid Book* (New York: McGraw-Hill Professional, 2005), 9.

[5] The goiter has its own rich history that deserves a study on its own. It would offer a prime example of the comparative histories of medicine, as Medvei states, organotherapy for treatment of goiter was introduced in Chinese medicine in 1493, and depictions of the goiter trace back to the reign of Cleopatra. Further, the use of goiter to depict "others" within print media deserves more attention. See Victor Cornelius Medvei, *The History of Clinical Endocrinology: A Comprehensive Account of Endocrinology from Earliest Times to the Present Day* (New York: Taylor & Francis, 1993). For a history of the depiction of goiters, see F. Merke, *History and Iconography of Endemic Goitre and Cretinism*, 1st ed. (New York: Springer, 1984); F G Vescia and L Basso, "Goiters in the Renaissance," *Vesalius* 3, no. 1 (June 1997): 23-32.

[6] Oliver T. Osborne, "The Therapeutic Uses of Thyroid Preparations," *Journal of the American Medical Association* 47, no. 18 (November 1906): 366.

[7] "Societies," *Journal of the American Medical Association* 34, no. 3 (1900): 164-173.

[8] I hesitate to separate out the categories of body biology and social performance. For thorough critiques of the

Disease

As many people suffer from thyroid disorders as diabetes.[9] Physicians generally recognize two major categories of thyroid disease: hypothyroidism and hyperthyroidism. The latter means that the thyroid gland is over-active (hyper), producing enough hormones to overwhelm the body. The symptoms include an increased heart rate (and an increased risk of heart attack), as well as nervousness and high cholesterol. Hypothyroidism is at the opposite end of the spectrum, because –for a variety of reasons – the thyroid does not produce enough thyroid hormones to keep the metabolic rate steady. The symptoms for hypothyroidism consist of a low body temperature, puffy skin (myxoedema), and slow cognitive function and reflexes.

This project concerns hypothyroidism and its treatment. Popular literatures have drawn connections between hypothyroidism and obesity, depression and unexplained pains. At once, hypothyroidism is a catchall disease. But it is also under diagnosed, particularly in women, according to several epidemiology studies.[10]

Though thyroid disease affects roughly the same number of people as diabetes, it receives much less popular media attention than diabetes as a serious chronic disease. While thyroid hormones are both "essential to every cell in the body," the definition for hypothyroidism is surprisingly narrow. Thyroid disease is diagnosed contemporarily through blood tests that

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divide between biology/culture and sex/gender, see Anne Fausto-Sterling, *Sexing the Body: Gender Politics and the Construction of Sexuality* (Basic Books, 2000); Donna Jeanne Haraway, "'Gender' for a Marxist Dictionary: The Sexual Politics of a Word," in *Simians, Cyborgs, and Women: The Reinvention of Nature* (New York: Routledge, 1991), 127-48.

[9] James Blackwell, "Evaluation and Treatment of Hyperthyroidism and Hypothyroidism," *Journal of the American Academy of Nurse Practitioners* 16, no. 10 (October 2004): 422. The AACE found that 27 million people suffer from thyroid disorders; diabetes affects roughly 26 million. The statistics on thyroid disorders vary widely because the range of blood diagnosis varies from clinic to clinic, and many people's thyroid conditions are undiagnosed.

[10] Gay J. Canaris et al., "The Colorado Thyroid Disease Prevalence Study," *Archives of Internal Medicine* 160, no. 4 (February 2000): 526-534; WM Tunbridge et al., "The Spectrum of Thyroid Disease in a Community: The Wickham Survey," *Clinical Endocrinology* 7, no. 6 (December 1977): 481-93.

usually measure how much TSH (the hormone sent out from the pituitary to the thyroid) is in the blood stream. If the TSH is too high, the patient is diagnosed as hypothyroid. Physicians claim that the symptoms of hypothyroidism are too unspecific to be a reliable measure of diagnosis. Patients diagnosed with hypothyroidism often express frustration because their symptoms were not taken seriously, or that they were misdiagnosed with a number of illnesses because they "failed" the TSH blood test.[11]

Thyroid disease is often described as a "woman's disease." A recent report found that the ratio of women to men who are diagnosed with hypothyroidism is 10:1; Hashimoto's thyroiditis, an autoimmune condition causing alternating periods of hypo- and hyperthyroidism, has a 50:1 female to male ratio.[12] The fields of women's medicine and endocrinology both accept the high prevalence of thyroid diseases in women as a fact without need of explanation. As shown in the overview of the thyroid itself, the interplay of gender categories and thyroid disease is not often remarked upon in current medical literature.

Treatment

The treatment for hypothyroidism usually involves giving thyroid hormones to the body. This form of treatment is usually called "thyroid hormone supplementation" or "thyroid hormone replacement." For the purposes of my research, I do not draw a strong distinction between the two, and thus describe the consumption of thyroid hormones to treat hypothyroidism as thyroid hormone therapy (THT). A physician will adjust a patient's dose of THT until either their

[11] For a sociological perspective on gender and chronic illness and interactions with physicians, see Anne Werner and Kirsti Malterud, "It is Hard Work Behaving as a Credible Patient: Encounters between Women with Chronic Pain and their Doctors," *Social Science & Medicine* 57, no. 8 (October 2003): 1409-1419.

[12] M. Sara Rosenthal, *The Thyroid Sourcebook for Women*, 1st ed. (New York: McGraw-Hill, 1999), 1; Matthew C Tews, Sid M Shah, and Ved V Gossain, "Hypothyroidism: Mimicker of Common Complaints," *Emergency Medicine Clinics of North America* 23, no. 3 (August 2005): 649-50.

symptoms are better, or their TSH test reads in the "normal" range.

A number of medical professionals can diagnose and treat hypothyroidism, from general physicians to specialized physicians, or endocrinologists. The former generally maintains a patient's dose once an endocrinologist establishes it. Endocrinology is a medical science, a subdiscipline of physiology, or the study of the processes of the body. It was established in the early 1920s, and THT provided much of the legitimization for the field's formation. Endocrinological associations establish the standards of diagnosis and treatment of thyroid disorders, which general physicians more or less follow. Throughout this thesis, I discuss mainly the discipline of endocrinology, as well as the differences in interpretations between general and specialist's understandings of thyroid disorders.

Prescription THTs take two major forms: desiccated and synthetic. Desiccated THT uses the dried and ground animal thyroids that undergo various forms of chemical assay and refinement.[13] Desiccated thyroid was used to treat severe hypothyroidism (then known as myxoedema) since the 1890s.[14] It was one of the first hormone treatments to be used. It remained the standard of care until the 1950s, despite the introduction of synthetic THT in 1926. Synthetic THT is created through the chemical manipulation of animal- and plant-based proteins, and pharmaceutical firms did not start producing it commercially until 1955. The compositional difference between synthetic and desiccated THT is that the latter contains two thyroid hormones – an "active" (T3 or triiodothyronine) and "dormant" (T4 or thyroxine) hormone – while the

[13]The major manufacturers of desiccated thyroid use porcine, or pig, thyroid. Pig thyroids were adopted over bovine (cow) or sheep thyroids around the 1940s. While whole desiccated thyroid is a controlled substance, which requires a prescription from a licensed medical practitioner, certain preparations of bovine, sheep and porcine thyroid are available over the counter as supplements. These preparations are less active meaning that they contain trace amounts of T3 or T4.

[14] As Chapter One discusses, desiccated THT was one of many preparations of animal thyroid used until the 1910s.

synthetic variety only contains the dormant (T4) hormone.[15]

Most medical associations, including the American Thyroid Association and the American Association of Clinical Endocrinologists, only recognize or approve the synthetic THT. These organizations describe desiccated THT to be "outdated" and "unpurified."[16] Still, a strong minority of patients and physicians advocate the use of desiccated THT, claiming that it relieves a majority of their hypothyroid symptoms because it contains T3 along with other ingredients that help the thyroid. THT is thus one of the only medications where the animal-derived and chemical forms are used today. The controversy between desiccated and synthetic thyroid medication continues to rage today, fueled by the recent shortage described above.[17]

The very descriptions of crude and outdated are based mostly on the presumption that animal-derived thyroid are impossible to control chemically or scientifically. As I discuss in Chapter Two, the 1920s invention of synthetic THT was legitimized by the assertion that desiccated THT had variable potency, and thus synthetic offered a constant and controlled therapy. Few studies show that what was supposedly constant or variable within desiccated THT is the amount of the two recognized thyroid hormones (T4 and T3) within the mixture.

Desiccated advocates contest that the activity of THT, and thus its effectiveness, depends on much more than the T3 and T4 content in a given pill. They cite that other compounds found only in desiccated THT (e.g. T1, T2, and calcitonin) contribute to the amelioration of symptoms, which are not adequately treated by the isolated synthetic therapies. The implicit contention is

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[15] There is a synthetic T3-only preparation, under the brand name of Cytomel and produced by the same manufacturers as Synthroid. T3/T4 combinations were popular during the 1970s, but have since ceased production. During the shortage, an alternative to desiccated was stated as combining synthetic T3 and T4 to match the ratio of desiccated THT (1:4.22).

[16] See, for example, American Association of Clinical Endocrinologists, "AACE responds to CBS The Early Show," *American Association of Clinical Endocrinologists*, October 18, 2005, http://www.aace.com/cbsletter.php.

[17] Shortages of either synthetic or desiccated thyroid are not unusual. Recalls of expired or mixed potency batches made and make a common enough occurrence on FDA websites of recalled medications. What made the 2009-10 shortage above so devastating was that it affected *all* strengths and preparations of Armour Thyroid.

that because desiccated THT is derived from animal glands, that it contains substances that are not considered essential to (the replacement of) thyroid function. To advocates of both treatments, these excess substances differentiate desiccated THT from synthetic.

As I argue throughout this thesis, the definition of what compounds or preparation methods makes THT effective or more efficient draws from the negotiations of the bodies of animals and women. Manufacturers of desiccated THT harvest thyroids from the bodies of livestock animals, clean them, dry them and combine them for maximum potency. Biochemists and medical researchers historically used these glands as well to isolate and define the active constituents of T3 and T4. Manufacturers of synthetic THT also use the by-products of livestock animals to form the base proteins and chemicals used in making synthetic THT. Thus, both forms of THT contain the bodies of animals, both in definition and material.

Because women make up the majority of people diagnosed with the disease, they also make up the majority of research subjects and case studies. Images of women before and after treatment populated treatment advertisements and medical testimony throughout the century. THT has been historically used to treat a wide variety of reproductive and menopausal ailments, as well as treating obesity, mostly in women. However, as stated in this overview, the connection between hypothyroidism, THT and women has yet to receive critical attention.

Animals also serve as mediums in which manufacturers and endocrinological researchers use to assay the potency of their products and given batches.[18] Assay measures usually involve the killing of the rat to measure its thyroid after treatment, called a goiterigenic assay. As I explore in Chapter 1, much of the basic research in developing definitions of myxoedema and THT was conducted on vivisected animals.

In this way, the activity of THT is determined through the bodies of animals and women,

[18] Rats are the preferred species of assay in thyroid research.

and the historical negotiations of these bodies affect and codify attitudes toward them. The preference of synthetic over desiccated in the past thirty years certainly draws on these negotiations. Thus, the descriptors of crude, outdated and even natural serve as starting places to historically analyze the definitions of THT's activity and effectiveness.

Theoretical Frameworks

As seen through this overview, images of women and animals are elided from the discourses of THT, yet actually form two primary sets of bodies that make THT possible. That is, animals have been used as both raw and research materials to treat a condition described as a woman's disease.[19] Analyzing these two sets of bodies allows for a deeper understanding not only of the current shortage, but also the medical preference for synthetic in general.

This project studies the bodies of animals and women through an analysis of the scientific and medicalized languages that endocrinologists and general physicians use to describe and study THT. These discourses draw on the rich history of negotiations around the bodies of animals and women in hypothyroidism. Rather than concentrate on the literal manifestations of these negotiations, I engage with what Catherine Waldby terms the "biomedical imaginary," or the "speculative, propositional fabric of medical thought, the generally disavowed dream work performed by biomedical theory and innovation."[20] By studying the biomedical imaginary, I analyze the historical procedures used in these negotiations of the effectiveness in the two forms of THT, and show how the otherwise erased bodies of animals and women are formed in the discourses surrounding THT. I insist on the material realities, and material deaths, which make

[19] I draw on the distinction of raw and research from the conversations of Nelly Oudshoorn and Adele Clarke (Nelly Oudshoorn, *Beyond the Natural Body: an Archaeology of Sex Hormones* (Taylor & Francis US, 1994), 159n1.
[20] Cathy Waldby, *The Visible Human Project: Informatic Bodies and Posthuman Medicine* (London: Routledge, 2000), 136.

the "theory and innovation" of endocrinology possible.

I argue along with Waldby that all medical practice and research draws on such supplemental knowledge work, and it is, in part, the disavowal of this work that defines the rhetoric of medicine and medical science. Because medical scientific thought is written in such "strictly systematic" language, the images and assertions generated by these disciplines should be investigated even more thoroughly. However, I contend that the biomedical imaginary is not something that is supplemental to the actual practice of medicine, but deeply embedded within it. Endocrinologists and general physicians, through drawing on the negotiations of animal and female bodies, codify these images within the very diagnostic and treatment decisions. This embeddedness only emphasizes the need to analyze these images within the biomedical imaginary.

The controversy over THTs is not merely a controversy between alternative and mainstream medical practices, but a recent iteration of an evolving negotiation of THT's effectiveness within the biomedical imaginary. The controversies surrounding the shortage above serve as ruptures within the strictly systematic discourses of THT. As Bruno Latour states in *Science in Action*, controversies are prime sites of "[medical] science in the making."[21] However, the controversies serve as a starting place within this project, as places to see the images of the biomedical imaginary in use. The presence of desiccated THT within the mainstream medical practice points to the crude images upon which endocrinology as a medical scientific field is based – animals used as therapeutic and assay mechanisms, and women's bodies receiving and defining conceptions of treatment and cure.

To define THT's effectiveness, medical practitioners and researchers call on images

[21] Bruno Latour, *Science in Action: How to Follow Scientists and Engineers through Society* (Harvard University Press, 1988), 4.

within the biomedical imaginary. These images serve as "liminal" figures, a phrase that Susan Squier deploys in her book *Liminal Lives* to describe "the state of being on the threshold of change."[22] Squier investigates how the areas of stem cell research, hormone replacement therapies, and xenotransplantation renegotiate the boundaries between life and death, human and nonhuman, and science and culture. In this project, I focus on the ways in which animals and women as liminal figures define and challenge the boundaries of what is proper, safe, and human in THT. The discourses around THT renegotiate its engagement with these liminal figures, and these negotiations have implications for the widespread areas of endocrinology and medicine as a whole. Thus, THT and its surrounding discourse constitute what I term "liminal medicine."

THT, as one of the first modern medicines to use animal organs, renegotiates the limits of life and death. The tension between THT as a living substance and a dead substance rests on a shift of understanding of the boundary between life and death. The thyroid taken to make animal-derived THT is a liminal figure: a tissue that has been taken from an animal corpse, but is alive or active enough to replace a dead thyroid in a living female body. Further, the tissue requires chemical manipulation to maximize desiccated THT's effectiveness; in synthetic, the active constituents need to be synthetically reproduced, combined and brought to life. Thus, THT is both living and dead, held in strict tension between meat and medicine, pure and effective.

Considering THT as a liminal medicine allows an exploration of how the bodies of animals and women both created and subverted definitions of THT's effectiveness. In one sense, THT's effectiveness was the foundation to the field of endocrinology. However, because endocrinology instigated a chemical understanding of the body, the ideal form of a therapy was

[22] Susan Merrill Squier, *Liminal Lives: Imagining the Human at the Frontiers of Biomedicine* (Durham: Duke University Press, 2004), 13-4.

one whose activity can be explained and produced easily in chemical terms. THT resisted this chemical definition and subsequent production until the 1950s. As such, physicians had to negotiate THT as an effective organotherapy, one that, as I explore in Chapter 1, was embedded within the practices of meat consumption and animal experimentation. Thus, THT was a liminal medicine that draws its notions of effectiveness from within and outside medical science.

Desiccated THT is one of the only pharmaceutical products used today that is derived from animal organs.[23] Premarin, a drug primarily used as estrogen replacement therapy, is derived from horses' urine, and has received critical attention from PETA and physicians alike.[24] Since the thyroid is viewed as a by-product of animal slaughter, desiccated THT receives little critical attention as a material that would likely already go to waste.

In this instance, however, harvested thyroids can point to a more complicated history of the politics that make rendering possible. Nicole Shukin in *Animal Capital* states that the politics of rendering requires "continuously complicating both the historical conditions and effects of power" to avoid falling into either the material politics of meat consumption or the cultural politics of "fetishizing" the origins of by-products.[25] THT, thus, is not simply an instance where animal-derived products are used for medicine, nor can it be described through the nostalgic return to a holistic, "natural" past. Yet THT is also embedded within the discourses that make

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[23] Insulin to treat diabetes was derived from the pancreas of pigs until the 1980s. In my brief review of the subject, there seems to be far less controversy over genetically human and animal insulin than is present within THT. For an example of discussions over human vs. pig insulin, see Amy T, "Wayback Wednesday: The Quest for Animal Insulin," *DiabetesMine: the all things diabetes blog*, September 30, 2009, http://www.diabetesmine.com/2009/09/wayback-wednesday-the-quest-for-animal-insulin.html.

[24] Specifically pregnant mare's urine, though, as Nelly Oudshoorn has pointed out, the concentration of estrogenic compounds is greater in stallion's urine (*Beyond the Natural Body*, 25). For an example of the concern over Premarin from a medical perspective, see D Cox, "Should a Doctor Prescribe Hormone Replacement Therapy which has been Manufactured from Mare's Urine?," *Journal of Medical Ethics* 22, no. 4 (August 1996): 199-203.

[25] Nicole Shukin, *Animal Capital: Rendering Life in Biopolitical Times* (Minneapolis: University of Minnesota, 2009), 75.

these processes possible. Terming desiccated as natural implies that the animal-derived THT is somehow separate from the industrialized logics that inform synthetic THT. And the insistence that synthetic THT is more precise and thus effective insists that the animal product within desiccated THT is antithetical to science. The biomedical discourses define THT's effectiveness by drawing on both of these conceptions. THT cannot be separated from the animal bodies, nor can it be reduced to them.

