# Perspectives on the Experimentation of Udo J. Wile: Insights into the Past and Considerations for Today

By Emily Vogel

## I. INTRODUCTION

Michael J. Franzblau, a 1952 University of Michigan alumnus, wrote and submitted a letter to *Medicine at Michigan,* a publication of the University of Michigan Medical School. The letter was published in the Summer 2002 edition under the title of "The Legacy of Udo Wile." It was accompanied by a response co-written by three of the school's most prominent figures, most notably Dean of the Medical School, Allen S. Lichter. In his letter, Franzblau revisited the "ethical cloud over the head of Udo Wile"[1] and questioned whether "it is reasonable, in view of his unethical experiments, even by 1916 standards, to honor Udo Wile?"[2] The very nature of Franzblau's question illustrates the mysterious "ethical cloud" shrouding Wile and his work. There is no simple answer to Franzblau's question, and any answer attempted is a subjective one. Therefore, it is important to investigate Wile's ethically disturbing experiment and to explore why, in today's retrospective discussions, the name Udo J. Wile is so entrenched with ethical misgivings.

Wile was one of the University of Michigan Medical School's most promising doctors. A specialist in both dermatology and syphilology, he was particularly interested in the promising future of syphilis research.[3] Wile conducted an experiment to investigate

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[1] Franzblau, Michael J. "The Legacy of Udo Wile." *Medicine at Michigan: A* Publication of the University of Michigan Medical School. Summer 2002, p.4.

[2] Ibid., p.5.

[3] Lederer, Susan E. Subjected to Science: Human Experimentation in America Before the Second World War. Baltimore: The Johns Hopkins University Press, 1995.

the viability of live spirochetes isolated from the brains of living syphilitic patients. His 1916 publication in the *Journal of Experimental Medicine* did not earn him the expected praise. Instead, the rest of the medical research community scolded him. Antivivisectionists[4] used him as an example of poor judgment and abuse of trust. City newspapers published the public's fiery opinions. Eighty-six years after the publication, Franzblau's letter is a testament to the continuing controversy.

A full understanding of Wile's experiment must consider what happened in the 1916 laboratory, newspapers, and scientific literature. The experiment is simple and straightforward. The reactions of his colleagues and adversaries speak for themselves. In reconciling the opposing opinions with each other and with the facts of the experiment, a conflict of ethical values and a historic battle between medical research and antivivisectionist interest emerge. Instead of questioning the ethical soundness of Wile's experiment, it is more valuable to ask what his experiment taught people in 1916 and continues to teach the scientific community and bioethicists in 2006.

Wile's experiment offers three insights. His experiment initiated the American Medical Association's effort to incorporate a research specific clause into its code of conduct, *The Principles of Medical Ethics.* Secondly, the fact that Wile's experiment was even conceived of is telling of the success-driven atmosphere of the early twentieth century research community. Finally, the experiment is a solid piece of scientific investigation and speaks to the effectiveness of the scientific method. While the ethical battle surrounding Udo J. Wile's 1916 experiment still rages, condemning the scientist

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p.95.

[4] Antivivisectionists were opponents of vivisection, the act of cutting into or otherwise injuring live animals, particularly for scientific research.

and his work tends to overshadow any lessons that can be learned from the past and impedes the progress of historically rounded scientific debate.

## II. THE EXPERIMENT

Udo Julius Wile, a professor of syphilology[5] and dermatology at the University of Michigan Medical School, published in the *Journal of Experimental Medicine* in February of 1916.[6] Wile's study, titled "Experimental Syphilis in the Rabbit Produced by the Brain Substance of the Living Paretic," was a follow up to the work of Edmund Forster and Egon Tomasczewski. Wile had previously worked with these two German researchers and was first author on their 1913 paper published in the *Journal of the American Medical Association*. The paper, "The Demonstration of the *Spriochaeta pallida*[7] in the Brain Substance of Living Paretics," marked a breakthrough in syphilitic studies.[8] Motivated by the renewed promise of effective antisyphilitic therapy specifically targeted at the newly localized live parasites, Wile continued Forster and Tomasczewski's work.[9]

In accordance with the germ theory of disease of the time, successfully infecting an animal with the serum of an infected person would satisfactorily identify the disease causing agent as being in the transferred fluid.[10] Additionally, the infected animal would serve as a model organism for further experiments and therapeutic research. Wile's work

[5] Syphilology is the study of syphilis.
[6] 4. Lederer, 1995, p.95.
[7] *Spriochaeta pallida* is the causative organism of syphilis.
[8] Udo J. Wile, "The Demonstration of the *Spirochaeta pallida* in the Brain Substance of Liing Paretics (Forster and Tomasczewski)," *JAMA*, 1913, *61*, p.866.
[9] Lederer, 1995, p.95.
[10] De Kruif, Paul. Gonzalez-Crussi, F. Microbe Hunters. Orlando: Harcourt, Inc., 1926.

demonstrated what Forster and Tomasczewski's work was unable to: that rabbits infected with the isolated cortical matter from live syphilis patients displayed symptoms of syphilis themselves.[11] In order to appreciate the debate that followed the experiment's publication, one must understand the methodology of Wile's work.