Similarly, it is also impossible to separate out images of women from the biomedical imaginary of THT. Women constitute – both historically and contemporarily- the primary bodily sites of myxoedema in humans. As such, this study offers an interesting case of comparison to historical studies of sex endocrinology, most notably Nelly Oudshoorn's *Beyond the Natural Body*. Many of the same processes – biological assays, production issues, and synthetization – occur within THT and sex endocrinology. As Nelly Oudshoorn suggests, the female body is the norm of the hormonal body, and THT offers a case study of how women's bodies are embedded as medical subjects within hormonal medical discourse.[26]

This thesis demonstrates how women and animal bodies are embedded within discourses surrounding THT. I argue that these discourses "become with" the bodies of women and animals. Donna Haraway uses this term in her 2008 book *When Species Meet* to discuss the multiplicity inherent in the category of human, which serves as a re-reading of her concept of the cyborg or liminal figure. Drawing on the fact that only ten percent of the human body actually contains the human genome, she states that "to become one is to become one with many."[27] I use this term to signal the reliance of endocrinology upon the bodies with which it demonstrates its findings, and to articulate the relationships between animals and women in past and present

[26] Oudshoorn, *Beyond the Natural Body*, 148.
[27] Donna J. Haraway, *When Species Meet*, vol. 3, (Minneapolis: University of Minnesota Press, 2007), 3.

configurations. My analysis attempts to show how animals and women constitute the material and imaginative realities of THT, and thus thyroid disease in general. Hence, I draw attention to their interdependence in the term "Cyborg Butterflies." Such an analysis pays attention to both the conditions of biomedicine's usage of these bodies, but also the images that inform these bodies in the biomedical imaginary.

Methodology

To study of the biomedical imaginary of THT, I draw from articles within the biomedical archive. I am primarily interested in how medical professionals and researchers engage with the images of animals and women throughout the history of THT. I look to a sample of general and specialized medical journals (see Table I.2 below) as sites where procedures and practice draw on these images. I take the articles I survey to be stylized rituals in medical meaning-making, what Bruno Latour and Steve Woolgar term "inscription devices" which mediate and codify the fleshy bodies of knowledge construction in particular ways.[28]

The journals themselves serve different voices at different times. General professional journals such as the *Journal of the American Medical Association* and the *British Medical Journal* are sites of reports of invention and minute negotiations of treatment in the early history of endocrinology (1890s-1940s), and later serve as sites of editorials legitimizing or critiquing synthetic and desiccated THT. They are also barometers for the popularity of a given treatment in the later history of endocrinology in this study (1940s-1970s). The specialized journals, in this case, *The Journal of Clinical Endocrinology and Metabolism* and *Thyroid*, emerge as sites for not only the more specialized knowledge constructions, but also deal increasingly with the

[28] Bruno Latour and Steve Woolgar, *Laboratory Life: The Construction of Scientific Facts* (Princeton: Princeton University Press, 1979), 245.

bodies of liminal figures. Summaries and receptions of the findings are reported within the more general journals.

Journal Title	**Abbreviation**	**Dates Reviewed**
British Medical Journal	*BMJ*	1880-1970
The Journal of the American Medical Association	*JAMA*	1890-1970
The Journal of Clinical Endocrinology and Metabolism	*JCEM*	1941-1970
Thyroid	*Thyroid*	1991-2010

Table I.2: Journals Reviewed in Establishing Medical Discourse

I take the notion of discourse to mean not only the text of the journals, but also the procedures and narratives the text describes. Within each chapter, I spend some time on individual articles. I take these individual articles not to represent an intellectual history of thyroid hormone treatment, but to represent major shifts and important moments within the medical discourses surrounding thyroid hormone treatment. For example, in Chapter Two, I spend time discussing the ways in which the synthetization procedures reflect images within the biomedical imaginary.

I take a departure from the approaches of historians of endocrinology such as Merriley Borell and Victor Medvei in that I pay less attention to singular authors, as I am interested in reading "above and below the text" (as Haraway advocates) for the translations of their work in the larger medical imaginary. The story of THT through the heroic and personal individuals within THT has already been quite exhausted. Because I am dealing with unwieldy bodies and fragments, an approach that seeks to explain the influences of personal bias and intentionality seems less convincing than one that explores the tacit images haunting the discourses themselves.

Limitations

My thesis focuses on the treatment, rather than disease, of hypothyroidism. By analyzing the treatment, I do not imply that the disease is any less important. Rather, my focus requires a discussion of the material realities of the disease, which implicates the bodies used in defining the disease and its treatment. Further, the disease of hypothyroidism is often a condition that is the result of a variety of disorders – including Hashimoto's thyroiditis, Grave's disease, and radiation exposure. Further, the complications present in treating hypothyroidism are often overlooked in the medical discourse.

While thyroid hormone treatment certainly served as a conduit for adopting the "scientific" medical practices of German and French physiologists, I study primarily the journals and discourses of the British and American researchers and physicians. I limit my study thus because THTs were tried first within United Kingdom, and the American meat manufacturers such as Armour made possible the wide dissemination of thyroid extract and powder. Often, the major actors from Germany and France, in particular, will appear in summary sections of the journals listed above. At times, I include the reception of these articles when more explanation is needed.

Further, the national and temporal limits of this project exclude the discourse and contributions of non-Western countries, where the treatments of goiter trace back to the first century. I've included some notable events in thyroid hormone therapy in Appendix A. Today, India and China are both major suppliers of various versions of desiccated thyroid to consumers across the globe, a fact discovered by many patients who used these suppliers for the first time in the shortage of 2009. The politics of this exchange are certainly worth discussing, but it requires another project entirely.

It is not my attempt to repeat the already extensive histories of endocrinology and the

hormone concept. These have already been done through the work of Victor Medvei and the dissertation work of Merriley Borell.[29] This project is rather an attempt to offer an example of an area of intersection between animal studies, gender studies and hormonal histories.

Finally, as discussed above, I limit my study to the history of myxoedema and hypothyroidism in adults. While the history of cretinism certainly is not easily distinguished, other than it's a disease of myxoedema that affects children, I suspect that the disease and treatment are situated within a similar biomedical imaginary. Many of the examples and articles I draw on Chapter 1 discuss cretinism alongside myxoedema.

Chapter Organization

This project historically contextualizes the debate between desiccated and synthetic THT as a negotiation of animal and women's bodies in the biomedical imaginary. By focusing on the gendered and special bodies neglected in the narratives of THT's history, this project brings to light the affective and imaginary dimensions of diagnosing and treating hypothyroidism. Further, this project's larger goal is to insist on the fleshy materialities of thyroid's history to trouble the medical discourses that divorce the imaginary from the material realms.

Chapter One, "Between Meat and Medicine" studies how early THT's success was established (1890-1910).[30] Drawing on the debates surrounding vivisection and meat consumption, I discuss how THT's effectiveness was established through the bodies of animals

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[29] See Merriley Borell, "Origins of the Hormone Concept: Internal Secretions and Physiological Research, 1889-1905" (History of Science, Ph.D. Dissertation, Hartford: Yale University, 1976); Medvei, *History of Clinical Endocrinology*.

[30] Constructing my chapters in chronological order serves two purposes: first, it attempts to offer an alternative genealogy from other histories of THT; secondly, it means to show how the images shown and displayed from the first chapter echo and haunt the discussions and choices in the second and concluding chapters. In this, I hope to both be as historically specific as possible, while drawing connections between discursive events and procedures and the images which they entail.

and women. Most historians state that THT served as the fodder for the increased interest in "internal secretions," or what Ernest Starling would later call "hormones."[31] Yet there was a persistent uneasiness that the origins of endocrinology were not as scientifically sanitized as later endocrinologists imagined them to be.

Within this chapter, I investigate THT as an organotherapy. As such, I analyze THT in terms of the actual fleshy and excessive bodies that were consumed to both produce knowledge about myxoedema (a more severe version of hypothyroidism) and the use of animal thyroids to treat it. As Merriley Borell states, physicians used animal-derived THT widely before physiologists, scientific medical practitioners, could determine the reasons of its effectiveness.[32] Thus, explanations for THT's effectiveness draw on the figures of animals already within the discourse in discourses around meat consumption and vivisection. I consider the tensions present in using animal organs as specific therapeutic as both becoming scientific with animals and becoming animal. That is, on one hand, both animal and female bodies were being used to demonstrate the power of medical research. On the other hand, the correlation between animals and women created uneasy tensions over medical researchers crossing tenuous special divides. Medical professionals combined both of these discourses to determine a measure of the activity of the thyroid gland.

While other historians have made connections between agriculture and endocrinology, few (if any) have made the connections between these two fields and the (anti)vivisection debates. Curiously, both the regulation of food and drugs and the vivisection debates occurred within the same decade as one another. The meat industry made the large-scale production of

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[31] Oudshoorn, *Beyond the Natural Body*, 15; Bernice L. Hausman, *Changing Sex: Transsexualism, Technology, and the Idea of Gender* (Durham: Duke University Press, 1995), 27.

[32] Merriley Borell, "Organotherapy and the Emergence of Reproductive Endocrinology," *Journal of the History of Biology* 18, no. 1 (1985): 3-4.

THT possible, while the (anti)vivisection debates both "assimilated" the popular gaze and those of the medical professionals and legitimated the increased role of experimental animals in medical research, specifically endocrinology. I conclude the chapter by showing how both discourses affected the definition of THT's effectiveness through the chemical compound iodine.

Chapter Two, "Pure and Efficient," chronicles two episodes in the push toward isolation and synthetization in 1920s and 1950s. While thyroid treatment predated other organotherapies in its adoption, the isolated and synthesized product was not widely adopted until 30 years after its invention. I argue that its slow adoption was due to the divergent definitions of synthetic THT's purity and desiccated THT's effectiveness. Thus, the adoption of synthetic THT depended on tests that emphasized chemical purity as more clinically effective. As other medical histories have found, the increased reliance on synthetic products paired itself with the emergence of quantitative diagnostic measures and controlled clinical trials. As desiccated THT was considered impure and inconsistent, it was elided from use in randomized clinical trials.

In this chapter, I trace how synthetic THT was defined as pure because it was composed of chemicals, rather than raw animal glands. With synthetic THT, the site of medical intervention was isolating the pure and active constituent within these glands. This emphasis shifted medical attention from the definition of treatment by the patient, to the control of activity in the gland. The bodies of women and animals increasingly were labeled as marginal and crude throughout the twentieth century, and medical regulators increasingly defined desiccated THT as a nonviable drug. The regulation of Marmola, an anti-obesity medication that contained desiccated THT, signaled a shift in the consideration of THT on both of these fronts. In what has previously been studied as an episode in quackery, I argue that Marmola "passed" as a legitimate medication because of the generalized effects of THT.

I conclude with a brief reflection on how this project can serve as a foundation for the study of patient perspectives in the biomedical imaginary. I then provide an example of a site of intervention in the current patient discourse, and how offering a critical historical lens can translate some of the contradictions within patient-centered discourses.

Chapter One
Between Meat and Medicine:
Women, Medical Animals and the Emergence of THT

In 1907, science was on trial. The Royal Commission on Vivisection commenced hearings regarding the experimentation on live animals. Medical scientists insisted that live animal experiments were necessary to create scientific knowledge about disease and the inner workings of the body. Animal rights advocates claimed that scientists created unnecessary suffering in animals, and that the practice was unethical and inhumane.

Medical scientists repeatedly listed the number of benefits that had resulted directly from animal experimentation. Thyroid hormone therapy (THT) was among them. When animal rights advocates, or antivivisectionists, were brought to testify, they were often asked if they had heard of or used THT before.

Such was the case with Arabella Kenealy, a medical student and key witness for the antivivisectionists. When asked if she had used thyroid or adrenaline to administer to sick patients, she replied that the medical establishment "had quite enough beautiful healing medical substances from the mineral and vegetable world, without going to the bodies of lower creatures. She thought there was a great deal of danger in it."[1] Such an objection to the use of animal organs was common among antivivisectionists, who protested the emerging method of using animal organs to treat diseases, what was termed organotherapy.[2]

Her testimony continues,

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[1] "Royal Commission On Vivisection (Continued)," *The British Medical Journal* 1, no. 2424 (June 1907): 1430.

[2] Merriley Borell states that the "outrage among antivivisectionists, who objected to the use of extracts of animal organs" was part of the reason for the lack of enthusiasm within the biomedical discourse for organotherapy. See Merriley Borell, "Organotherapy, British Physiology, and Discovery of the Internal Secretions," *Journal of the History of Biology* 9, no. 2 (Autumn 1976): 238.

> Asked if she would carry that so far to include cod liver oil, she said that was a food. It was not given subcutaneously [under the skin]; it was given via the stomach, and the stomach was a very *intelligent organ*, and discriminated between things which were bad and which were good to be passed into the system.[3]

Kenealy's disapproval of organotherapy centers on the distinction between the injection and the consumption of animal substances. The intelligent organ in her testimony serves as a mediator in distinguishing between meat and medicine, what is good for the system and what is dangerous.

Medical practitioners and researchers also interpreted THT through these two categories. Kenealy's testimony serves to show the controversies surrounding the injected and ingested forms of treatment, between the "new" use of animals for medicine and the "old" use of animals for food. THT, as one of the first of these organotherapies, is situated at the intersection of both of these uses of animals. Physicians prescribed forms of THT to be injected or ingested – used under the skin or through the stomach. THT blurs the border between meat and medicine.

This chapter investigates how the medical discourse interprets THT's effectiveness as types of meat consumption and medical vivisection. Both of these discourses depend on the bodies of animals and women, but they both configure these bodies differently. THT was conceived in the processes of vivisection, as well as transplantation and glandular grafting, where the animal tissue is kept alive; the conversation of meat consumption interprets THT as a by-product of animal slaughter, and thus a piece of (dead) meat to be consumed. THT embodies both of these interpretations simultaneously, and I conclude the chapter by showing how this liminal position between dead and living tissue is codified into measures of THT's effectiveness.

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[3] Ibid.

The distinction between the ingested and injected organotherapies has received little attention from historians of endocrinology. With most other organotherapies, one administration was usually lauded as more potent or more efficacious than the others.[4] In the case of THT, both ingested and injected forms were used simultaneously until the 1920s, each considered equally successful. However, the injected forms more directly engaged with the image of the living animal and woman because they draw on the methods of vivisection. The ingested forms allowed for a more complete elision of the bodies of the slaughtered animal and woman.

The desiccated THT that is used today is one of the only organotherapies still in use.[5] Other organotherapies were dismissed as viable medical therapeutics in the 1920s, as their chemical synthetic counterparts were more potent or less costly to produce. Because physicians considered desiccated THT so effective at treating hypothyroidism, it was not largely (nor entirely) dismissed until the 1960s. As such, the study of what makes THT a *scientific* organotherapy is paramount to understanding its subsequent dismissal in the late twentieth and early twenty-first centuries. As such, I explore how the ingested and injected forms affect medical interpretations of THT's effectiveness, and thus its adoption, in the decade before and after the turn of the twentieth century.

After exploring how THT and organotherapy emerge, I discuss how THT emerged from the practice of vivisection and then how THT was adopted within the discourses of meat consumption and industrial meat manufacturing. I conclude by examining the ways in which these discourses converge to chemically measure THT's effectiveness in the early twentieth century.

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[4] For example, testicular extract was understood to be more potent injected, and worthless through oral administration. Nelly Oudshoorn cites the same for ovarian preparations. Nelly Oudshoorn, *Beyond the Natural Body: An Archaeology of Sex Hormones* (London: Routledge, 1994), 45.

[5] The desiccated THT contemporarily used is assayed chemically, while preparations of the 1890s were not assayed, usually at all. At base, both are the dried and powdered glands of livestock animals.

Background: Murray's Extract

In 1891, British physician and budding physiologist George Murray injected a patient with the extract of sheep thyroid. The patient, Mrs. S, had become so swollen and lethargic that she could not do her housework. She had not menstruated in over four years, and her skin was swollen and hard. Murray diagnosed her with myxoedema, or thyroid deficiency.[6] Three months after her treatment, Murray stated that Mrs. S now menstruated regularly, and her beauty had returned.[7] All her symptoms had subsided so that she could return to normal life.

Murray's extract drew implicitly on the method of organotherapy. Two years earlier, Charles-Édouard Brown-Séquard introduced the method of organotherapy by injecting himself with the extract of "vigorous young mammal" testicles.[8] Brown- Séquard's extract received a good deal of press in Russia and the United States, but not in the United Kingdom. The little attention his findings received in the major British medical journals was negative, usually dismissing his findings as the "ramblings of a medieval natural philosopher" or the product of a "senile mind."[9] Despite some confirming reports, the *British Medical Journal* editorial staff would not extensively report on Brown-Séquard's extract until 1892, and quite a few medical professionals objected to the practice entirely.[10]

THT brought scientific merit to the method of organotherapy and the study of internal secretions, which would later solidify as the field of endocrinology. Unlike Brown-Séquard's

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[6] Myxoedema is the precursor to hypothyroidism. It is generally understood as more advanced case, and today it is used only in conjunction with a coma (myxoedemous coma). See Introduction.

[7] 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 (October 1891): 796.

[8] He and his assistant, d'Arsonval, did preliminary tests on guinea pigs and rabbits before Brown-Séquard injected himself. For a more detailed description of Brown-Séquard's experiments, see 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): 309-320.

[9] Borell, "Organotherapy, British Physiology, and Discovery of the Internal Secretions," 238.