Wile selected six clinically insane patients housed in Michigan's Pontiac State Hospital as the sources of the live *Spriochaeta pallida.* Positive Wasserman reactions verified their syphilitic condition.[12] Wile obtained the parasitic matter using Forster and Tomasczewski's method, "a modification of the Neisser-Pollak trephining operation."[13] Procuring the sample involved accessing the patients' brain and cerebral spinal fluid, which he did after cleaning and anesthetizing the site. The desired area was trephined[14] and a needle and syringe appliance was used to remove a small portion of white and gray matter and ventricular fluid[15]. Wile studied the samples via dark-field microscopy and confirmed the presence of live spirochetes.[16]

Wile then transferred the spirochetes from Petri dishes to the testes of a single rabbit. Within two weeks, the infected rabbit displayed syphilitic symptoms. Upon aspirating the rabbit's syphilitic nodules, Wile was delighted to find live spirochetes in the sample. Injecting samples of the first rabbit's parasites into the testes of a second rabbit, Wile successfully transferred the disease and again confirmed the presence of live

[11] "Experimental Syphilis in the Rabbit Produced by the Brain Substance of the Living Paretic," *J. Exp. Med*, 1916, p.199-202.
[12] Lederer, 1995, p.95
[13] Wile, 1916, p.199.
[14] To trephine is to operate using a trephine instrument, which is a small saw used with the intention of removing disks of skull.
[15] Ventricular fluid is the cerebral spinal fluid which bathes, provides nutrients to, and protects the brain.
[16] A spirochete is a motile bacteria causing syphilis.

spirochetes, this time within the second rabbit. He conducted several more 'generations' of infection and verification, all of which yielded similar results.[17]

The experiment was a success. Not only did Wile demonstrate that *Spirochaeta pallida* was indeed the disease causing agent of syphilis but he also created an animal model of the disease upon which to test future hypotheses and therapies. Furthermore, Wile observed: "The spirochaetes in these experiments differ in morphology from those ordinarily seen in mucous and cutaneous lesions[18]. They were similar to those described by Nichols" which "seem to indicate the existence of a neurotropic strain of spirochaetes."[19] This central nervous system-localized neurotropic strain was novel, even according to Henry J. Nichols. Nichols, a member of the Department of Pathology at the Army Medical School in Washington, affirmed that "no [other] observations have been made on a similar strain."[20]

The success of the experiment would soon be clouded by controversy. The experiment raised questions and concerns regarding the use of human subjects in non-therapeutic studies, consent of incapacitated and vulnerable parties, and the boundaries of researching doctors. Throughout the public ordeal, Wile steadfastly supported his work and stated: "You may quote me as having absolutely no interest in the matter…[of] whatever people may wish to think regarding the experiment."[21] For many of Wile's adversaries, his use of hospitalized patients was objectionable. Yet how Wile obtained his

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[17] Wile, 1916, p.201.

[18] Mucus and cutaneous lesions refer to the somatic locations from which spirochetes had previously been isolated. This is in contrast to the spirochetes Wile isolated in the central nervous system, which refers to the brain and spinal cord.

[19] Wile, 1916, p.201.

[20] Henry J. Nichols, "Observations on a Strain of *Spirochaeta Pallida* Isolated from the Nervous System," *J. Exp. Med,* 1914, p.362-371.

[21] Quoted in "Human Vivisection- the Betrayal of a Sacred Trust," *Our Dumb Animals*, 1916, *49*, 34. [cited in Lederer, 1995, p.96.]

subjects is significant in assigning blameworthiness. Wile thanked Dr. Edmund A. Christian, medical superintendent of the general paralysis patients of Pontiac State Hospital,[22] for the "facilities that he placed at my [Wile's] disposal."[23] Christian did not deny his role in the experiment and was quoted in the *Chicago Daily Tribune* explaining, "The consent of the guardians or relatives of the patients was not secured, as it was not necessary. Paresis was inevitably killing the patients anyway, and the operations did not retard or hasten the course of the disease."[24] Christian and Wile's use of incapacitated subjects without secured consent erupted in controversy.