[10] Ibid.

rejuvenation studies, Murray applied thyroid extract to cure myxoedema, a specific disease of one particular organ: the thyroid. British and German physiologists recreated myxoedema in animals by removing their thyroid gland throughout the 1880s, and so the disease was understood as the lack of a functioning thyroid. A committee of the Clinical Society of London had appointed a committee to its study in 1883, and the committee had released *The Report of the Committee on Myxoedema* five years later. The report systematically chronicled the histology and pathology of the disease in extensive animal and human cases. Based on the human cases, it found that the disease affected six women for every man diagnosed.[11]

Like myxoedema, THT emerged from the physiologist's lab. Murray worked closely with Victor Horsley, a prominent member of the Committee on Myxoedema. In 1890, Horsley suggested that grafting or transplanting a lower animal's thyroid might cure a myxoedemous patient.[12] Murray took up this suggestion, but instead of a transplant, used an extract. The administration of a thyroid gland for a deficiency in thyroid served as an exemplary application of the logic of physiology. Unlike testicular extract, thyroid received a large amount of attention within the *British Medical Journal* (*BMJ*) and the *Journal of the American Medical Association* (*JAMA*).

By 1897, H. Gideon Wells cited that THT was "one of the most striking examples of the success of ration[al] and experimental methods in therapeutics that can be cited."[13] In citing that THT was a specific therapeutic, Wells contrasted THT with the extensive list of unspecific conditions for which physicians and quacks applied other organotherapies (e.g. testicular,

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[11] Clark T Sawin, ed., *Report of a Committee Nominated December 14, 1883 to Investigate the Subject of Myxoedema*, Facsimile Edition. (Boston: The Francis A. Countway Library of Medicine, 1888), 64.

[12] Horsley chose sheep out of the eight other species in which thyroid had been studied, due to the similarity in suffering and progression of the disease.

[13] H. Gideon Wells, "The Physiology and Therapeutics of the Thyroid Gland and its Congeners," *Journal of the American Medical Association* 29, no. 18 (October 1897): 897.

ovarian, and brain extracts). Yet Wells also listed a number of other conditions THT treats that were unrelated to myxoedema.[14] However, physiologists could not find reasons why THT was effective in treating these conditions.

The tension between ingesting and injection was also a divide between therapeutic and physiological effectiveness. Physiologists used vivisection to make knowledge claims around THT, and thus THT was embedded in the methods of vivisection. Physicians altered Murray's extract to administer it by mouth. This alteration is based on making THT easier to administer and prepare, as well as the interpretation of THT as an animal meat therapeutic. Thus, physicians made sense of THT's effectiveness using the discourses of meat consumption.

THT and Vivisection

THT was invented in the physiologist's lab from the processes of vivisection, the experimentation on animals. As such, it used not only thyroids of animals, but experimental animals as well.

Physiology depended on vivisection. Vivisection used the bodies of live animals, as opposed to dissection that used corpses. Claude Bernard, one of the figureheads of the field of physiology, claimed that without being able to witness the live inner workings of animals, physiology would have no foundation at all.[15] As Nicholaas Rupke states, "vivisection met the requirements for recognition as a true experimental science which mere anatomical observations on dead bodies had never been able to do."[16] Vivisection was thus a part of the larger reform of

[14] Ibid, 1007-1009
[15] Nicolaas Rupke, ed., *Vivisection in Historical Perspective* (New York: Croom Helm, 1987), 7.
[16] Ibid.

medicine from an art to a science.[17] The study of internal secretions was also carried out through vivisection, and its subsequent discoveries were attributed to this practice.

Rather than eschewing the live and fleshy bodies that constituted the methods of knowledge production, the excessive liveness of the animal bodies *made possible* the scientific inquiry into the disease of myxoedema and its treatment, bolstering its prestige within medical research.[18] As expressed by Rupke, vivisection emphasized the witnessing of the live processes, rather than the dead states, of the animal/human body. The physiologist who witnessed the inner animations of a living organism, could, theoretically, learn how to control them.

All of the thirteen members of the Committee on Myxoedema were physiologists. George Murray was clinician and a physiologist, as were most researchers on thyroid issues across the nineteenth and twentieth centuries.[19] Physiologists had learned how the disease was caused through removing the thyroid gland; THT was the process of restoring thyroid function to the body.[20] THT was thus considered a rational therapy because it replaced one organ with the transplantation or substitution of a functioning one. In his 1890 suggestion to cure myxoedema, Victor Horsley states,

> the transplantation of a thyroid gland from one of the lower animals into the peritoneal cavity, or into the subcutaneous tissue might be followed by the

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[17] Ibid.

[18] I term liveness as excessive from the assertions of Catherine Waldby. In *The Visible Human Project*, she states, "The living body is excessive, unpredictable, organised through unquantifiable forces of meaning and desire." (144) The living body within vivisection is set in direct opposition to the post-mortem examinations upon which most of medicine is based. I investigate the dead body as the ideal form at the end of this chapter, as well as Chapter 2. Clearly, vivisection as a discipline depends upon the liminal state of the body being vivisected. It is through the eventual sacrifice that the living body can be contained within the vivisection theater.

[19] Endocrinology was what Nelly Oudshoorn describes as a "New Physiology." As endocrinologists conduct the most research on issues of THT, most of them are also physiologists.

[20] In the 1856, Moritz Schiff had transplanted one dog's thyroid to the chest of another. The transplanted thyroid had vascularized when the thyroid was examined a few weeks later. This suggestion was played out with a myxoedemous woman who received a grafting of a thyroid above her breast in 1890. Horsley published his suggestion (see n21 below) after the grafting had taken place, but had suggested this method of treatment to Murray a few months before its publication.

> successful growth of the grafted gland, and so bring about the arrest of the disease process by reason of the restoration of the lost function.[21]

Horsley imagined that the animal gland would vascularize and begin functioning as the patient's. When thinking about which animal thyroid would be best suited for the transplantation into the myxoedemous patient, Horsley chose the sheep, as it resembled the human in the disease progression and duration, and it was roughly the same size as a human's.[22] Thus, THT in its proposed form at the beginning of the 1890s depended on the logics of xenotransplantation, or the transplantation from an animal to a human.

THT, in this sense, transgressed the special divide through the transplantation of one living tissue in the body of another.[23] Antivivisectionists questioned physiologists's power to cross the already-tenuous divide between animals and humans. Antivivisectionist protest caused the first Royal Commission on Vivisection hearings in 1876.[24]

Arabella Kenealy's testimony, quoted at the beginning of the chapter, was part of the second set of hearings that called into question the extent and ethics of the practices on vivisection in England.[25] These hearings questioned the treatment of animals in scientific

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[21] Victor Horsley, "Note on a Possible Means of Arresting the Progress of Myxœdema, Cachexia Strumipriva, and Allied Diseases," *British Medical Journal* 1, no. 1519 (August 1890): 6.

[22] Ibid.

[23] In this project, the term "special" most often represents the adjective form of "species," thus resurrecting an antiquated usage.

[24] The first hearings resulted in the passage of the 1878 Cruelty to Animals Act, an act that stated that, among other provisions, the same animal could not be used for the same experiment. The passage of the law was monumental, but it was loosely enforced. Members of the regulatory board practiced vivisection themselves. See Coral Lansbury, *The Old Brown Dog: Women, Workers, and Vivisection in Edwardian England* (Madison: University of Wisconsin Press, 1985), 9-10.

[25] These hearings had started with an incident known as the Brown Dog Affair. In 1903, William Bayliss and Ernest Starling conducted a vivisection on a small brown terrier. Bayliss, who would develop insulin a decade later, and Starling, who would term internal secretions 'hormones,' were attempting to stimulate the dog's salivary glands. Unknown to them, two antivivisectionist medical students had infiltrated the audience to witness the experiment. They were horrified to see that the terrier had another scar from a previous experiment, a violation of the 1878 Cruelty to Animals Act. After the experiments, the news of the brown dog drifted through the town of Battersea, England. The antivivisectionist organization erected a statue, which was subsequently vandalized by the medical students. Upon hearing of a large group of medical students trying to take the statue down, the antivivisectionists and the labor activists uncharacteristically demonstrated together until the statue was replaced. For a detailed

experimentation. However, as stated above, the use of animals as experimental subjects formed the basis of medical research. Because of this, the Royal Vivisection Hearings were also an attack on the institution of science itself.[26] While the anti-vivisection movement primarily fixated on the undue suffering of animals kept alive during surgical demonstrations, it was also a movement whose participants expressed a growing concern for the increasing social power of scientific meaning-making.[27]

During these hearings, as stated at the beginning of the chapter, pro-vivisectionist testimonies repeatedly cited THT as an advancement of science. The most direct and chronicled testimony was that of William Osler, who had "an unusually large experience" dealing with issues of the thyroid.[28] He testified that THT had "come directly from experiments on animals," citing The Committee of Myxoedema and Horsley's work.[29] He stated that it was one of the strongest cases in favor of the benefits derived from the experiments on animals.[30]

At the apex of his testimony, he produces a set of portraits of patients taken before and after the treatment, similar to Figure II.1.[31] He states,

> Take a woman, for instance, who, with advanced myxoedema, may be reduced to a condition of imbecility, dementia, to a simple frog-like or a toad-like caricature of her former self, and in a hopeless, helpless condition. Within six months that

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study of the Brown Dog Affair, see Lansbury, *The Old Brown Dog*.

[26] Rupke, 8.

[27] Rupke, *Vivisection in Historical Perspective*, 4. The Antivivisectionist movement found support from the clerical and noble classes of British society, who felt that their power as figureheads in society was dwindling with the rise of science.

[28] "Royal Commission on Vivisection: Fourth Report," *British Medical Journal* 1, no. 2470 (November 1908): 1444.

[29] Ibid. Osler's testimony is a bit jumbled and riddled with errors. For example, he states that the extract was trialed on dogs rather than humans, but its first use was George Murray's. Because his testimony was summarized, it is hard to tell whether the transcriber, Osler or the editorial board made these factual errors.

[30] Ibid.

[31] The specific plates that Osler used weren't noted in the *BMJ*.

> woman may be perfectly well. And she stays well. Here, for instance, is an illustration of what may be done in eleven months.[32]

The phrase "frog-like" here seems commonplace, but given that frogs constituted a primary medium in the vivisector's lab, this phrase deserves closer inspection. Osler also included the words "hopeless" and "helpless" – both characterizations of the antivivisectionist's descriptions of the state of the vivisected animals (some of which Osler almost certainly had read or borne witness to). While the patient Osler discusses is a woman, he frames the patient in terms of the experimental animals.

Osler's choice of words is further emphasized by the fact that it coincides with the production of the photographs. These before/after photographs pervade physiologists' case studies of administering myxoedema, and have escaped much critical analysis.[33] Photographs such as Figure II.1 coincide with tales of transformation from a swollen creature to a distinguishable and healthy woman. While they create a cinematic effect through the before/after snapshots, it is the before state that garner the most attention, both rhetorically and affectively. Many physiologists beside Osler use metaphors of the beastly appearance of the patients before they receive treatment. One physiologist states that the patient suffering from myxoedema as "one of the lowest forms of animal existence."[34] Another states that the patients with myxoedema parallel so closely the "dumb brutes" in the vivisection theater.[35] In each of these descriptions, the female patient is described as an animal, and thus requires the

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[32] "Royal Commission," (1908): 144

[33] For other cases of before/after portraiture, see William M. Ord, "On Myxœdema, a term proposed to be applied to an essential condition in the 'Cretinoid' Affection occasionally observed in Middle-aged Women," *Medico-Chirurgical Transactions* 61 (1878): Plate VII; Archibald Church and Frederick Peterson, *Nervous and Mental Diseases* (Philidelphia and London: W.B. Saunders Co., 1911), 468; Clark T. Sawin, "The Invention of Thyroid Therapy in the Late Nineteenth Century," *The Endocrinologist* 11, no. 1 (2001): 1; Thos. F. Raven, "Myxœdema Treated With Thyroid Tabloids," *The British Medical Journal* 1, no. 1723 (January 1894): 12.

[34] Wells, "Physiology of the Thyroid Gland," 959.

[35] Victor Horsley, "The Brown Lectures On Pathology," *The British Medical Journal* 1, no. 1255 (January 1885): 114.

interventions of science to transform her into an acceptable member of society. Like Osler's testimony, these photographs conflate the female patient and the experimental animal to be vivisected.

Figure II.2: Sailor's Widow, Before and After Treatment, 1894

Women and animals as experimental subjects were also deeply embedded within the wider cultural imaginary. As Coral Lansbury points out, pornographic novels often featured women not only in the role of domestic animals, but also in the place of the vivisected animal. Lansbury traces the emergence of the vivisector within the pornographic novel as drawing on the riding master, both taming their female subjects with the whip or the knife. "[A]s a vivisected animal," Coral Lansbury notes, "[the] woman [in the novel] was made to satisfy a delight in the

spectacle of pain."[36] Medical and pornographic discourses at the turn of the century reciprocally fed off one another. For example, Victor Horsley's electric stimulation experiments in particular were retraced by replacing various animals with women. Reciprocally, the contraptions used to tie women down or "break them at the bit" within pornographic novels predated, but were structurally similar to, the gynecological devices used at that time (e.g. "stirrups").[37]

Images of xenotransplantation called on these images of interchangeability. For the physiologist, the bodies of the (female) patient and the donor animal had to be similar enough for the organ to be absorbed. In choosing the sheep, Horsley drew on the "deep metaphors between women as domestic animals" present within Victorian culture.[38] As presented at the beginning of the chapter, Kenealy presents the difference between subcutaneous injection and ingestion as a clear barometer to test the cultural acceptability of an animal organ preparation. The injection of any animal part was a "danger[ous]" transgression of the special divide.

This transgression haunted the cultural reception of xenotransplantation from the start. Lansbury investigates the xenotransplantation in Orson Wells' *The Island of Dr. Moreau* and Mary Shelly's *Frankenstein.* Both can also be considered early critiques on the scientification of (non)human vivisection. Dr. Frankenstein's monster is both the emblem of science and its inability to control its creation. The monster is the grotesque chimera, which corresponds to the virago who kills its creator in Well's *Dr. Moreau.* Both of these narratives, widely popular by the turn of the century, were part of the biomedical imaginary. The hybrid figure of the chimera represents science out of the control. These hybrid figures served as figureheads of the social response critical of xenotransplantation, popularized by the antivivisectionist movement.

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[36] Lansbury, *The Old Brown Dog*, 110.
[37] Ibid. These terminologies continue today.
[38] Evelleen Richards, "Redrawing the Boundaries: Darwinian Science and Victorian Women Intellectuals," in *Victorian Science in Context*, ed. Bernard V. Lightman (Chicago: University of Chicago Press, 1997), 133.

The chimera, then, represents both the productive and dangerous encounter of thyroid grafting. At once, the woman receiving THT is both becoming animal through xenotransplantation and becoming woman with the treatment. That is, the bodies of experimental women and animals make the physiological inquiry possible, constituting a relationship of "becoming with." I draw the term of "becoming with" from Donna Haraway in her 2008 book *When Species Meet*, where she describes the tacit multiplicity of the category of human. Drawing on the biological claim that only ten percent of cells in the human body actually hold the human genome, she states that "to become one is to become one with many."[39] Vivisection offers a literal way in which medical research becomes scientific with the animal bodies and excessive living processes it attempts to describe and control.

Yet, at the same time, the logics of xenotransplantation also literally and figuratively represent a notion of "becoming animal." The uneasy equation of humans (and more specifically, women) and animals under the vivisector or surgeon's knife manifests itself within an anxiety that these procedures cross an already tenuous divide between human and nonhuman animals. Thus, becoming with animals argues for a co-construction of difference, an explicit dependence upon an already and iteratively defined *other* species as well as the acknowledgement and dependence upon that difference. Becoming animal, on the other hand, represents undertow, the always-in-formation, rarely articulated point of excess. This excessiveness speaks to the simultaneously becoming not-human and never-human status of the medical creation (the patient receiving THT). Yet this desire/fear also holds within it the assertion that the subject has never been completely human in the first place.

The simultaneous transformation of the patient in Figure II.1 shows both of these relationships held in tandem, and thus a point of tension within the discourse around implanting

[39] Haraway, *When Species Meet*, 3.

animal organs. As Catherine Waldby points out in *The Visible Human Project*, "[T]he deployment of images marks points of tension, knots of paradox or ambiguity within a system which are not resolvable within its terms."[40] The bodies of animals and women are culturally controversial, but also serve as the foundations for physiological, and thus THT inquiry. As I show in Chapter 2, these before/after photographs embed this tension deeply within the biomedical imaginary of THT.

The prevalence of these photos speaks also to the literal inability of physiologists to pinpoint an exact physiological response to THT. As Merriley Borell notes, THT was measured therapeutically, rather than physiologically.[41] Medical professionals used body temperature, urine volume and the regrowth of hair, but none of these measures provided a comparable measure across individuals and species. The photographs stood in the space between medicine's ability to prove THT as a viable therapeutic and explain its effectiveness through empirical measures.

The next section focuses on how general physicians altered the form of THT to make it more digestable to their colleagues and their patients. Such ingested forms of THT drew on already well-established traditions of meat consumption and industrialized slaughter. As such, it did not pose as direct a challenge to the similarities between the bodies of animals and women as injected/grafted THT.

Meat Eating and THT

While THT was invented in the physiologist's lab as an injected extract, THT would be widely adopted as an ingested powder. This adaptation of THT happened within the first two

[40] Waldby, *Visible Human Project*, 137.
[41] Borell, "Organotherapy, British Physiology, and Discovery of the Internal Secretions," 238.

years following Murray's report on his extract. Two of the reports confirming George Murray's extract over 1892 were in the form of thyroid feeding. One of the authors, Hector MacKenzie, wrote that the labor, bacterial dangers and extreme side effects of Murray's treatment presented significant drawbacks to injection of the extract.[42] Alternatively, feeding fresh thyroid glands was "altogether so very much simpler and safer, and so very easily carried out."[43]

Among the plethora of THT preparations used in the 1890s, the majority of forms were consumed orally. In fact, the numerous methods to make thyroid palatable signal the reliance on the consumption methods of THT. A list of THT preparations sounded more like a cookbook than medical therapeutics. Thyroid on toast, thyroid minced with brandy and seltzer, dried thyroid, thyroid powder, thyroid extract, elixir of thyroid, thyroid sandwich, and thyroid lightly fried.[44] The prevalence of preparations that were consumed deserves a better interpretation and analysis than they were simply safer or less laborious for the preparing physician. Conceptions of THT's effectiveness drew on the rich tradition of meat eating. This conception of THT's effectiveness received less attention from critics of organotherapies because of its reliance on this tradition.