## III. THE RESPONSE TO WILE'S PAPER

Wile's 1916 publication was not met with praise but was recognized as a "regrettable lapse of judgment."[25] The voices of Wile's quiet defenders are rarely remembered and the notably adverse reactors to the experiment instead obscure the historical image and reputation of Wile and his work. To understand Wile's experiment and legacy, it is behooving to learn of, and furthermore to understand, the strong and vocal reactions of the medical research community, the antivivisectionists, and the American people. In doing so, one must be wary of allowing the visceral language of the detractors to obscure the science and the central controversial issue. To illustrate this point, perhaps a comparable and recently familiar event was the 1997 announcement that Dr. Ian Wilmut and the Roslin Institute of Edinburgh, Scotland had cloned the first mammal, Dolly the sheep. The story was objected to, misconstrued, and fretted over by

[22] "Vivisection on Human Beings," *Chicago Daily Tribune*, 12 Apr. 1916.
[23] Wile, 1916 p.202.
[24] Chicago Daily Tribune.
[25] Lederer, 1995, p.96.

the press, animal rights activists, religious figures, scientists and citizens alike. Yet at the root of both Wilmut and Wile's work was a single, logical experiment based upon the widely accepted scientific method.

The medical research community of the early twentieth century was, as it is today, associated with the forward movement of technology and knowledge acquisition. Wile's experiment threw a hiccup into this progression. While research did not cease altogether, the publication threatened the certainty of its future and the pace of its progress, and outspoken representatives of this professional community reacted accordingly. As referenced earlier, the Rockefeller Institute, the very publishers of the *Journal of Experimental Medicine*, "considered [the paper's publication] a regrettable lapse of judgment."[26] So regrettable that Simon Flexner, the journal's editor and previously outspoken voice on the AMA's Council on Defense of Medical Research,[27] essentially washed his hands of the Wile fiasco and skirted responsibility for the paper's publication. Recognizing the enormity of the situation they instigated, Henry James, Jr., the Institute's business mind, emerged as the leader of their response, or lack thereof, and ordered that no representative from Rockefeller issue any comment.[28]

Embarrassed as the research community was, Walter Bradford Cannon boldly addressed the situation in hopes of salvaging the reputation of American medical research. As chairperson of the AMA's Council on the Defense of Medical Research, Cannon was no stranger to controversy and devoted much of his career to defending researching physicians against the fierce attacks of the antivivisectionists.[29] In

[26] Lederer, 1995, p.96.
[27] Lederer, 1995, p.78.
[28] Lederer, 1995, p.97.
[29] Lederer, 1995, p.92.

considering the appropriate response, James recognized that the future of research might come at the price of sacrificing the bright successful scientist and accordingly advised Cannon, "It is surely more important for you to maintain your position correctly, than it is to hush up the attacks on Wile…Nothing could be more fatal to the defense of research in the long run than an unvarying, thick-and-thin defense by you and others of all doctors attacked by the press."[30]

Cannon chose to issue an advisory statement in the *Journal of the American Medical Association* which openly outlined proper, and admonished improper, use of human subjects in experimental studies.[31] Although Cannon's response respectfully omitted the incriminating name of Udo J. Wile, the timeliness of its publication was as discrete as the twenty two unreferenced ethically questionable case studies examined in Henry Beecher's 1966 article "Ethics and Clinical Research."[32] In addition to his public address in *JAMA*, Cannon sent a chiding letter to Wile and the Dean of the University of Michigan Medical School, Victor C. Vaughan. The letter attacked both the ethical unsoundness of the experiment and Wile's nonchalant attitude toward the study's repercussions. Cannon charged Wile of jeopardizing "the freedom of research which had been enjoyed in this country up to this time – a freedom which has had important values for the progress of medicine."[33] William Williams Keen, past president of the AMA,

[30] Henry James, Jr., to Walter Bradford Cannon, 24 Apr. 1916, W.W. Keen Papers, American Philosophical Society, library, Philadelphia. [cited in Lederer, 1995, p.97.]

[31] Lederer, 1995, p.97.

[32] Henry K. Beecher, "Ethics and Clinical Rsearch," *New England Journal of Medicine,* 1966, *274(24)*, p.1354-1360. Beecher's publication is often considered to mark the birth of bioethics and publications on ethical research. His paper highlighted and discussed many studies which practiced questionable ethics.