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[42] H. W. G. Mackenzie, "A Case of Myxoedema Treated with Great Benefit by Feeding with Fresh Thyroid Glands," *The British Medical Journal* 2, no. 1661 (October 1892): 940.

[43] Ibid.

[44] For reference to the preparations: for thyroid on toast, see E. Cresswell Baber, "Feeding With Fresh Thyroid Glands In Myxœdema," *The British Medical Journal* 1, no. 1671 (January 1893): 10. For thyroid minced, see Constantine Holman, "Case Of Myxœdema Treated By Thyroid Feeding," *The British Medical Journal* 1, no. 1673 (January 1893): 114-115. For dried thyroid, see "Annual Museum," *The British Medical Journal* 2, no. 1858 (1896): 351. Elixir or extract of thyroid were by far the most popular throughout the 1890s, and the distinction between them is not well defined. For various methods of preparation, see J. Hawtrey Benson, "Case Of Myxœdema Of Long Standing Treated By Administration Of Thyroid Extract By Mouth," *The British Medical Journal* 1, no. 1685 (April 1893): 795; Murray, "Note on the Treatment."; W. H. Neilson, "A Study of Thyroid Extracts," *Journal of the American Medical Association* 29, no. 15 (October 1897): 722 -723; P. Blaikie Smith, "Thyroid Extract as a Remedy, with Illustrative Cases," *The British Medical Journal* 1, no. 2094 (February 1901): 388-389; S. Taylor, "Thyroid Extract," *The Lancet* 277, no. 7172 (February 1901): 332-333. For reference to the thyroid sandwich, see Thomas Schlich, *The Origins of Organ Transplantation, Surgery and Laboratory Science, 1880-1930* (Rochester, NY: University of Rochester Press, 2010), 52.

The consumption of thyroid drew on the long-standing tradition of meat as both a national practice, as well as a therapeutic one. Meat renderers and manufacturers were keen to emphasize and sponsor medical research that emphasized meat eating as both nutritional and rejuvenating. David Cantor and Christian Bonah note in their introduction to *Meat, Medicine and Human Health* that meat producers in both the United Kingdom and United States "promoted meat as crucial to national and military efficiency and effectiveness."[45] Beef tea advertisements were prevalent particularly in Britain, where soldiers are often portrayed as being revitalized through the consumption of meat.[46]

This revitalizing or fortifying activity was also widely held by the medical community throughout the nineteenth century. Cantor and Bonah also state, "Physicians often regarded consuming meat or meat extracts as ways of fortifying the constitution, and extracts such as beef tea were popularly used as stimulants."[47] Meat extracts already served in the medical and cultural imaginary as stimulants, or givers of vitality. This medical and cultural notion provided further evidence of the fortifying powers of THT and other organotherapies, which were constituted the active constituents of meat.

Because of their general stimulating effects, meat extracts were prescribed for a wide variety of conditions from tuberculosis to infertility. THT followed this tradition. Even though THT was originally used to treat myxoedema, physicians began prescribing it for a large variety of conditions. Like the female hormones in the 1920s, THT was considered effective in treating conditions ranging from obesity to psoriasis, receiving promising results in each case study. The majority of non-myxoedemous applications of THT involved women.

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[45] David Cantor, Christian Bonah, and Matthias Dorries, eds., *Meat, Medicine and Human Health in the Twentieth Century*, 1st ed. (Pickering & Chatto Ltd, 2010), 9.
[46] Lori Anne Loeb, *Consuming Angels: Advertising and Victorian Women* (New York: Oxford University Press, 1994), 64.
[47] Ibid, 12.

The wide applicability of THT to many diseases also resulted from its low cost and availability. Ingested forms of THT were easy to procure and could be administered in a variety of forms. If one wanted the prepared versions of thyroid juice or dried thyroid, these were available through a pharmacist or by mail order. Meat manufacturers also began producing these forms in large quantities by 1895. For those that wished to procure their own glands, the physician or the patient could travel to the butcher or slaughter grounds. Thus, the patient could be easily instructed to procure or prepare their own preparation, and the idiosyncrasies of its preparation did not widely affect the cumulative results.

Ingested forms of THT perpetuated the role of the physician in establishing THT's effectiveness through therapeutic, rather than physiological means.[48] The consumption of raw glands took place entirely outside of the pharmacy or physiologist's laboratory. As long as the thyroid was properly removed from the food carcass, and it was fresh, there were no obstacles to its active effects. Any dangers posed by THT were most likely the result of a diet that was too high in other meats, which over stimulated the patient's constitution when administered.[49]

THT as a meat engaged with the animal body already contained within the current cultural traditions of slaughter and meat consumption. Ingested forms of THT were considered "dead product[s]" whose stimulating effects had to be renewed through continued consumption.[50] The product was also dead in that it was divorced from the bodies of the animals from which it was harvested. As Carol Adams points out, "An animal cannot be alive if it is meat."[51]

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[48] Borell, "Organotherapy, British Physiology, and Discovery of the Internal Secretions," 236.
[49] Few doctors warned about the effects of overstimulation by eating too much thyroid, and one doctor ascribed this error to a patient's misunderstanding his instructions.
[50] Osborne, "The Therapeutic Uses of Thyroid Preparations," 1478.
[51] Carol J. Adams, *The Sexual Politics of Meat: A Feminist-Vegetarian Critical Theory*, Tenth Anniversary Edition. (New York: Continuum, 2000), 59.

Nelly Oudshoorn, Naomi Pfeffer and Adele Clarke have discussed how medical researchers used the slaughterhouse or abattoir to procure of raw materials for organotherapies and research specimens.[52] Yet, as Naomi Pfeffer notes, the formalized relationships between the meat manufacturer and research labs did not widely occur until the "endocrinology gold rush" of the 1920s.[53] In this sense, ingested THT serves as a precursor to other organotherapies being produced completely within the slaughterhouse, as meat manufacturers began producing it in 1895. The last mention of a dead sheep or the preparation of the tissue itself within the *BMJ* or *JAMA* was in 1897.[54] After then, THT was discursively separated from the circumstances of its manufacture.

The bodies of animals served as absent referents in THT. The removal of slaughterhouses from town centers paralleled the movement of the production of THT to the meat manufacturers. Animal slaughter became less of an olfactory and visual reality for the residents of cities.[55] Animals thus became absent referents from the cityscape, and the consuming of THT followed this trend. Rather than raw glands, more prepared forms were being made. Thus, the slaughtered animal was increasingly distant from the body of desiccated THT. While this mediation was riddled with its own problems in determining the activity of the product, the medical establishment did not overtly question the administration of THT by mouth. Its

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[52] See Oudshoorn, *Beyond the Natural Body*; Adele Clarke, *Disciplining Reproduction: Modernity, American Life Sciences, and "The Problems of Sex"* (Berkeley: University of California Press, 1998); Adele E. Clarke, "Reflections on the Reproductive Sciences in Agriculture in the UK and US, ca. 1900-2000+," *Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences* 38, no. 2 (June 2007): 316-339; Naomi Pfeffer, "How Abattoir 'Biotrash' Connected the Social Worlds of the University Laboratory and the Disassembly Line," in *Meat, Medicine and Human Health in the Twentieth Century*, ed. David Cantor, Christian Bonah, and Matthias Dorries (London: Pickering & Chatto Ltd, 2010), 63-76.

[53] Pfeffer, 65

[54] Neilson, "A Study of Thyroid Extracts," 722.

[55] See Chris Otter, "The Vital City: Public Analysis, Dairies and Slaughterhouses in Nineteenth-Century Britain," *Cultural Geographies* 13, no. 4 (October 1, 2006): 517 -537.

regulation coincided with that of meat, increasing the biochemical definitions of its effectiveness or adulteration.

The act of ingesting configures recognizable bodies and recognizable organs as belonging to a process of slaughter or a process of killing. Ingesting animal thyroids did not call into question the categorization of human, but rather reaffirmed it. Ingesting THT thus configured the bodies of animals and women that made/ingested THT as "becoming with" without the threat of "becoming animal" discussed in the previous section. Not only was ingested THT embedded within the rational logics of treatment, but it was also situated within the rational logics of slaughter.

Conclusion: The Rise of Chemical Meaning-Making

After the Royal Hearings on Vivisection, reports on thyroid grafting disappeared completely from the *BMJ* and *JAMA*. However, reports on raw thyroid feeding did as well. The two major forms of thyroid that remained were the more mediated forms that were ingested or injected: desiccated thyroid and thyroid extract. Meat manufactures supplied both of these therapies. Thus, ingested and injected forms of THT were embedded in the meat rendering production line. Meat manufacturers prepared batches of the therapeutic from large numbers of glands, as they had access to a seemingly endless supply of "food animals" from which THT was derived.[56] The selling of therapeutics was virtually an entirely profitable business for these manufacturers, as the thyroid was easily removed from the slaughtered animal in the disassembly

[56] The two written references for the preparation of desiccated THT and thyroid extract were the British and US Pharmacopeias. Both of these sources defined that THT should be derived from "food animals" or sheep.

line.[57] In the perspective of the meat manufacturer, the thyroid constituted a product that was made out of "biotrash," or waste.[58]

As the donor livestock thyroids were moved further away from the final product of THT, the physician lost control over the preparation of the product and matching the donor animal to the patient. During gland transplantation, this variability was viewed as a benefit rather than a hindrance, as some physiologists touted that "matching" the donor animal to the human in age (and sometimes sex) was preferable.[59] As THT became more pre-prepared, physicians voiced doubts about how to determine the activity of the gland. Yet, as stated above, a large number of glands were combined into one batch of desiccated THT or thyroid extract. Individual matching was no longer possible.

The editors of the *BMJ* cited in 1909 that "Since there are no tests for quality, or even identity, of these powdered products, the physician, unless he can himself supervise their preparation, is forced to rely on the general reputation of the manufacturer."[60] Yet the reputation of the manufacturer – in particular, the meat manufacturer, was being questioned by the aftermath of the 1906 Pure Food and Drug and Cosmetic Act in the United States.

This act responded to the increased distance between the producers and consumers of food and drugs, leaving possibility for dangerous diseases. As Jonathan Simon and Christoph Gradmann stated in their introduction to *Evaluating and Standardizing Therapeutic Agents*, "Units of measurement and, in particular, numbers served as a means for regulating these

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[57] I state easily removed in comparison to the other ductless glands such as the kidney, ovaries or pituitary. For the difficulties in procuring these glands, see Clarke, "Reflections."; Oudshoorn, *Beyond the Natural Body*; Pfeffer, "How Abattoir 'Biotrash' Connected the Social Worlds of the University Laboratory and the Disassembly Line." For the diagram of where the glands are located, see Rudolph Alexander Clemen, *By-Products of the Packing Industry* (Chicago: University Of Chicago Press, 1927), 214 and 218.

[58] Pfeffer, 64.

[59] "Current Medical Literature: Thyroid Medication for Children," *Journal of the American Medical Association* 37, no. 1 (July 1901): 1567.

[60] "New and Nonofficial Remedies: Organs of Animals," *Journal of the American Medical Association* 52, no. 24 (June 1909): 1928.

domains where personal contact and judgment of character no longer sufficed."[61] The 1906 Pure Food Drug and Cosmetic Act placed emphasis on chemical units of measurement. In his analysis of the concept of adulteration and purity, Ben Cohen noted, "As concerns about adulteration grew, scientists and chemical analysis started to emerge as …the 'border patrol' between pure and adulterated products."[62] While governmental regulation relied on chemical analysis to determine what was pure and adulterated, physiologists increasingly understood the body in terms of chemical reactions. The same physiologists that were involved in vivisection described internal secretions as "hormones," or chemical messengers. Thus, both the frameworks of meat consumption and physiology increasingly relied on the field of biochemistry.

As Chapter Two discusses, iodine served as such a quantitative measurement. This measurement merged THT as a living and decaying substance, both meat and medicine. Biochemists and physiologists attempted investigations into what was the most iodine-rich, and hence living part of the dead tissue. The dead tissue represented the crude tissue that had to be refined to bring it to regular and chemical life. Further, measuring THT's activity in iodine precluded the bodies of animals and women, as it was a test that was completed on the preparation, rather than experimental animals or the patient. This new method of measurement became the focus of the determination of THT's effectiveness, and the before/after photographs faded from the biomedical discourse. The focus on the gland itself, rather than the bodies which show its effectiveness, elided both relationships of becoming and becoming with – both the

[61] Jonathan Simon and Christoph Gradmann, *Evaluating and Standardizing Therapeutic Agents, 1890-1950* (New York: Palgrave Macmillan, 2010), 4.
[62] Earl Lane, "Benjamin R. Cohen: Long-Ago Conflicts Over Food 'Purity' Echo in Today's Controversies," *AAAS News Archives*, July 30, 2009, http://www.aaas.org/news/releases/2009/0730food.shtml.

images of the chimera and the experimental subjects of science. It was the gland that would go through the transformation into a chemically purer substance, not the experimental subject.

Thus, the "New Physiology" of endocrinology increasingly considered the bodies of animals and women crude and variable at best, despite their presence in early THT. The presence of THT as an animal-derived product or organotherapy would thus become increasingly marginalized over the twentieth century. As the next chapter explores, the introduction of synthetic, a "pure" chemical compound emphasized the distinction between the variable bodies of treatment and the pure gland. Endocrinologists increasingly assumed that a constant and pure treatment would create constant and pure bodies. Those bodies which were variable or outside of this ideal would be elided from the medical discourse throughout the twentieth century.

In this chapter, I have shown how the medical discourses make sense of THT's effectiveness as an organotherapy through the discourses of vivisection and meat consumption. Animals and women were fundamental to the invention and adoption of THT as a successful organotherapy, as their associations with both of these discourses show. The role of animals and women within the emergence of THT thus sheds light on how these bodies are reconfigured as THT progresses into a specific therapeutic, discussed in the next chapter.

Chapter Two
Pure and Effective: Biochemical Definitions of THT

In a 1991 article in the journal *Thyroid*, a group of epidemiologists discussed the use of desiccated and synthetic THT (thyroid hormone treatment).[1] The graph (Figure III.1) shows the first medication, desiccated thyroid [natural], beginning its decline in 1966, while the synthetic form of the treatment rose over the entire course of the study, 1964 to 1988. The authors explained this phenomenon by arguing that the synthetic form was "clinically superior" to the natural form of the treatment.[2]

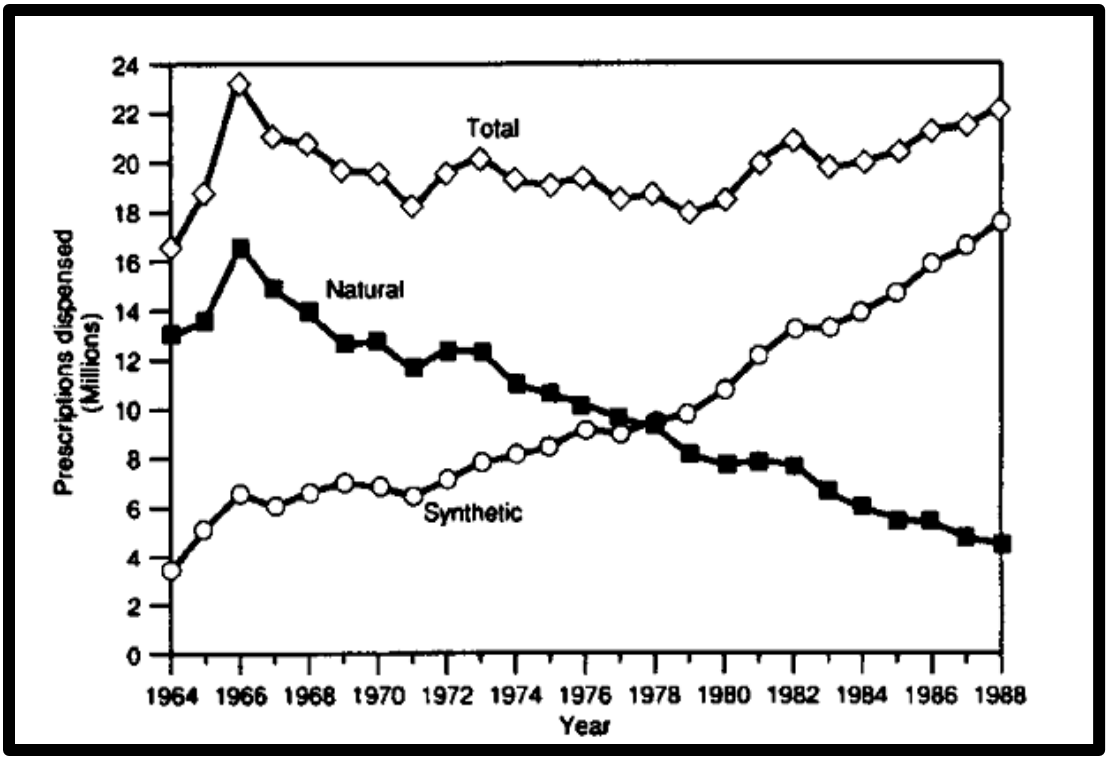

Figure III.1: Number of THT prescriptions dispensed by retail pharmacies in the US, 1964-1988. Used under fair use guidelines, 2011.

This chapter explores why these epidemiologists and the larger mainstream medical

[1] Steven C Kaufman et al., "Thyroid Hormone Use: Trends in the United States from 1960 through 1988," T*hyroid: Official Journal of the American Thyroid Association* 1 (1991): 285-91.
[2] Ibid, 285.

community consider synthetic THT clinically superior. While the preference for synthetic seems to be universal today, this preference took shape over the course of sixty years, between 1915 and 1979. As the graph shows, synthetic THT did not actually outpace desiccated THT until 1979, sixty years after its invention and thirty years since its viable commercial preparation.