[33] Copy of letter sent to Udo J. Wile also sent to Victor C. Vaughan, 27 Apr. 1916, Victor C. Vaughan Papers, Michigan Historical Collection. [cited in Lederer, 1995, p.97.]

"insisted that Wile's case demanded explicit condemnation."[34] Keen issued his own personal statement on the issue which was published in the same volume of *JAMA* as Cannon's. Together the articles were a forceful and reproving response to Wile's non-therapeutic human subject research.

In addition to the guidelines published in *JAMA* and Wile's private chastisement, Cannon advised amending the AMA's Code of Ethics to "explicitly address the use of human subjects in research." While not the first revision since its institution in 1847, a revision motivated by a single publication is demonstrative of the paper's far reaching consequences.[35] It furthermore speaks to the severity of the threat the scientific community was experiencing in the wake of Wile's work.

Given that two of the medical profession's most well-respected public figures personally involved themselves in the unified response to Wile's paper, the medical community must have felt that the future of research was in serious jeopardy. The threat was coming from the horrified reactions of the antivivisectionists. Just four years prior to news of Wile's experiment, the antivivisectionists issued an anticipatory pamphlet "warning about the dangers that unregulated experimentation posed for an unsuspecting public." While the pamphlets of 1912 merely posed the question, "Are the helpless people in our hospitals and asylums to be treated as so much material for scientific experimentation, irrespective of age or consent?",[36] the Vivisection Investigation League's pamphlets of 1916 were unrelenting and charged, "how far this use of patients

[34] William Williams Keen to Henry James, Jr., 29 Apr. 1916, Antivivisection Files, Rockefeller University Archives, North Tarrytown, New York. [cited in Lederer, 1995, p.97.]
[35] Lederer, 1995, p.97.
[36] *Human Vivisection* (New York Anti-Vivisection Society, n.d.); *What Vivisection Inevitably Leads To* (Vivisection Investigation League, n.d.). [cited in Lederer, 1995, p.83.]

in our hospitals for purely experimental purposes will extend before public feeling is sufficiently aroused to take action?"[37] The antivivisection response was evinced not only by their words and publications, but also by the defensive reaction of the medical community. Cannon's 1914 memorandum to journal editors requesting "that original papers submitted…be edited to eliminate expressions that could be misunderstood by antivivisectionists" is evidence that the antivivisectionists were maintaining a watchful and unforgiving eye.[38] Additionally, Keen's official written response underwent several purposeful revisions before publication to explicitly avoid attack from the antivivisectionists.[39]

A tribute to the antivivisectionist response and the effectiveness of their effort is the amount of negative press coverage Wile's experiment received.[40] Not yet having access to the Internet and the conveniences of Pub Med, the biased antivivisectionist pamphlets were a significant source of information available to interested people. In fact, the "editors of one Charleston newspaper apparently believed that Wile had abstracted the entire brain contents of the six insane patients upon whom he had operated."[41] While several newspapers did admonish Wile's actions there were also those that defended his work.

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[37] *Human Beings Vivisected* (New York: Vivisection Investigation League, 1916), p.4. [cited in Lederer, 1995, p.96.]

[38] "Report of the Committee on the Protection of Medical Research," *Jama*, 1914, *63*, 94. [cited in Lederer, 1995, p.94.]

[39] W.W. Keen, "The Inveracities of Antivivisection," *JAMA*, 1916, *67*, 1390-91. William Williams Keen to Victor C. Vaughan, 15 June 1916; and Vaughan to Keen, 25 Apr. 1916, Victor C. Vaughan Papers, Michigan Historical Collection. [cited in Lederer, 1995, p.99.]

[40] Susan E. Lederer, "The Right and Wrong of Making Experiments on Human Beings": Udo J. Wile and Syphilis, *Bulletin of the History of Medicine*, Fall 1984, *58:3*, p.388.

[41] Lederer, 1984, p.388.