The slow adoption of synthetic THT corresponds to the change in tests that determined clinical superiority. Clinical superiority came to apply to synthetic THT over time. This change depended on how physicians and endocrinologists interpreted synthetic THT's effectiveness in tension with its chemical purity. When synthetic THT was invented in 1919, it promised a departure from the associations with organotherapy discussed in Chapter One. Unlike animal-derived THT[3], synthetic THT offered biochemists and physiologists a chemically pure substance that could help physiologists pinpoint the physiological responses of the body to thyroid hormone. However, physicians did not initially adopt synthetic THT into general use because its chemical purity did not translate into clinical effectiveness. Physicians observed that synthetic THT could not be consumed by mouth, and it did not produce as immediate effects as animal-derived THT. In the 1920s, animal-derived THT was relatively well standardized by assays on iodine, and physicians considered it dependable because of the chemical and biological assays required for its manufacture. Thus, two definitions of clinical superiority emerged in evaluating the THTs: the chemically pure and the clinically effective. These two definitions of clinical superiority would evolve over the next sixty years, and the adoption of synthetic THT in the 1960s would coincide with the merging of these two definitions within biomedical discourse.

Like the logics of vivisection and meat consumption discussed in Chapter One, the definitions of THT's effectiveness as chemical and clinical also configured the bodies of animals

[3] In this chapter, I use desiccated THT and animal-derived THT interchangeably. Thyroid extract, as discussed in the previous chapter, slowly became a digested form. Proloid, discussed at the end of this chapter, is such a form. The distinction between the two forms is not as prevalent as it was during the Vivisection debates.

and women differently. Synthetic THT was considered pure because it was not derived from animal thyroids. Yet the pure THT also had to prove its effectiveness in the bodies of female patients and experimental animals. During the twentieth century, endocrinologists (formerly physiologists) continued their reliance on the bodies of experimental animals in biological assays, with greater uniformity and quantity than during the vivisection debates. Yet clear articulations of endocrinology's dependence on these animals faded from the biomedical discourses. The role of animals in defining therapeutics thus came to be known as the "hidden standard" of drug regulation because large numbers of animals were used to create the statistically normal measurements.[4] Women's bodies stayed present within the biomedical imaginary, but increasingly became associated only with desiccated THT.

This chapter explores how the adoption of synthetic THT as the standard of care in hypothyroidism depended on how general physicians and specialists interpreted its effectiveness and purity compared to desiccated THT. This interpretation centered on the bodies of animals and women. I discuss the adoption of synthetic THT in two episodes: the invention of synthetic THT in the formation of biochemistry, and the rise of synthetic THT in the development of the controlled clinical trial. Between these two episodes, I explore how the regulation of a particular patent medicine, Marmola, renegotiated these two interpretations. The rise of the randomized clinical trial merges these two interpretations of effectiveness and purity in the 1970s. I show that the adoption of synthetic THT depended on the elision of female and animal bodies from measures of clinical effectiveness.

[4] The phrase "hidden standard" is drawn from A. A. Miles's discussion on how standards are kept by the World Health Organization. In his book *Trust in Numbers*, Ted Porter draws on Miles's statement that the familiarity with animals is what makes assay measures so precise. See Theodore M. Porter, *Trust in Numbers: the Pursuit of Objectivity in Science and Public Life* (Princeton: Princeton University Press, 1996).

Episode 1: Pure, but effective?

The emergence of biochemistry as a discipline had a more immediate effect on the standardization of desiccated THT than the emergence of synthetic THT. In the early 1910s, the new *Journal of Biochemistry* published a few studies about the variability of iodine in animal thyroid glands, based on the location and season of slaughter.[5] German biochemists reported that the "active" constituents of the gland contained iodine, and thus claimed their preparations of the iodine-rich colloid constituted a more uniform and standardized dose than preparations of the whole gland.[6] Thus, variability in iodine translated to variability in potency. As discussed at the end of the last chapter, the chemical assay of iodine combined the conception of THT's effectiveness from the traditions of meat eating and vivisection. The increased biochemical regulation of THT would only increase as medical specialists and physicians within the UK and US pushed for their respective pharmacopeias to standardize animal-derived THT preparations by measuring the "organic iodine" content. As pharmacopeias were the reference manuals that all pharmacists were required to follow, publishing the standardization measures in these publications theoretically ensured that all reputable preparations would meet the same iodine content, and thus activity level. By 1916, the British and the United States pharmacopeias defined desiccated THT's activity by measures in organic iodine.[7]

Iodine assay was equally accessible to large manufacturers and small pharmacies, and

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[5] Christine R Squire, "Methods for the Investigation of Thyroid Function," *Methods in Molecular Biology (Clifton, N.J.)* 324 (2006): 91-108; Atherton Seidell and Frederic Fenger, "Seasonal Variation in Iodine of the Thyroid Gland," *Journal of Biological Chemistry* 13, no. 4 (January 1913): 517 -526.

[6] Robert Hutchinson, "On the Active Constituent of the Thyroid Gland," *British Medical Journal* 1, no. 1882 (January 1897): 194-7; Wells, "Physiology of the Thyroid Gland," 901.

[7] United States Pharmacopoeial Convention, *Pharmacopoeia of the United States of America*, Ninth Decennial Revision. (United States Pharmacopoeial Convention, Inc., 1820-1975., 1916), 443.

provided what Ted Porter has described as a "technology of trust."[8] This measure allowed for pharmacists to test the raw thyroids or prepared substances they bought, and for large-scale manufacturers to test the lots they shipped. THT was thus part of the rapidly expanding pharmaceutical market, which relied less on general reputation of particular pharmacists, and more on the reputability of particular firms, supplemented by assays such as iodine.

With the adoption of the iodine assay in 1916, the standardization of animal-derived THT preparations was better defined than those of estrogen preparations or insulin. These preparations largely relied upon biological assays for measurements of their activity. These assay mechanisms required defining specific physiological responses to a given preparation that could be measured among members of the same species.[9] Finding a specific measurable response in another species, however, was often difficult. As Nelly Oudshoorn notes, "A growing number of reports based on studies in animals of both sexes indicated that ovarian and testicular extracts produced similar effects."[10] As discussed in the previous chapter, physiologists had trouble defining a specific physiological response of THT in women and animals. Pulse rate, urine volume or body temperature varied between individuals. The rejuvenating effects of THT (e.g., the return of menstruation, regrowth of hair, weight loss) were variable among both human and nonhuman recipients. Thus, in the 1890s and 1900s, before/after portraits stood in for a specific physiological definition of THT's effectiveness.

The level of iodine as a measure of potency was appealing because it did not require experimenting on the bodies of animals or women, but rather offered a method of assay that could distinguish physiologically active and inactive raw glands. Iodine assay seemed so well

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[8] Porter, *Trust in Numbers*.
[9] For most therapeutics, researchers usually use(d) rats, mice or guinea pigs.
[10] N Oudshoorn, "On Measuring Sex hormones: The Role of Biological Assays in Sexualizing Chemical Substances," *Bulletin of the History of Medicine* 64, no. 2 (1990): 246.

defined in the case of THT that the Committee for Biological Standardization, appointed by the International Health Organization (later to become the World Health Organization [WHO]) in the 1920s, paid relatively very little attention to the standardization of animal-derived THT.[11]

Though iodine was generally adopted, it also posed its own problems. Iodine provided a measurement for the potency of unadulterated THT, but iodine levels could not determine whether or not the preparation was pure. It was possible for a manufacturer to add iodine to the preparation to meet specifications, thereby selling a product with potentially no potency.[12] When possible adulteration was suspected, the Committee of Biological Standardisation suggested pharmacists test the preparation with a bioassay involving rats.[13] However, the effects of an impotent preparation were not as dangerous as an overly potent one in the eyes of regulators.[14] Because iodine assays kept the preparations from being too powerful, but not from being too weak, they were acceptable as methods of standardization.

General practitioners and drug regulators accepted the iodine assay as an adequate standardization method for THT; however, for biochemical researchers, the goal was not an adequate standardization procedure, but a pure substance that did not require standardization at all. Rather than finding ways of measuring the active ingredient within THT preparations through secondary measures, biochemists wished to isolate and produce the active ingredient and compound. In 1915, Edward Kendall claimed that he had found such an active constituent of

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[11] "The Second International Conference on the Biological Standardization of Certain Remedies," *Public Health Reports (1896-1970)* 41, no. 12 (March 19, 1926): 505-515.

[12] Ibid, 510.

[13] Ibid. Reid Hunt developed the assay, called the aceto-nitrile test. Hunt had found that rats who received thyroidectomies had a lower tolerance to aceto-nitrile than other rats who had thyroids. This assumption also confirmed the theory that the thyroid removed toxins from the body, or neutralized certain poisons by combining them with iodine. Other methods of bioassay (not suggested by the committee, but prevalent in the biomedical discourse) included measuring feathers on a fowl and whether or not the axolotl, a South American salamander, could transform into a distinguishable frog. The axolotl assay seemed to gain a bit of momentum, as it is referenced in popular as well as medical texts. For references to these biological assays, see "Scotland: Effects of Thyroid on Aged Fowls," *The British Medical Journal* 2, no. 3366 (July 4, 1925): 34; "Current Medical Literature," *Journal of the American Medical Association* 75, no. 16 (October 1920): 1020.

[14] Ibid.

thyroid, what he termed as "thyroxin."[15] In a brief overview of his experiments in the *Journal of American Medical Association* (*JAMA*), Kendall claimed that this pure compound would allow physiologists to clearly identify its corresponding physiological activities, which had hitherto eluded medical researchers.[16] As physiologists tested the physiological activity of THT by administering preparations of the entire gland, they could not be sure that the physiological reaction they witnessed was due to the "active constituent" of the gland, or some impurity. If physiologists used a chemically pure substance, physiologists could theoretically pinpoint the physiological effects of the thyroid. Thus, Kendall argued that this pure substance, thyroxin, would lead the way for endocrinology to be more grounded in chemistry.

However, the isolation of thyroxine did not ultimately lead to a more specific measurement of the physiological activity. Rather, Kendall measured the activity of his preparation by comparing it to the wide variety of effects of desiccated THT: loss of weight, increased heart rate, and agitation among others. In 1926, Charles Harington succeeded in producing a synthesized version of thyroxin, thyroxine. Unlike Kendall, Harington measured the physiological activity of thyroxine in terms of basal metabolic rate, a quantitative assay used on both animals and humans.[17] He found thyroxine was far less potent than thyroid extract, taking at least ten days to show its effects.

When editors of the *BMJ* and *JAMA* discussed Kendall and Harington's synthetic THT, they labeled thyroxine as a chemically pure, but relatively ineffective, substance. In other words,

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[15] E. C. Kendall, "Isolaation of the Iodine Compound which Occurs in the Thyroid," *Journal of Biological Chemistry* 39, no. 1 (1919): 125 -147; E. C. Kendall and A. E. Osterberg, "The Chemical Identification of Thyroxin," *Journal of Biological Chemistry* 40, no. 2 (December 1, 1919): 265 -334; E. C. Kendall, "The Isolation in Cyrstalline Form of the Compound Containing Iodin, which Occurs in the Thyroid," *The Journal of the American Medical Association* 64, no. 25 (June 1915): 2042-2043. Kendall was one of the few biochemists who published articles in both the *JAMA* and the JBC. Most biochemists published in the JBC, and the editorial staff

[16] Kendall, "Isolation," *JAMA,* 2043.

[17] Charles Robert Harington and George Barger, "Chemistry of Thyroxine: Constitution and Synthesis of Thyroxine," *Biochemical Journal* 21, no. 1 (1927): 182-3.

thyroxine may be the pure active ingredient of THT, but impure desiccated THT was better suited for general use as a therapeutic. A *BMJ* article which chronicled Harington's production of thyroxine stated, "The isolation of thyroxine, though a big laboratory success, does not make to medicine so immediate a contribution... Therapeutically there is no impediment to the oral administration of the whole gland or simple extracts of it."[18] In the opinion of the editors of the *BMJ*, thyroxine was of use to the chemical researcher, or, at best, the physiologist – not the general practitioner.[19]

The difference between clinical and biochemical work was further reinforced by the description methods of Harington. During his chemical identification and production of synthetic thyroxine, Harington did not test the physiological or clinical effects of his work. Instead, he included the analysis of physicians, Dr. Hetzel and Dr. Lyon, as appendices to the chemical work. The only depictions of thyroxine Harington used were chemical diagrams. While such depictions were well within the realm of biochemistry, Harington's formal depictions of thyroxine were significant when compared to Kendall's depictions of his synthetic substance, thyroxin.

In his three articles, Kendall included an unusually large number of photographs. His discussions of thyroxine showed not only the liquid from which he isolated thyroxin, but also the vats that boiled down the three tons of hog glands (Figure III.2). While possibly making the case for the differences between biochemical work and physiological work, these photographs demonstrated also the crude origins of the purified substance of thyroxin. In his paper on the chemical identification of thyroxin, Kendall and his co-author E. Oesterberg included thirty photographs of a step-by-step progression of purifying thyroxin. Kendall included the first photo

[18] "Thyroxine," *The British Medical Journal* 1, no. 3416 (June 26, 1926): 1093.
[19] Ibid.

of the crystalline substance in his *JAMA* article (Figure III.3). This photograph was reprinted in a multitude of textbooks, despite the fact that Kendall's chemical identification of thyroxin was incorrect.

The presence of these photographs played two roles in the medical discourse concerning thyroxin(e). First, as mentioned above, photographs provided touchstones for the non-specialist medical community to access the work of the biochemist. Rather than providing an abstract diagram of the chemical composition of the thyroxin, Kendall used a photograph as evidence to the *actual* existence of the active constituent of thyroid. By showing the crystalline form, Kendall also allowed a non-specialist medical reader to see thyroxin, an otherwise abstract chemical component. Kendall's act of making visible was part of science's drive "towards the production of images which are held, through strict procedures of referentiality, to reveal the natural world."[20] Kendall's inclusion of the photograph was a process of both making visible, but also naturalizing this novel chemical substance. Through the photograph, Kendall portrayed thyroxin not as a substance which was the product of years of chemical procedures and filtration, but as a substance which was already there, part of the natural world.

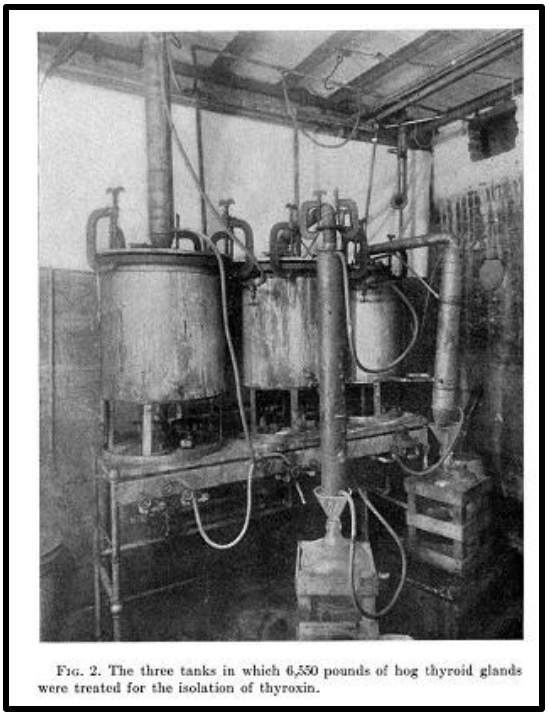

FIG. 2. The three tanks in which 6,550 pounds of hog thyroid glands were treated for the isolation of thyroxin.

Figure III.2: Kendall's Vats, 1919

Secondly, Kendall's photographs serve as a discursive bridge between the therapeutic traditions and biochemical inquiry. While gesturing to the purity of chemical processes, they also drew from the tradition of before/after portraitures discussed in Chapter 1. Editors of the

[20] Waldby, *Visible Human Project*, 137.

BMJ, while discussing the contributions of synthetic THT, stated, "When the student first acquires a textbook of physiology his earliest reconnaissance is likely to be among the illustrations to the text. One of these which will surely capture his interest will be that of the contrasting photographs of a cretin *before and after a course of thyroid feeding*."[21] Kendall did not include the photographs of the women and animals he uses in testing thyroxin; rather, the *compounds themselves* become the bodies being transformed. The sequence of thirty photographs represents the reality of chemical intervention and purification, the transformation of a gland into the recognizable substance of activity.[22] The image, through its reprinting in endocrinology and biochemistry textbooks, becomes implanted within the biomedical imaginary as its own embodiment of the chemical purity of thyroxin(e).


Crystals of the iodin-containing compound which occurs in the thyroid.

Figure III.3: Kendall's Crystalline Thyroxin, 1915. Used under fair use guidelines, 2011.

The deployment of such photographs also represented what, according to Catherine Waldby, "marks points of tension, knots of paradox or ambiguity within a system which are not resolvable within its terms."[23] The framing of each of these photographs also argued for the inability of chemistry to capture THT's effectiveness. The isolation of thyroxine was not simply a matter of finding an already-defined chemical principle. To find thyroxin, Kendall chronicled

[21] "Thyroxine," 1092; emphasis mine.
[22] In this sense, it is notable that the Kendall chooses the first, rather than the last, photograph in this sequence to widely distribute.
[23] Waldby, *Visible Human Project*, 137.

testing the activity of each group of substances on animals and otherwise healthy women to see which material mimicked the actions of animal-derived THT.[24] The chemical identification of thyroxin, then, could not be completely separated from the bodies that also proved desiccated THT's effectiveness.

Seven years after Kendall's isolation and chemical identification of thyroxin, George Harington corrected Kendall's thyroxin to thyroxine.[25] He claimed that "a careful study of Kendall's paper reveals the very slender nature of the evidence from which the chemical formula is deduced. …[F]rom a chemical point of view, there is no evidence."[26] The subsequent *BMJ* review of Harington's thyroxine states, "If the work of Harington is accepted it must be conceded that the physiological behavior of the synthetic compounds of Kendall can have no relation to the function of thyroxine."[27]

While both Harington and the *BMJ* editors pointed out errors in Kendall's chemical methodology, they implicitly criticized his inclusion of photographs as evidence. As stated above, Harington did not include photographs of thyroxine; he used chemical diagrams. The BMJ editors stated that Harington's discussion served as "one of the prettiest examples of the application of classical methods of organic chemistry to a definite biochemical problem," in contrast to the elusive findings of Kendall. Biochemical work, both Harington and the *BMJ* implicitly stated, does not include photographs. Yet this elision had implications for the presence of the animal thyroids within the synthetization of THT. By eliding the photographs, Harington erased all visual gestures to the animal glands from which he derived thyroxine.[28]

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[24] Kendall, "The Isolation in Crystalline Form of the Compound Containing Iodin, which Occurs in the Thyroid."
[25] C R Harington, "Chemistry of Thyroxine: Isolation of Thyroxine from the Thyroid Gland," *The Biochemical Journal* 20, no. 2 (1926): 293-299.
[26] Ibid, 293
[27] "Thyroxine," *BMJ*, 1093.
[28] Kendall's photographs remain the only pictorial demonstration of the isolation of any active constituent of the thyroid until present day. The image of the crystalline form in the JAMA was repeated within textbooks,

This elision of the crude glands had effects on the reception of thyroxine. It is in part this elision that divided Harington's biochemical work from its general use by physicians. Thus, the adoption of thyroxine was considered separate from the concerns of animal-derived THT, which had "no impediments to its widespread usage."[29]

The isolation and synthetization of thyroxine did not make an immediate contribution to the general treatment of patients with hypothyroidism. While considered a success of the field of endocrinology, Harington's thyroxine would not be adopted as the standard of care until the 1970s. Paradoxically, the deficiencies of thyroxine as a treatment were rarely discussed explicitly in either the *JAMA* or the *BMJ* before the 1950s. One of the only instances was a question posed by a practicing physician as to whether thyroxine or desiccated THT was better for the treatment of myxoedema, asking that the editor omit his name. The editor replied,

> Desiccated thyroid would be superior because it contains all the thyroid secretion and has been found to possess greater calorigenic activity than an amount of thyroxine of equal iodine content when administered by mouth. …. It is to be supposed that as replacement therapy the desiccated thyroid containing [other thyroid] substances would more nearly serve as a complete substitution process.[30]

The question being raised not only alludes to the separation between the discourses constructing knowledge about synthetic thyroid, but also the belief that thyroxine missed a substance which desiccated THT possessed. "Greater calorigenic activity" meant a higher basal metabolic rate (BMR). The test involved measuring heart rate and oxygen consumption in a

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histories of thyroxine and synthetic THT, lodging itself as the accurate representation of thyroxine.

[29] "Thyroxine," 1093.

[30] "Queries and Minor Notes: Thyroxine or Desiccated Thyroid," *Journal of the American Medical Association* 103, no. 21 (November 1934): 1645.

relatively neutral state. This form of measurement would continue as one of the only ways to measure the relative activity of synthetic or desiccated THT. However, the diagnosis and measurement of treatment was still subjective, and as the BMR was perceived to have significant limitations as a barometer for hypothyroidism, as by the time the patient's levels decreased to a point that couldn't be attributed to error, hypothyroidism could already be pronounced. The most precise method of diagnosing hypothyroidism was feeding small amounts of thyroid to see if the symptoms were ameliorated. If thyroxine could not be dependably absorbed through the stomach, then it did not assist physicians in treatment or diagnosis better than existing methods. Thus, the crude substance of desiccated THT continued as the standard of care. Synthetic THT remained, throughout the 1930s and 1940s, a pure "beautifully crystalline," but clinically inferior, substance.[31]

Intermission: Marmola and the FDA Amendment of 1938

> ...[T]o be an endocrinologist among the practicing profession today means too often to be primarily concerned with making fat ladies thin (Herbert Evans, 1933)[32]

As discussed in the last chapter, Upton Sinclair's *The Jungle* and the tainted meat served to soldiers during the Spanish-American War in 1898 pushed Theodore Roosevelt and his Congress to pass the Food Drug and Cosmetic Act of 1906.[33] The Act placed investigative

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[31] Kendall and Osterberg, "The Chemical Identification of Thyroxin," 277.

[32] Merriley Borell, "Setting the Standards for a New Science: Edward Schäfer and Endocrinology.," *Medical History* 22, no. 3 (1978): 283n3. Herbert Evans also made the infamous comment that endocrinology had suffered an obstetric deformation in its very birth." This concern over the relationship between endocrinology and quackery is also expressed in England during the 1920s. 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 (October 1976): 269-285.

[33] See "The Long Struggle for the Law," *Centennial of the FDA*, May 13, 2009, http://www.fda.gov/AboutFDA/WhatWeDo/History/CentennialofFDA/TheLongStruggleforTheLaw/default.htm.

power into the hands of the Bureau of Chemistry, demonstrating the rise of biochemical meaning-making in the early part of the 20th century. Yet the legislative battles that ensued were difficult and time-consuming. As FDA historians note, the amendment contained less enforcement power than was necessary to enact "real reform."[34]

The 1938 Food, Drug, and Cosmetic Act was signed into law to bolster the Bureau of Chemistry's enforcement power. The act moved enforcement activities into a new organization called the Food and Drug Administration, and left research and analytical practices within the Bureau of Chemistry.[35] Alongside controlling adulterated products, the new act increased regulatory power over direct-to-consumer medications, or patent medicines. Of the many therapies targeted, the first one to come under legal scrutiny was the anti-fat medication, Marmola. Its first appearance in the medical discourse was in the Questions and Answer section of *JAMA* shortly after the FD&C Amendment passed in 1908.[36] Marmola represented a particularly dangerous patent medication because it contained desiccated THT, a substance that medical professionals advocated only be used under their supervision. Marmola, by marketing directly to consumers, bypassed the physician's authority to regulate how much THT the patient received. The dangers of taking too much desiccated THT without doctor supervision manifested in the biomedical discourse as an emerging syndrome called "thyrotoxicosis."[37]

Marmola also underscored the tension between physicians and laboratory researchers. The bioassay proposed by the Committee on Biological Standardisation served a double function as a test for thyroid preparations enhanced with iodine, but also for the presence of THT in anti-fat medications. While Marmola could be mail-ordered without the need of a physician's

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[34] Ibid.
[35] Ibid.
[36] "Queries and Minor Notes: Thyroxine or Desiccated Thyroid," 1439.
[37] Cases of thyrotoxicosis, despite their strong associations with Marmola, happened under physician's supervision as well.

prescription, many physicians prescribed desiccated THT for weight loss, in case of hidden hypothyroidism.[38] THT had been associated with metabolic function since the turn of the century, and throughout the 1920s the thyroid was considered a "chief gland" over the functions of growth and metabolism.[39] At once thyroid patients were women, many of them swollen or overweight, and the transformations that took place in patient narratives clearly suggested that there might be something more to thyroid than simply a cure for myxoedema.[40]

The assertion that thyroid cured obesity was popular throughout the 1920s and 1930s, and Marmola advertisements aimed to capitalize on that claim. Thus, they advertised that their preparation had been "scientifically proven" to cure obesity.[41] This claim was truer than the American Medical Association (AMA) would like to admit.[42] Marmola passed so well as a legitimate medication that six AMA-certified physicians testified in its favor during the 1942 FTC (Federal Trade Commission, working with the FDA) trial.[43]

The news of physicians testifying for patent medicines sounded calls of treason within the AMA. In the words of the editors of *JAMA*, "Here, then, is a sweet spectacle: the American Medical Association attempting to protect the public against quack remedies, while individual members testify in behalf of the exploiters of quack remedies!"[44] Most of the physicians who testified for Marmola issued public apologies and explanations for their mistake. In the fall-out, medical reformers established that the "unspecific" complaints of women – such as obesity –

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[38] R. G. Hoskins, "Progress and Problems in Endocrinology," *JAMA: The Journal of the American Medical Association* 105, no. 12 (Sept, 1935): 948.
[39] Clemen, *By-Products*, 209.
[40] See I. N. Love, "Thyroid Extract in Juvenile Obesity: A Clinical Note," *Journal of the American Medical Association* 34, no. 16 (April 1900): 975 -976. The treatment of obesity was also believed to be present within the synthetic THT. Kendall claimed his thyroxin caused a decrease in weight for healthy individuals.
[41] "Bureau of Investigation: Marmola," *Journal of the American Medical Association* 108, no. 8 (February 1937): 658.
[42] Ibid.
[43] "Lending Aid and Comfort to Quackery," *Journal of the American Medical Association* 91, no. 18 (November 1928): 1377.
[44] Ibid., 1378.

should not be considered valid symptoms in proper endocrinology or medical practice. Reports of desiccated THT curing any condition other than deficient thyroid function disappeared from *JAMA* and the *BMJ* after the FTC trial.

In the view of Anti-Quackery council of the AMA, the therapeutic application of a medication had to be justified by specific physiological measurement. The prescription of a medication for a non-specific condition, in this case obesity, would only promote quackery and the image of endocrinologists as dietary gurus rather than medical professionals. They argued that use of such a medication must be administered through a medical practitioner, who could determine the dose of THT.[45]

For the case of thyroid in the first half the century, there was no easy method in which to diagnose hypothyroidism. As discussed in Chapter 1, medical professionals connected a number of conditions, from psoriasis to infertility, to deficient thyroid hormones. These generalized rejuvenating effects corresponded to the physician's understanding of THT's effectiveness as a meat medicine. Yet, within a medical discourse which increasingly emulated and valued contributions from physiology and biochemistry, the presence of Marmola gestured again toward the liminal space between quackery and endocrinology.

While the experiences of consumers of Marmola certainly testified to its dangers, the prosecution, and its extensive coverage in *JAMA*, also dampened the excitement around the use of desiccated THT. The fact that physicians testified *in favor* of Marmola thus underscored the need for medical reform of unspecialized, general practitioners. Such reform was possible only through the increased presence of laboratory methods and techniques in daily medical practice, and the publication of improper uses of medications. Between 1945 and 1950, many cases of "misuse" or "abuse" of thyroid therapy were published, including treatments for obesity,

[45] Ibid.

infertility and psoriasis, all conditions for which thyroid had been suggested as a medication in the 1930s.[46] The articles that mentioned desiccated thyroid did so with greater constraint than in the previous "golden years" of endocrinology.

The Marmola incident, like other crises that called for governmental and medical intervention, further associated the anxieties over organotherapy with the animal-derived therapy and female patients. Marmola's advertisements targeted women, and Herbert Evans cites the obese woman's presence as the literally excessive body that undermined endocrinology's reputation. Here, the image of the (obese) female body served as the antithesis to the pure chemical compounds that endocrinology touted as its achievements. Similar to the chimerical figures discussed in Chapter 1, Marmola served as a rupture point within the science of endocrinology.

Unspecialized, general practitioners also were increasingly viewed as at the borders of medicine; their ignorance could cause them to stray into quackery in prescribing desiccated THT for invalid conditions. After 1950, endocrinologists increasingly worked toward specifying more objective and technical procedures for diagnosing hypothyroidism. The emergence of a commercially viable, meaning oral administration, of synthetic THT provided endocrinologists with more power to advocate that physicians use the more controlled synthetic THT.

Episode 2: Why Doesn't Everyone Use L-Thyroxine?

In 1949, a group of British pharmaceutical chemists developed a more "commercially

[46] See, for example, R. G. Hoskins, "Progress and Problems in Endocrinology," *The Journal of the American Medical Association* 105, no. 12 (September 1935): 948-951; J. H. Means, "Therapeutics of the Thyroid," *The Journal of the American Medical Association* 105, no. 1 (July 1935): 24-8; Samuel F Haines and Robert D. Mussey, "Certain Menstrual Disturbances Associated with Low Basal Metabolic Rates without Myxoedema," *The Journal of the American Medical Association* 105, no. 8 (August 1935): 557-560; Emil Novak, "The Uses and Abuses of Modern Gland Products in Gynecologic Disorders," *Journal of the American Medical Association* 105, no. 9 (1935): 662 -667.

viable" form of synthetic thyroxine (T4).[47] This preparation was commercially viable because it could be consumed and absorbed through the intestines. Four years later, using similar synthetization methods, a second thyroid hormone, triiodothyronine (T3), was isolated and synthesized by Rosalind Pitt-Rivers and John Gross, former students of Robert Harington, who had isolated and synthesized T4 in 1926.[48] Unlike thyroxine, triiodothyronine's action was almost immediate, paralleling the effects that physicians were accustomed to seeing with desiccated THT preparations.

Over the next twenty years these chemical and synthetic compounds would come to stand for THT's effectiveness. The technologies of trust that had ensured desiccated THT's effectiveness over the twentieth century were called into question by comparing iodine assays to measurements of T3 or T4. Synthetic THT would thus double as an assay mechanism for clinical effectiveness and a pure therapeutic.

The adoption of synthetic THT as a viable therapeutic thus depended on the merger of both specialists' and general practitioners' methods towards measuring the effectiveness of THT. Due to the restriction on published reports of desiccated THT in the 1940s, the definition of hypothyroidism became increasingly narrow over the 1950s. Simultaneously, the symptoms that physicians sought to relieve also became increasingly specific. After the Marmola incident discussed in the last section, obesity was no longer recognized as a symptom for hypothyroidism, and patients' symptoms generally had to be confirmed by blood tests for treatment to go forward. Dangers of over-prescription or improper prescription of THT populated medical texts.

As the *Thyroid* graph at the beginning of the chapter suggests, the adoption of synthetic

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[47] Benjamin Arthur Hems and John Charles, "Preparation of Thyroxine and Its Derivatives", July 1949; Charles W. Turner and Ezra P Reineke, "Production of Thyroxine from Diiodotyrosine", February 10, 1948.

[48] J. Gross and Rosalind Pitt-Rivers, "3:5:3′-Triiodothyronine, Isolation from Thyroid Gland and Synthesis," *Biochemical Journal* 53, no. 4 (March 1953): 645-652.

THT was made possible by the abandonment of desiccated thyroid. In the previous section, I focused on how technologies of trust, such as standardization and biological assays, allowed desiccated THT's effectiveness to be adequately measured. In this section, I focus on how the technologies of trust were categorized as inadequate in the face of synthetic THT's assumed consistency.

One particular editorial offers a strong articulation of these phenomena: Alain MacGregor's 1961 "Why Does Anybody Use Thyroid B.P?"[49] MacGregor, a research clinician and endocrinologist, emphasized the need for chemical purity within the clinic, thus merging the physician and specialist's view of THT's effectiveness. Within his editorial, he summarized his previous study on the effects of l-thyroxine on patients. In this study, he identified seven patients in his practice who were "clearly hypothyroid" on their current animal-derived THT. He took them off their animal-derived therapy and switched each one over to synthetic. Through these case studies, using blood test results, he graphically showed each patient's improvement on the "consistent" l-thyroxine.[50]

MacGregor's editorial used a few important rhetorical devices to appeal to both general and specialized readerships. He used the format of the case study, a well-established format of report among general physicians. Yet in his discussion of each of these studies, MacGregor used a new laboratory measure, the protein-bound iodine blood test (PBI), to show the improvement of the thyroid. He took care not to mention the symptoms of his specific patients, but rather relied on both of these blood measurements to provide evidence for his claims. Also, he cited reports from both general physicians and biochemical researchers, providing a link between

[49] Alain G. MacGregor, "Why Does Anyone Use Thyroid B.P.?" *Lancet* 227 (1961): 329. MacGregor embodied both the endocrinological scientific researcher and the physician, having been trained in endocrinology and seeing patients on a regular basis. In this sense, he is the product of the medical reforms that had taken place over the twentieth century.

[50] Ibid.

chemical and therapeutic data. The appearance of his editorial in the *Lancet* also targeted a wider readership than his other publications in endocrinological journals, such as the *JCEM*.

MacGregor's editorial supported synthetic THT by questioning the chemical and biological assays of desiccated THT. He stated point blank that these assays are "indirect indices of probable biological activity," and thus physicians should not trust them to give accurate readings.[51] He pointed to the fact that iodine content of the gland varied by species; sheep and cows had less iodine in their thyroids than hogs. He accused manufacturers who use various animal thyroids in their preparations are producing THT with variable potency. As for the use of biological assays, he stated, "the vital biological assay is the biological response of the hypothyroid patient."[52] He argued that desiccated THT should not be used because medical practitioners cannot determine, even secondarily, the potency of their preparation. He further made the argument that variability in potency resulted in inconsistent treatment in patients. Desiccated THT, MacGregor argued, is clinically inferior.

Thus, MacGregor attacked not only the use of animals as raw materials, but also the ability to use animals as research materials. Underlying MacGregor's analysis was the assumption that animals have innate variability, and this variability was antithetical to modern medicine. Synthetic thyroid hormone, MacGregor reasoned, would not require any standardization at all. He concluded that standardization of desiccated THT "would become redundant if the profession as a whole used thyroxine instead."[53]

On both sides of the Atlantic, MacGregor's editorial was widely cited by both specialized and general practitioners who promoted synthetic thyroid.[54] Desiccated THT, whose crudeness

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[51] Ibid, 330.
[52] Alain Macgregor, "Why Does Anyone Use Thyroid BP?," *The Lancet* 277, no. 7172 (February 1961): 331.
[53] Ibid, 332.
[54] See, for example, "Editorial: Thyroid Outdated," *The Pharmaceutical Journal* 168 (1961): 131-2; V. J. Pileggi, O.

was once expected and tolerable, discursively transformed into a liminal and variable figure in the biomedical imaginary. That is, the control mechanisms for desiccated THT's innate variability had failed. Throughout the 1960s, the methods of this failure would only increase. Several reports that studied the variability of desiccated THT cited MacGregor's editorial as cause of their investigation. The last of these was a study that tested the amount of T3 and T4, the active thyroid hormones, in preparations of thyroid USP.[55] The report concluded, "The results obtained on the clinically ineffective desiccated thyroid preparations further emphasize the importance of knowing the T4 and T3 contents of the preparations."[56] None of these reports used human or animal assay to confirm that the effects of variable T3 and T4 translated into variable effects on the living organism.[57] The report signaled not only the variability of desiccated in comparison to T3 and T4, but also demonstrated that T3 and T4 were the emblems of THT's activity within the biomedical imaginary.