The *Detroit News* ran a column titled "Silly Uproar" which introduced the study's circumstances by claiming, "An attempt has been made to stir up a scandal." The column emphasized that only "minute portions of matter" were withdrawn from the subjects' brains, as was customary in other "skillfully done" experiments. Furthermore, the *Detroit News* considered the pain inflicted upon Wile's subjects "not as painful, as drawing off specimens of blood…and no one thinks of complaining [of a blood test]." The column doubted that any other researcher would refuse to do this work and claimed such a researcher would even "permit much more extensive probings into his own brain" should such an imminent cure be at hand. With a final jab at antivivisectionist objections, the column ended professing that if the University of Michigan's researchers "discover a method of arresting paresis…they will feel fully repaid for all the censure that may be launched against them by the ignorant."[42]

While the *Detroit News* defended the work and circumstances of Wile's experiment, the *Chicago Daily Tribune* presented a different perspective, and chose to emphasize the cruelty of the "ordinary dental drill" which "bored holes into the brains of six living people." The column took a disparaging stance against the whole medical community, against Wile's "colleagues [who were] rallying to his support" and "physicians [who] consider[ed] the act of entering a hospital for treatment implied assent to any experiments." The column also incited its readers by stating that future disease research may present the need to "have to experiment with a child" so as to "be able to study the disease as we please", and in doing so it may be necessary "to allow another to contract the disease."[43]

[42] "Silly Uproar," *Detroit News,* 13 Apr. 1916.
[43] *Chicago Daily Tribune.*

Examining the public's response to Wile's paper presents a new take on the study, specifically as it pertains to syphilis. To many traditionally conservative Americans, experimentation and open discussion of syphilis was representative of a new and more liberal age. Previously considered a "conspiracy of silence," syphilis was a "venereal disease [that] for many Americans remained a divine punishment for sins of the flesh."[44] While a regrettable disease to contract, it was a scarlet letter of shame. Therefore, in addition to considering the human rights issue involving "concerns about doing harm in the hope of helping someone avert a worse disease", some public sectors were also contending with the idea that syphilis was a disease that should remain an untouchable marker of sin.[45]

While the medical research community and the antivivisectionists each responded to Wile's experiment with boldly united fronts, the newspapers suggested a divided public, torn between defending altruistic research, defending themselves from vicious attacks of ruthless doctors, and defending a collapsing moral value of American society.

## IV. THE RESPONSE TO WILE'S PAPER-JUSTIFIED & CONTEXTUALIZED

The previous section of this paper identified and separated the reactions of three categories of significant players in the Udo Wile controversy. The next step in understanding Wile's experiment and its repercussions is contextualization and rationalization of these reactions. While exploring motivations behind each significant adverse reaction, it becomes apparent that no two reactions were motivated by the same factor. This suggests that not a single aspect of Wile's paper was morally or ethically

[44] Lederer, 1995, p.83.
[45] Lederer, 1995, p.83.

objectionable, and instead that the timing of the experiment was what prompted the magnitude of negative response.

As previously noted, Udo Wile's colleagues were not concerned with preserving his career and reputation. Protecting years of research and guaranteeing its place in the future was of higher priority than protecting the man who nearly destroyed it all. The idea that Walter Cannon's reaction was motivated by personal anger is not as outlandish as it may seem. Before Wile's paper was published, Cannon had "confronted the issue of human vivisection in a series of pamphlets organized to educate physicians about the benefits of animal experimentation."[46] He personally "monitored incidents that could be used against the medical profession for the purpose of curtailing laboratory freedom."[47] His proactive effort to thwart controversial human subject research proved ineffective when Wile's paper made it to press. The young researcher's work was an insult to a seasoned AMA advisor's career's worth of work. This idea that Wile's actions personally embarrassed and insulted Cannon's pride justifies the admonishing letter he sent to Wile. That Flexner's journal did not heed Cannon's earlier advice cautioning editors against publishing potentially offensive and treacherous wording further incited him. "In any case of diagnosis or treatment when the procedure is novel or might be objected to," Cannon suggested editors "let the fact be stated that the patient or his family were fully aware of and consented to the plan."[48]

While Cannon may have reacted out of personal embarrassment, the Rockefeller Institute of Medical Research may have been motivated to keep a tight lip based on fear

[46] Lederer, 1995, p.92.
[47] Lederer, 1995, p.93.
[48] "Report of the Committee on the Protection of Medical Research," *JAMA*, 1914, *63*, 94. [cited in Lederer, 1995, p.94.]

of having exhausted the public's good graces on previously waged and won battles. The years between 1896 and 1911 were most trying for the medical research field. Its leaders successfully defended its reputation from the imminent risk of federal and legislative involvement and waged a verbal and printed war on the relentless, yet justifiably concerned, antivivisectionists. When situations arose that questioned the ethical principles of researchers, the blanket statement issued was that "the abuse of patients in scientific research was rare."[49] When Johns Hopkins' William Osler defended the reputation of medical research in light of Henry J Berkley's 1897 thyroid extract experiment, Osler "condemned improper experimentation on patients" and "insisted that the medical profession absolutely opposed non-therapeutic experiments on patients."[50] While research and medical leaders could have confronted the issue or taken responsibility for the past and for a change in the future, they instead sought to "deflect allegations of human vivisection and to dismiss legislative efforts to establish protections for human subjects…Leaders of the profession believed, however, that both patient interests and professional concerns would be best served by preserving free access to animals for medical research."[51]