MacGregor's editorial signaled not only the failure of technologies of trust to properly standardize desiccated THT, but also to contain what he viewed as the danger in the variable desiccated product. In 1961 the Marmola trials, the last crisis around desiccated THT, were more

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J. Golub, and N. D. Lee, "Determination of Thyroxine and Triiodothyronine in Commercial Preparations of Desiccated Thyroid and Thyroid Extract," *Journal of Clinical Endocrinology & Metabolism* 25, no. 7 (July 1965): 949-956; Selahattin Kologlu, Harold L Schwartz, and Anne C Carter, "Quantitative Determination of the Thyroxine, Triiodothyronine, Monoiodotyrosine and Diiodotyrosine Content of Desiccated Thyroid," *Endocrinology* 78, no. 2 (February 1966): 231-239; J.-F. Dymling and D. V. Becker, "Occurrence of Hyperthyroidism in Patients Receiving Thyroid Hormone," *Journal of Clinical Endocrinology & Metabolism* 27, no. 10 (October 1967): 1487-1491; Herber A Selenkow and Marvin S Wool, "A New Synthetic Thyroid Hormone Combination for Clinical Therapy," *Annals of Internal Medicine* 67, no. 1 (July 1967): 90-99; Joel I. Hamburger, *Your Thyroid Gland--Fact and Fiction* (Springfield: Thomas, 1970); C. N. Mangieri and M. H. Lund, "Potency of United States Pharmacopeia Desiccated Thyroid Tablets as Determined by the Antigoitrogenic Assay in Rats," *Journal of Clinical Endocrinology & Metabolism* 30, no. 1 (January 1970): 102-104.

[55] Pileggi, Golub, and Lee, "Determination of Thyroxine and Triiodothyronine in Commercial Preparations of Desiccated Thyroid and Thyroid Extract."

[56] Ibid., 995.

[57] This is in contrast to the methods that established iodine content as ineffective in contrast to the biological assay. That is, that iodine content did not translate into biological effects or effectiveness with either human or nonhuman test subjects.

than 20 years old. Yet the bodies of women and animals were certainly present within the biomedical discourse, and being called upon by an unlikely voice: animal-derived THT manufacturers.

For example, MacGregor extensively cited studies and responses from the manufacturers of Proloid, an animal-derived THT. In 1953, four years after the commercial production of synthetic THT, Proloid began two series of advertisements in the *JCEM*. With the first series, the title for each of these advertisements reads "Predictable thyroid therapy" underneath pictures of women, a uterus and ovaries, or all three (see Figure III.4). Each ad touts, "Proloid, *the improved thyroid*" and "Proloid, virtually *pure* thyroglobulin."

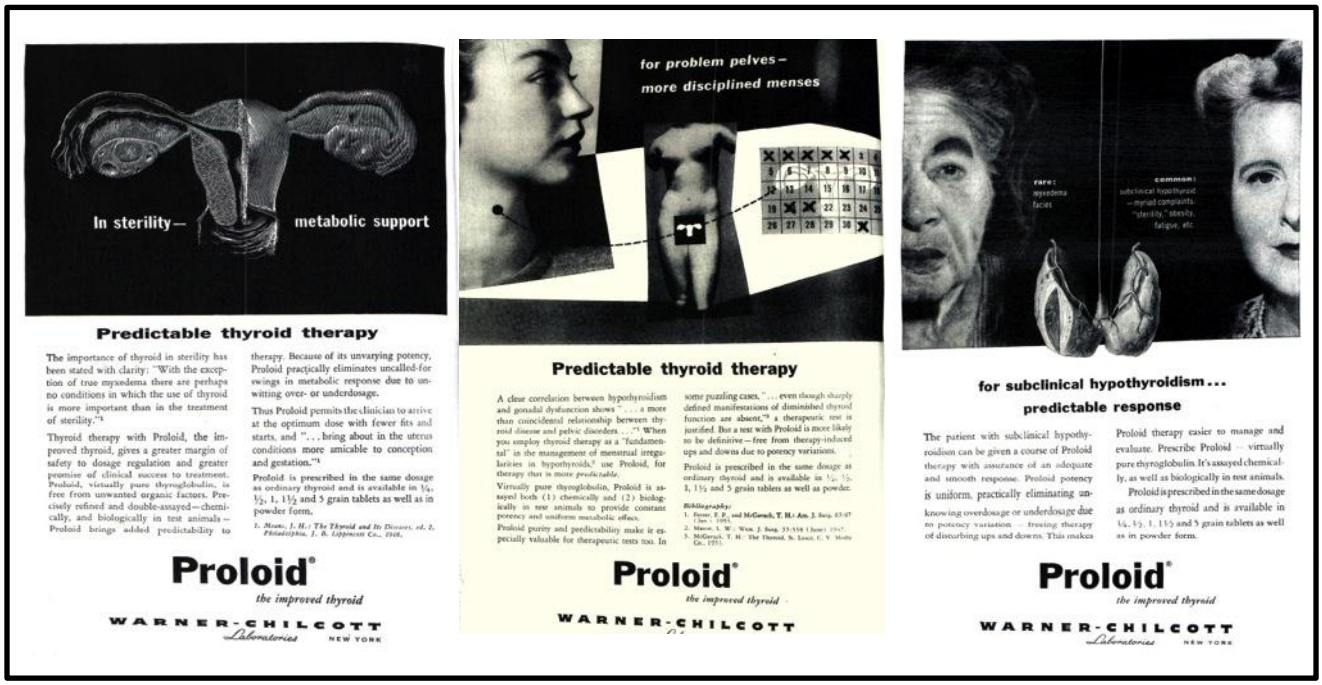

Figure III. 4: Proloid Ads, "Predictable Thyroid" Series, *JCEM* 1953-6. Used under fair use guidelines, 2011.

The second series involved a rendition of before/after shots so prevalent within earlier medical discourses. One (Figure III.5, right) showed a modern variation on the before/after pictures of the early 20th century women treated with animal-derived THT. In the other (Figure III.5, left), a trans-species analogy between "man" and "dog." Within each of these, Proloid touted itself as "smooth," and "predictable." In some issues of *JCEM*, representatives of both of these series appeared together. In the print below the photographs, the text reads that the Proloid was doubly assayed, using both the biological and chemical tests.[58] It was both of these assays that MacGregor attacked in his 1961 editorial.

Figure III.5: Proloid Ads, second series, *JCEM* 1953-6. Used under fair use guidelines, 2011.

[58] Warner-Chilcott labs, manufacturers of Proloid, used an anti-goiterigenic assay and the USP-specified organic iodine content for their two assays.

Proloid, more visibly than other animal-derived products, reflected and determined both the specialist and general physician's interpretations of THT's effectiveness and purity. It differentiated itself from desiccated THT as more pure, more refined, than other products. At the same time, it insisted on the superiority of animal-derived THT. These advertisements appeared in a specialized journal, whose submission standards had changed over the past decade to include more statistically based studies. Quantitative measurements and charts often qualified the rare appearance of before/after portraits.[59] Thus, the reliance of the before/after effects invoked the early-twentieth century photographs while translating these results into a discourse that emphasized predictability, consistency, and reliability. These advertisements reminded physicians that women are their main consumers of THT, and to transform these women into recognizable figures, they needed "predictable," but animal-derived, therapy.

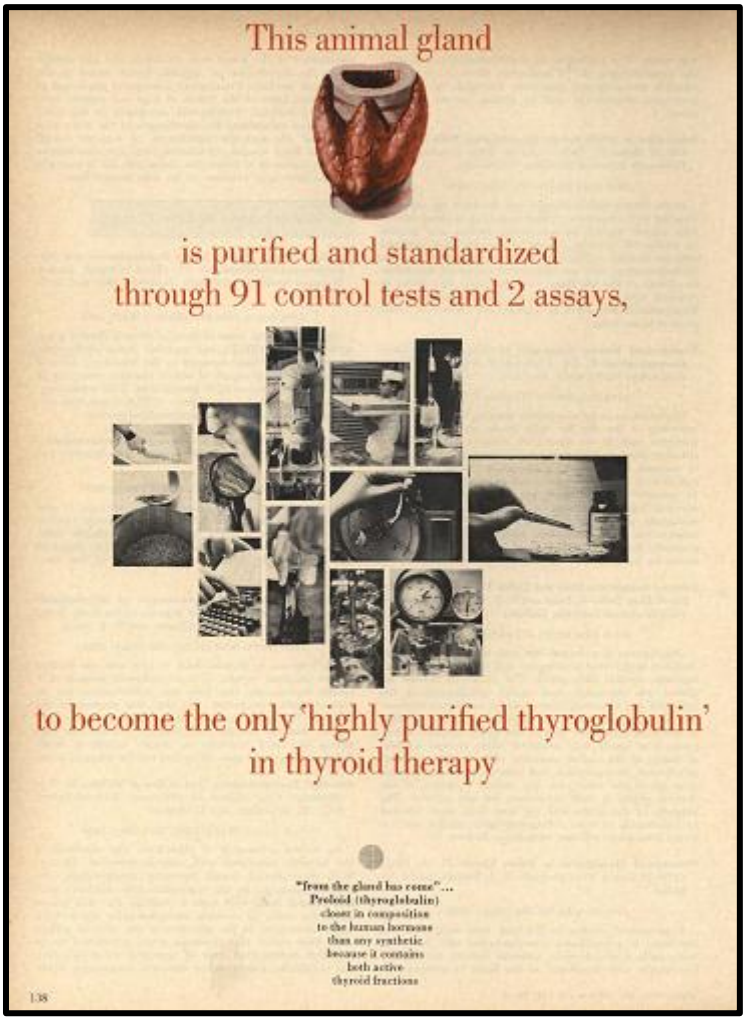

Figure III. 6: Proloid Ad, "This animal gland" *JAMA* 1965. Used under fair use guidelines, 2011.

After the MacGregor study that attacked desiccated thyroid USP, Proloid put another

[59] See, for example, Lawrence C Wood et al., "Syndrome of Juvenile Hypothyroidism Associated with Advanced Sexual Development: Report of Two New Cases and Comment on the Management of an Associated Ovarian Mass," Journal of Clinical Endocrinology & Metabolism 25, no. 10 (October 1965): 1289-1295.

advertisement out in the *JAMA* (Figure III.6). Published in 1965, this advertisement reached a wider range of physicians, and more general practitioners than in the *JCEM*.[60] Curiously, it was and is the *only* picture of an animal thyroid present in the *JAMA*, *BMJ* or *JCEM* between 1890 and 1980.[61]

This advertisement reflected the mounting evidence of animal-derived THT's variability. The contrast of the animal thyroid with the almost-abstracted photographs of control devices demonstrated the strict tension between fleshy bodies and the technologies of trust that erased them. Within this advertisement, the mediation between the actual thyroid and Proloid's name responded to the increased concern over variability, while at the same time asserting that animal-derived THT was clinically superior to synthetic. The animal thyroid, the advertisement stated, "is the closer to the human thyroid" than synthetic, responding to MacGregor's accusation that animal assays were incompatible with biological activity.

In both sets of advertisements, the increased emphasis on standardization and purification applied to both women's and animals' thyroids. Proloid's emphasis on its effects as predictable and consistent implied the normalization of the hormonal body as well. As Bernice Hausman notes in *Changing Sex*,

> endocrinology participated in the development of a medical vision that privileges an ideally functioning body, harmoniously regulated by a system of internal secretions (the hormones). Within its purview the ideal became conflated with the normal, or statistically average, as was espoused by doctors as a possibility available to all subjects during the life span.[62]

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[60] Warner-Chilcott Labs, Proloid Advertisement, *Journal of the American Medical Association* 196, no 9 (May 1965): 138. Also appears in several issued throughout 1964 and 1967.
[61] Based on my own observation and research. See Methodology in the Introduction for qualifications to this claim.
[62] Hausman, *Changing Sex*, 27.

Thus, both animal-derived and synthetic THT participated in the perpetuation of the ideal body as one whose measurements of hormones did not vary considerably. Rather than focusing on the improvement of subjective symptoms, the larger medical trend in the 1960s also advocated an increase in statistically standardized methods of measuring the effects on the human patients. While the variability of desiccated THT was demonstrated in 1965 through the measurement of T4 and T3, it was the exclusion of animal-derived THT from clinical trials that signaled the merger of biological and chemical meanings of clinical superiority, and general practitioner and specialized understandings of methods of measuring THT's effectiveness.

Conclusion: "A Valid Comparison," Synthetic THT in the Clinical Trial

In 1962, a year after MacGregor's editorial, news of gross birth defects in Europe made headlines in the United States.[63] Reportedly, these defects were caused by the pregnant mothers taking thalidomide, a sedative drug used to help treat morning sickness. Spawned by the public debate over the effectiveness and safety of the currently marketed drugs, Congress passed what would be known as Kefauver-Harris Amendments, which required all new drugs to offer "substantial evidence" of their efficacy. In his discussion of the amendment, William Curran notes that the "efficacy requirement had significant effects on the need for and the scope of government controls over clinical investigation."[64] "Substantial evidence" was defined as "evidence consisting of adequate and well-controlled investigations . . . by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved."[65] What came to be realized as "substantial evidence" was the randomized clinical trial.

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[63] William J. Curran, "Governmental Regulation of the Use of Human Subjects in Medical Research: The Approach of Two Federal Agencies," Daedalus 98 (1969): 542-3.

[64] Ibid, 552.

[65] Ibid.

The rise of the randomized clinical trial (RCT) as a gold standard within medicine signaled the final merger of the specialized and general perspectives on THT. Unlike drugs adopted after 1963, neither synthetic nor desiccated THTs had to show their effectiveness, meaning that they did not have to submit clinical trials proving both their efficacy and their safety to the FDA.[66] However, the RCT pervaded the biomedical discourse outside of FDA regulation. As RCTs became the "gold standard" of medical knowledge-creation, clinical researchers adopted this framework to study controversies within the literature.[67]

One such controversy was alluded to by the 1965 Proloid advertisement – whether or not a combination therapy with both T3 and T4 was better than T4 alone. A report was published in 1970 that aimed to address this controversy.[68] The investigator, R. N. Smith, stated that undertaking a RCT of the subject would provide a "valid comparison" to be made between the T4-only or a T4/T3 combination. Rather than comparing an animal-derived THT and the synthetic T4 therapy (thyroxine), he used a thyroxine and a T4/T3 synthetic combination.

By using only synthetic THTs, Smith implicitly argued that desiccated THT was unpredictable and unfit for the "gold standard" of medical research. He ended his study by stating that at the bare minimum, all patients should be switched from desiccated THT to synthetic THT.[69] Yet this assertion was based on an *assumption* of the study rather than the actual results of the study.

For the combination T3/T4 therapies, which represent the absent desiccated THT, Smith

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[66] In 1997, the FDA cited that synthetic preparations had potency problems and requested that manufacturers reapply for FDA approval. See Food and Drug Administration, "Compliance Policy Guides - 440.100 Marketed New Drugs Without Approved NDAs and ANDAs," http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074382.htm.

[67] For a discussion on the rise of the RCT, see Jeremy A. Greene, *Prescribing by Numbers: Drugs and the Definition of Disease* (Baltimore: JHU Press, 2007); J. Rosser Matthews, *Quantification and the Quest for Medical Certainty* (Princeton: Princeton University Press, 1995).

[68] R. N. Smith, S. A. Taylor, and J. C. Massey, "Controlled Clinical Trial of Combined Triiodothyronine and Thyroxine in the Treatment of Hypothyroidism," *British Medical Journal* 4, no. 5728 (October 1970): 145-148.

[69] Ibid, 148.

argued that the benefits were not supported by "objective" measures of blood PBI. He stated that the "subjective comments …of benefit from the combined treatment [of T3 and T4] may be valid but equally may be due to other factors which cannot be excluded and which are inherent in uncontrolled therapeutic studies."[70] By contrasting the patient narrative and the quantifiable results of the PBI, Smith gestured to the incommensurability of medical certainty and subjective therapies. The need for RCT in this sense was no different than other technologies of trust before it (e.g. iodine or biological assay).

However, what made the RCT different was that it extended the procedures of control from the THT preparation to the patient. The ideal patient, in this context, was one who could be easily quantified through blood tests. These tests represented the elision of variability in the therapeutic effects of THT. Eight subjects were excluded from the results because they didn't take more than 25% of the prescribed tablets, and several more were excluded because they developed ill side effects when taking the medication[71]. Smith argued that a T4/T3 combination produced somewhat misleading blood test (he, like MacGregor, traced clinical effectiveness using PBI), and thus argued that thyroxine held advantages over the combination therapy.[72] Smith thus defined the clinical advantages as producing a reliable blood test, rather than the subjective experience of the patient.

Through the RCT, endocrinologists found ways of proving THT as effective outside of the bodies of animals, and focused on specifically narrow conceptions of THT's effectiveness in the bodies of women. Endocrinologists and general physicians relied increasingly on laboratory mechanisms, such as PBI tests, to assay the effectiveness of THT. As Smith states, synthetic

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[70] Smith, Taylor, and Massey, "Controlled Clinical Trial of Combined Triiodothyronine and Thyroxine in the Treatment of Hypothyroidism," 147.
[71] Ibid, 143.
[72] Smith, Taylor, and Massey, "Controlled Clinical Trial of Combined Triiodothyronine and Thyroxine in the Treatment of Hypothyroidism," 148.

THT matched this definition of clinical effectiveness better than combination therapies. The blood tests thus superseded the patient in determining the effectiveness of THT. While the increased quantification of the patient led to an establishment of clinical certainty of THT's effectiveness, it was a narrower definition than used previously. The variable bodies and variable treatments were controlled by the RCT.

No reports would question synthetic THT's constant potency until 1997.[73] Thus, Smith's usage of synthetic THT as the more constant preparation was not an issue within the period's discursive climate. After Smith's trial in 1970, the continued use of the RCT solidified synthetic THT's presence within the frameworks of modern medicine.[74] Yet synthetic THT's usage in clinical trials only perpetuated the belief that synthetic was clinically superior and desiccated was clinically inferior. Desiccated THT's exclusion from the clinical trial implied that it was not a valid tool within proper modern medicine. By the time the official standardization of desiccated THT would shift from iodine to T3/T4 methods in the 1990s, desiccated THT would not be used with the gold standard for more than twenty years.

Other historians have noted that the emergence of RCT in biomedical research stabilized and formalized the meaning of "control" to those trials which did not employ the methods of the RCT.[75] The increased attention to RCTs, quantitative diagnosis, and prescription levels based on test results narrowed conceptions of THT's effectiveness within the biomedical discourse. Physicians and endocrinologists determined THT's effectiveness in patients through hormone

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[73] See note 67, this chapter.

[74] See, for examples of the RCTs used to construct knowledge around synthetic THT, see John P. Walsh et al., "Combined Thyroxine/Liothyronine Treatment Does Not Improve Well-Being, Quality of Life, or Cognitive Function Compared to Thyroxine Alone: A Randomized Controlled Trial in Patients with Primary Hypothyroidism," *Journal of Clinical Endocrinology & Metabolism* 88, no. 10 (October 2003): 4543-4550; Simona Grozinsky-Glasberg et al., "Thyroxine-Triiodothyronine Combination Therapy Versus Thyroxine Monotherapy for Clinical Hypothyroidism: Meta-Analysis of Randomized Controlled Trials," *J Clin Endocrinol Metab* 91, no. 7 (July 2006): 2592-2599.

[75] Martin Edwards, "Good, Bad or Offal? The Evaluation of Raw Pancreas Therapy and the Rhetoric of Control in the Therapeutic Trial, 1925," *Annals of Science* 61, no. 1 (January 2004): 79-98.

levels in the blood, rather than before/after photographs or symptomatically. Desiccated THT was standardized through the chemical assay of recognized biochemical hormone levels, outside of the effects on a group of animals or a particular patient. New inscription devices and technologies of trust allowed for increasing mediation between the bodies of animals and women and the medical discourses. Blood levels, rather than patients, became the sites of medical intervention.

Those physicians who supported animal-derived THT or did not always use the most up-to-date blood tests began publishing in other journals increasingly over the 1970s. As the set of discourses and procedures that applied to desiccated and synthetic THT divorced from one another, the particular interpretations of the history of THT would also differ. As these discourses became isolated, their denunciation of the opposing therapy became more extreme, and the border between "alternative" and "mainstream" became more heavily guarded. As I will discuss in the conclusion, by focusing on the bodies of animals and women, this study offers a more sustained engagement with the middle ground between synthetic and desiccated THT and their long *shared* history.

Conclusion
Future Directions and Reading Contradictions

This project historically contextualizes the debate between desiccated and synthetic THT as a negotiation of animal and women's bodies in the biomedical imaginary. By focusing on the gendered and special bodies neglected in the official narratives of THT's history, this project brings to light the affective and imaginary dimensions of diagnosing and treating hypothyroidism. Further, this project's larger goal is to insist on the fleshy materialities that trouble the medical discourses that divorce the imaginary from the material realms.

In Chapter One, I analyzed how the physicians and medical researchers used the procedures of meat consumption and vivisection to make sense of animal-derived THT's effectiveness. Physiologists invented THT transferring procedures of vivisection on animals to female patients. In this framework, THT was a living tissue whose use depended on the logics of xenotransplantation. Women taking THT were cured both by the animal-derived product and by becoming animal. This notion received extensive critique by anti-vivisectionists because of the conflation of the woman and animal on the vivisector's table, whereas the ingested forms of THT did not. Ingested forms, used mostly by general physicians, drew on the logics of meat consumption to explain THT's effectiveness. Just after the turn of the century, both of these frameworks would combine to determine that there was some chemical activity within the mostly dead meat. Scientific work increasingly focused on purifying and isolating this constituent within THT, rather than tracing its generalized effects on the patient.

In Chapter Two, I explored how these purification, isolation and synthetization procedures further altered notions of THT's effectiveness. The methods for assay increasingly elided the bodies of women and animals from the medical discourse. This elision depended on

the rise of statistical measures of both THT's effectiveness in the pill itself and the patient. As physicians and specialists focused on the measure of chemicals in the pill and patient bodies, the indescribable effectiveness of animal-derived THT lost importance in the treatment of hypothyroidism. In this way, chemical purity was paired with clinical effectiveness.

Future Directions: The Biomedical Imaginary of Patient Discourse

I began this project by calling attention to a particular place of rupture: the shortage of desiccated THT in 2009 and 2010. During this shortage, patients taking desiccated THT organized using social media cites such as Facebook and list-serves to provide advice, support and resources for one another. Mary Shomon, one of the figureheads of this movement, started a Facebook group called "Save Natural Thyroid." This group was dedicated to finding out information from manufacturers and governmental bodies as to why the desiccated THT shortage occurred, as well as finding resources on supplies of medicine.

In the study thus far, I have examined the biomedical imaginary by investigating the medical discourses from myriad voices in both general and specialized journals. These voices are comprised mainly of endocrinologists, medical practitioners and physiologists. I have explored the tacit images, narratives and procedures of these professionals because they constitute the means by which the biomedical imaginary instantiates itself as the commons sense of THT's definition and therapy. Also, they represent the narratives most consistently recorded, as there is no consistent historical collection of narratives of patients who lived with thyroid disorders before the 1970s.

Figure IV.1: "Save Natural Thyroid" Banner from campaign website. Used under fair use guidelines, 2011.

However, the number of organized patient advocacy groups has increased considerably over the past three decades. Just as the figures of animals and women within the biomedical imaginary define(d) the forms of thyroid disease and its treatment, the inclusion of patients' voices is certainly well warranted. This iteration of the project lays the historical groundwork for an oral history project that will include the *actual* voices of patients and physicians. These narratives draw on the historical images, narratives and procedures from biomedical discourses to assert their own viewpoints today. By analyzing these narratives, I will trace the historical images of animals and women to their current iterations within the debate between synthetic and desiccated THT.

Including the actual voices of patients should not be confused with a holistic picture of thyroid disorders and the contestations of their treatment. The point is not just to get the other narratives associated with THT. As I discussed in the Introduction, few patient-centered sites include the reference to the animal bodies of the source thyroids. While acknowledging the unqualified symptoms of their own experiences, I hope to demonstrate that THT discourse has more ramifications and associations than the just the dismissal of women's bodies within

industrialized medicine. For example, pro-synthetic THT advocates state that desiccated THT is crude, and this word appears several times throughout both sides of the treatment debate. Yet this project demonstrates how crude speaks across the history of THT to embody a multiplicity of events –its origins in organotherapy, the association to Marmola or "fat fighting" drugs, the large amounts of thyroids that were once used to arrive at just a handful of "pure substance."

Categories within the medical discourse are re-deployed within patient-centered THT discourse. In the case of THT, patient narratives draw and respond to medical discourses, which feed back into the biomedical imaginary. Rather than discounting patient discourse for the physician's (or vice versa), it is important to explore the liminal spaces within physician and patient space, the mainstream and alternative communities. This passage is meant to point to future directions of the project in establishing the biomedical imaginary from the oral and written narratives of patients and physicians.

Both camps of THT discussion engage with the term natural as both an explanation for and critique of why patients use desiccated THT. Explanations that desiccated THT is natural are not enough. More research is needed to understand how patients make sense of THT's effectiveness for themselves, as this could shed light on some of the limitations of a quantitative conception of clinical effectiveness discussed in Chapter 2. However, terming and thus choosing the "all-natural" desiccated THT has contradictions in it as well, and shows also some of the limitations of advocating desiccated THT-only therapy as the answer. Such an example is provided by Janie Bowthorpe's sourcebook, *Stop the Thyroid Madness!*. Bowthorpe includes an investigation of some difficult areas of consuming an animal-derived "natural" product. In her Addendum B, Bowthorpe investigates vegetarian and religious responses to eating porcine

thyroid. She offers an example of a patient who uses desiccated THT despite her religious and dietary choices. Serene, the patient, states:

> All the evidence points to this [Armour desiccated THT] being the superior medication for this illness, although most docs want to give the synthetics. Armour is all natural, which appeals to me in spite of the fact that it is derived from pigs. As you know, being vegan and Messianic, this doesn't sit well, but I have come to believe that what makes my body/brain/temple perform optimally takes precedence over the desire to exclude all animal products from my diet as well as the mitzvah against pork. It is a very tiny amount and I am already feeling incredibly better: my thinking is clearer, I feel more in control of my emotions, and I am having frequent moments of real joy![1]

Bowthorpe concludes this narrative by stating, "since the use of desiccated thyroid saves a life, it might not be a problem."[2]

This project has demonstrated how the ineffable effectiveness of animal-derived THT was elided in the rise of the synthetic alternative. This passage demonstrates how that effectiveness of THT, which escapes scientific bounds, is so important to an individual patient that she is willing to reconsider some of the most important foundations to her identity. The body of the pig, in this case, is a site of renegotiation of other (religious, dietary) imaginaries.

As within the medical discourses this project studies, this reflexive moment of contradiction shows the complications of coming to terms with the raw material of thyroid. As Bowthorpe states, the life-saving potential of desiccated THT holds in tension the specters of dead animal bodies on one hand and transformed becoming-healthy human bodies on the other.

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[1] Janie A. Bowthorpe, *Stop the Thyroid Madness!: A Patient Revolution Against Decades of Inferior Treatment* (Boulder Springs: Grape Publishing, 2008), 198.
[2] Ibid.

Such a pausing and reflecting, rather than being a point of closure, is a point of potentiality. That is, the consideration of the animal body and animal thyroid serves as a point of possibility that embraces the complexity of THT rather than eschews it.

Subversive and Productive

The frameworks of this project are particularly helpful in thinking about such contradictions as presented in Serene's narrative. For example, the phrase "superior" offers a distinct metric from the tests and assays in claiming that synthetic THT was clinically superior. Further, the appeal of Armour thyroid speaks toward the simultaneous desire and repulsion that parallels physicians' interpretations of preparing THT at the turn of the century.

Such contradictions are not visible within the current essentialist natural and scientific discourses, which interpret the natural to mean innately better or worse. Within endocrinology especially, the images of animals and women both engage productively and subversively with the biomedical imaginary. THT cannot be separated, nor reduced to, the bodies of animals and women. Neither can most former organotherapies or medicaments that are produced from the bodies of animals. Bringing these material bodies forward is vital to understanding the logics that implicate(d) them within the study of THT. As Catherine Waldby points out

> [M]edicine relies upon productive encounters with corpses, donor cadavers, foetal tissue, and other forms of marginal life and near-life. Such entities act as research matter and as a source of organs and tissues, crucial elements in the biomedical enhancement of vitality for the more properly alive. This implication of living and the dead becomes more profound in medicine's continuing reliance on a

concept of the living body as a mechanical system.[3]

Medicine, then, depends on the corpse for the definition and maintenance of the living body. In the case of THT, the corpse is harvested for thyroids and used as explanations for THT's generalized effects. This productive encounter with the corpse also holds with it the implicit anxiety over the excesses of the living and decaying body – the irreducible remainder that escapes medical and mechanical logics. This irreducible remainder informed the general stimulating effects of meat, the logics of xenotransplantation, as well as the slow abandonment of desiccated THT over the twentieth century. The animal thyroid has historically held and contemporarily holds within it an excessive effectiveness that resists medical witnessing.

Through paying attention to the productive and subversive relationships between the biomedical discourse and the images of animals and women, this project's framework serves as a helpful place to begin thinking about the contradictions and excessiveness inherent within the current debate between desiccated and synthetic THT. Each of the issues discussed within current iterations of the debate between synthetic and desiccated THTs is an argument around how to negotiate and conceptualize these bodies. In the dismissal of desiccated THT as outdated or crude, the mainstream medical community does not simply disavow the variable potency of desiccated THT, but also disavows its dependence on these bodies. As Merriley Borell notes, later workers in endocrinology were quick to dismiss the previous discipline-building work of physiologists on animal organs as "rash empiricism."[4] The same trend is iterating itself again in the present controversy and shortage, as specialists attempt to dismiss the viability of animal-derived THT as a treatment for thyroid conditions.

It is this dismissal that unnecessarily narrows the conception of hypothyroidism. To open

[3] Waldby, *Visible Human Project*, 23.
[4] Borell, "Brown-Séquard," 320.

up this under-diagnosed disease, a middle ground must be explored between desiccated and synthetic, between patient and physician, between the material realities and the biomedical imaginary.

Appendix A: Timeline of Hypothyroidism and THT[1]

Date	Description
1600 BC	The Chinese treat goiter with burnt sponge and seaweed
30-50 BC	Egyptian Relief of Cleopatra showing goiter
c. 650 AD	Sun Ssu-Mo used combined seaweed, dried powdered mollusk shells and thyroid gland (organotherapy) for goiter.
1475	Wang Hei describes the thyroid gland and recommended treatment for goiter by taking dried/minced thyroid
c. 1530	Paracelsus attributes goiter to mineral impurities in drinking water. He also realizes the connection between cretinism, endemic goiter and congenital idiocy.
c. 1606	Shakespeare mentions goiter in *The Tempest*
1656	Thomas Wharton names gland "thyroid" after the shape of an ancient Grecian shield
1792	Desault (Paris) describes successful surgical removal of part of the thyroid
1811	Bernard Courtois discovers iodine by oxidizing burnt seaweed
1844	Johannes Mueller calls the thyroid 'bloodgland.'
1850	Curling (London) describes defective cerebral development due to the absence of the thyroid body
1857	Moritz Schiff successfully performs total thyroidectomies in dogs
1873	Gull gives a classical account of myxoedema in women
1878	Ord coins the term 'myxoedema' in reference to the mucous which forms under the skin
1884-86	Horsley confirms Sermon's postulates that thyroid removal (cachexia strumprivera), cretinism and myxoedema are connected, as does the Committee On Myxoedema, of which he is a member
1891	Murray reports on his successful treatment of myxoedema with thyroid extract

[1]Drawn from my own research, Medvei, *History of Clinical Endocrinology*; A M Ahmed and N H Ahmed, "History of Disorders of Thyroid Dysfunction," *Eastern Mediterranean Health Journal* 11, no. 3 (May 2005): 459-469; American Thyroid Association, "ATA Thyroid Timeline", http://www.thyroid.org/professionals/education/timeline.html.

1895-96	Baumann (Germany) isolates "thyroiodin" (later called "iodothyrin") from the thyroid. This serves as the iodine-rich colloid material that is claimed to be more pure than traditional desiccated THT. Proloid is a part.
1897-1925	Oswald studies of the iodine content of the thyroid
1906	Thyroid USP is grandfathered in under Pure Food, Drug and Cosmetic Act
1907-8	Royal Committee on Vivisection Hearings held in London
1914	Kendall isolates thyroxin, what he believes to be the active constituent of the thyroid gland, in crystalline form
1918	Herman Zondek publishes his studies of the heart in myxoedema
1926	Harington determines the chemical structure of thyroxine, correcting Kendall's thyroxin.
1927	Harington and Barger synthesize thyroxine. While Kendall makes 33 grams out of three tons of glands, they make roughly 88 grams out of the equivalent amount.
1938	Thyroid USP (and tacitly thyroxine) grandfathered in under 1938 Food, Drug and Cosmetic Act
1942	Marmola, an anti-fat medication that contains THT, is tried and receives a cease and desist order from the FDA
1949	Commercial synthesis of laevo-thyroxine (l-thyroxine) is achieved by a group of chemists from Glaxo Labs. They draw on the work of chemists with Quaker Oats, Inc and the American Dairy Association, who have synthesized a constituent that increases milk production in dairy cows.
1953	John Gross and Rosalind Pitt-Rivers isolate triiodothyronine (T3) from the thyroid gland and synthesize it (lio-thyronine); Pitt-Rivers works under Charles Robert Harington, who synthesized thyroxine in 1926.
1961	MacGregor publishes his editorial "Why Does Anyone Use Thyroid BP?"
1962-1969	DESI (Drug Efficacy Study Implementation) conducted on all drugs introduced between 1938 and 1962. Desiccated thyroid/synthetic thyroid are not studied.
1970	L. Baverman, S. Ingbar and K. Sterling discover T4 to T3 conversion.
1970	RN Smith conducts his the first randomized clinical trial on THT.

1997	Synthroid and other synthetic THT asked to apply for NDA (New Drug Application), as they have been found to have variable potency.
2001	Synthroid found by FDA to not be GRAS/GRAE (generally recognized as safe/effective)
2009-2010	Unexplained shortage on desiccated THT

Appendix B: Citations for Figures

Figure I.1: [public domain] United States National Institute of Health, *SEER Training Modules*, "Endocrine Glands & Their Hormones," http://training.seer.cancer.gov/anatomy/endocrine/glands/ (accessed Mar 2, 2011). Works by the US government are not eligible for US copyright protection.

Figure II.2: [public domain] Raven, Thos. F. "Sailor's Widow Before and After Treatment," in "Myxoedema Treated With Thyroid Tablets," *British Medical Journal*, 1 no. 1723 (Jan 1894): 12. [This work was created before 1923; it is also included in the Memoranda section, which is does not retain permissions.]

Figure III.1: [fair use] Steven Kaufman et al., "Thyroid Hormone Use," *Thyroid*, 1 (1991): 286. Fair Use Documentation Attached.

Figure III.2: [public domain] Kendall, Edward. "Fig. 2. The tanks in which 6,300 pounds of hog thyroid glands were treated for the isolation of thyroxin." in "Isolation of the Iodine Compound which Occurs in the Thyroid," *Journal of Biological Chemistry*, [1919]: 136. [This work was created before 1923, and no copyright was attached.]

Figure III.3: [fair use] Kendall, Edward. "Crystals of the iodin-containing compound which occurs in the thyroid." In "The Isolation in Crystalline Form of the Compound Containing Iodin, which Occurs in the Thyroid," *Journal of the American Medical Association* 64, no. 25 (1915): 2042. Fair Use determination attached.

Figure III.4: [fair use] Warner-Chilcott Labs, "Predictable Thyroid" series, *Journal of Clinical Endocrinology and Metabolism*, (1953-6). Fair use determination attached.

Figure III.5: [fair use] Warner-Chilcott Labs, "in every species" and "sisters under the skin." Advertisements. *Journal of Clinical Endocrinology and Metabolism*, (1953-6). Fair Use determination attached.

Figure III.6: [fair use] Warner-Chilcott Labs. "This animal gland" Advertisements, *Journal of the Americal Medical Association*, (April 1965). Fair Use determination attached.

Figure IV.1: [fair use] Save Natural Thyroid, Campaign banner. http://www.savenaturalthyroid.com (accessed: Nov 2, 2010). Fair Use determination attached.

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