When the story of Wile's experiment broke, the medical research field had just controlled the damage resulting from Hideyo Noguchi's 1911 luetin experiments.[52] Cannon had tried to start over and "recommended that colleagues exercise good judgment in reporting the results of human experiments."[53] Preceding the Noguchi experiment,

[49] Lederer, 1995, p.51.
[50] Lederer, 1995, p.63.
[51] Lederer, 1995, p.52.
[52] Lederer, 1995, p.82.
[53] "A Caution to Medical Writers," *JAMA*, 1901, *37*, 1120. [cited in Lederer, 1995, p.94.]

researchers had narrowly escaped the consequences of proposed Senate Bill 3424, "for the regulation of human experimentation in the District of Columbia." If the bill was passed, an "investigator's purpose and procedures in any *nontherapeutic* experiment on human beings, as well as the written consent of the subjects" would need to be secured beforehand.[54] William Williams Keen, then president of the AMA, made a "private appeal" to Senator Jacob H. Gallinger of New Hampshire to avert disaster. Keen vowed "the moral sense of the profession may well be relied upon to prevent any extension of such an objectionable method without any law to restrain it."[55] Evidently, the research leader's motive was not the preservation of the ethical soundness of their research. Instead it was to hold on to public confidence and to the liberties that practitioners and researchers enjoyed in their daily work. Clearly, Wile's work jeopardized this vision and therefore received a reproachful response.

While the doctors were reacting to Wile's experiment out of shame and fear, the antivivisectionists were reacting out of rage from past wrongdoings and years of unappreciated foresight. Year after year their efforts for legislative protection were thwarted by lying doctors who maneuvered themselves out of claiming responsibility and upholding ethical standards. Wile's non-therapeutic research not only used humans but also rabbits. According to the antivivisectionists, the unethical use of both subjects could have been avoided had Michigan Senator James MacMillan's Cruelty to Animals Bill of 1895 ever come to a vote.[56] The antivivisectionists again threw their support behind a 1913 bill introduced in Pennsylvania. "Its purpose was to prevent physicians from

[54] Lederer, 1995, p.71
[55] William W. Keen to Senator Gallinger, 21 Mar. 1900, Keen Papers, College of Physicians of Philadelphia, library. [cited in Lederer, 1995, p.72.]
[56] Lederer, 1995, p.57.

making experiments, procedures that had nothing to do with the patients' treatment."[57] However, a group of testifying physicians soiled antivivisectionist success yet again.

To appreciate the perspective of the American people's response to Wile's experiment, it is again important to consider their sources of information. Inflammatory catch phrases such as scientific "torture houses" and "halls of agony", from biased antivivisectionist pamphlets altered readers' perspectives.[58] Aside from inserted commentary, antivivisectionists committed "literary forgeries."[59] Keen claimed the authors of these pamphlets "simply select those sentences which, to a diseased imagination savor the sensational, deliberately omitting the setting of the sentences quoted, and then publish these statements with innumerable additions, exaggerations, and material of their own manufacture."[60] In addition to pamphlets, people often look to newspapers as resources. There is simply a different language and level of depth addressed in newspapers as opposed to scientific journals. Trying to explain the complexities of syphilis research to a broad range of people in one column is nearly impossible to do without misconstruing some factual information and would rarely be written about if the author did not have an agenda in the debate. In the past, the Darwinian theory of evolution had been so improperly communicated that one writer, thinking that the theory only applied the development of humans, claimed "No sufficient analogies exist in the animal kingdom from which to draw useful conclusions."[61] It is

[57] Lederer, 1995, p.87.
[58] W. W. Keen, "Influence of Antivivisection on Character," *Boston Med. Surg. J.*, 1912, *166*, p.653. [cited in Lederer, 1995, p.64.]
[59] Lederer, 1995, p.65.
[60] Wilcox, "The Anti-Vivisection Agitation,' p.787. [cited in Lederer, 1995, p.64.]
[61] Quoted in E. V. Wilcox, "The Anti-Vivisection Agitation," *J. Comp. Med. & Vet. Arch.*, 1898, *19*, p.792. [cited in Lederer, 1995, p.59.]

therefore not difficult to reason why the American public was divided over Wile's experiment and confused all together.

## V. CONSIDERATIONS FOR TODAY

In today's acronym dominated research world of PCRs, RAIs, and induced GFP tagged SDM, it is easy and even laughable to reflect seriously on the once revolutionary germ theory of disease and its requisite rudimentary laboratory setups. Research has entered a whole new league, one of strict Institutional Review Board regulations, limited and competitive National Institute of Health funding, and politically driven competition. Such remarkable changes have taken place since 1916 that one can assuredly reflect on Wile's work and confidently proclaim "that'll never happen again here." It is equally easy to understand how the responses of the past seem so dissociated from and incomparable to, the relevant issues of today. Medical research is now a cherished and safeguarded institution. What marks the time between 1916 and 2006 are small pockets of progress initiated by research procedures and results, and acted upon by those who genuinely valued human life and fully believed in the promising future of research. Udo J. Wile was a researcher whose work started such a movement. Regardless of whether Wile cared or was even conscious of the change in which he was a part, that he instigated it is indisputable. With this in mind, it is equally challenging to affirm that Wile's "dental drill" experiment was a valuable contribution to medical research, as it is to ignore the unethical work entirely. However, as with most historical situations, it can be said with confidence that there is a lesson to be learned. Wile's experiment and legacy contributed to both the content of medical research and the progress of the entire

researching field. His experiment was the driving force behind the implementation of a human subject protection clause in the AMA's *The Principles of Medical Ethics* and is also the link to understanding how the atmosphere of his professional field could have ever given rise to his use of human subjects. Finally, Wile is a testament to the effectiveness of research and the scientific method.

In conducting his non-therapeutic human subject experiment, Wile was not in violation of any AMA codes. Introduced in 1847, the first AMA *Code of Ethics* made no mention of rights and responsibilities surrounding human subject research. The *Code* instead outlined physicians' duties to bedside patients, to each other, and to the honor of the profession.[62] More a physician's code than a protection of human rights, it supposed "every duty or obligation implies, both in equity and for its successful discharge, a corresponding right" and declared:

> "that the physician… in whose judgment and discretion under Providence, life is secured and death turned aside- should be allowed free use of his faculties, undisturbed by a querulous manner, and desponding, angry, or passionate interjections, under the plea of fear, or grief, or disappointment of cherished hopes, by the sick and their friends."[63]

While two minor amendments were made to the *Code* between its implementation and Wile's experiment, most notable of which was the document's 1903 name change to *The Principles of Medical Ethics*, it remained free of any research guidelines.[64] Walter Cannon's 1916 suggestion to revise the AMA's *Principles* was one which implied more

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[62] "AMA History," American Medical Association, 1995-2006. **www.ama.assn.org/ama/pub/category/1854.html.** Accessed 19, Apr. 2006.

[63] "Code of Medical Ethics of the American Medical Association: Originally Adopted at the Adjourned Meeting of the National Medical Convention in Philadelphia." Chicago: American Medical Association Press, May 1847. p.84.

[64] "AMA History," website.

than a simple rephrasing of the existing text. His formal change would professionally address medical research and the physician's role and responsibility to patients. The suggestion was hotly contended and was met both with supporters and objectors,. Henry James, Jr. articulated the most pressing issue raised, that of "where to draw the line between unjustifiable experiments on human beings and those procedures that, although unrelated to an individual's treatment, contributed significantly to clinical research."[65]

The significance of the AMA's suggested restructuring as it pertains to this paper is that Wile and his experiment were the driving forces behind the ethically motivated change. The leaders of medicine were addressing important and difficult questions regarding the future of advanced scientific work as they realized the research field was not a static one and that the 1847 rules would no longer suffice. Cannon's suggestions pertaining to the "obligations of a researcher to a subject" were not officially incorporated into the AMA's *Principles* until 1946, but the history of the revision dates back to 1916 and Udo J. Wile's experiment.[66]

The second lesson that can be gleaned from Wile's work is a lesson on community responsibility. Shifting perspective from Wile in order to assess other, often disregarded, ethical deviations will demonstrate two things: first, Wile was made a scapegoat for an entire researching field and second, although it was ardently disputed, Wile's experiment was in good company. Even in his own study, Wile was not a lone conspirator, others were instrumental in the logistics of his experiment and also indirectly involved in the permissive circumstances of his experiment. Recognizing greater participation and responsibility does not atone for the wrongs committed, but rather

[65] Lederer, 1995, p.98.
[66] Lederer, 1995, p.98.

contextualizes the experiment within a community permissive of ethically questionable behavior.

Although the only author of the 1916 publication, Wile was not the sole person involved in the experiment's execution. While he may have been responsible for collecting data, several parties contributed to the other aspects of the study. As a relatively new member of the University of Michigan Medical School faculty, Wile would have had to answer to an authority figure. Someone at Michigan must have known the nature of his project, even if just to oversee the channeling of funding. Victor Vaughan, Dean of the Medical School, may have been one such figure, as he was a strong defender of Wile's work.[67] Secondly, Dr. Edmund A. Christian's cooperation in securing the patients and justifying a lack of consent was a crucial factor in the experiment's setup.[68] Furthermore, Wile himself even thanked Dr. Frederick Novy and Mr. Paul de Kruif "for many laboratory courtesies extended" to him.[69]

The players involved in the permissive circumstances of Wile's publication are more telling of the research community's atmosphere in 1916. Just five years prior was a tremendous precedent setting experiment, that of Hideyo Noguchi in 1911. With the sponsorship of the Rockefeller Institute for Medical Research and "with the aid of fifteen physicians…Noguchi obtained four hundred subjects" upon which to test luetin's effectiveness as a syphilitic diagnostic agent.[70] Although Noguchi's work drew criticism, "For the most part, antivivisectionists directed little criticism at the Japanese physician

[67] Medicine at Michigan, 2002, p.6.
[68] *Chicago Daily Tribune.*
[69] Wile, 1916, p.202
[70] Lederer, 1995, p.82.

himself."[71] Henry James, Jr., representing the interests of the Rockefeller Institute, affirmed: "Noguchi would not be held liable for the experiments."[72] While not denying some severe repercussions Noguchi experienced, his debauched experiment was essentially excused by the community thereby setting a precedent of ethically questionable practices.

Further contributing to the permissive circumstances was the failure of the peer review system. Without so much as a raised eyebrow, Forster and Tomaczewski's work was published in America in 1913.[73] Editors review journal submissions carefully; had Forster and Tomaczewski's work been ethically upsetting, *JAMA* should not have published it. Moreover, if the research community were sincerely passionate about upholding the highest standards of ethical practices, they would have noted this value in the earliest versions of the AMA's *Code of Ethics/Principles of Medical Ethics*. Given that Cannon's 1916 recommendation "introducing a requirement that physicians obtain explicit permission for research struck investigators as not only unnecessary but potentially damaging to the entire research enterprise,"[74] suggests that researchers preferred the "ambiguous ethical and legal status of human experimentation during the period."[75] This ambiguous status would allow circumstances to be distorted as necessary, such as editing "original papers submitted for publication…to eliminate expressions that could be misunderstood by antivivisectionists and the public."[76] The suggested selective editing came from Cannon, and is a practice excusing of ethical misconduct. Such

[71] Lederer, 1995, p.84.
[72] Lederer, 1995, p.92.

[73] Wile, 1913.
[74] Lederer, 1995, p.100.
[75] Lederer, 1995, p.90.
[76] Lederer, 1995, p.94.

factors all contributed to the success oriented, ethically questionable atmosphere surrounding medical research in the early twentieth century. There were many guilty players who nurtured a research field ripe for Wile's experiment.

Exploring different guilty parties and trying to distribute blameworthiness distracts focus from the experiment itself. When the debates of morality and judgment are temporarily set aside, Wile's experiment is a testimony to the scientific method and a shining example of scholarly excellence. What is today's casually transmitted and easily treated venereal disease was the early twentieth century's "public health disaster," infecting between ten and fifteen percent of the United States' population.[77] Before the 1928 discovery of penicillin, there were frantic research efforts to find the causative agent of syphilis. Noguchi's 1913 discovery of the "long suspected…organic link between paresis and somatic syphilis" was a great discovery in its time.[78] An active syphilis researcher, Wile claimed "it is not too much to hope that the demonstration of the spirochete in cases in which the cortical centers are as yet not greatly involved…may be followed by an arrest of the course of the disease under appropriate treatment."[79]

Wile's 1916 curative therapy-motivated experiment was regarded as the next necessary step in syphilis research. According to colleague Henry J. Nichols,

> "If there is any special strain of pallida, the proper way to study it would seem to be to work back from the clinical condition to the experimental animal and to carry on the strain long enough to determine its peculiar characteristics." Nichols further explains, "Most of the work in

[77] Nicholas Jabbour, "Syphilis from 1880 to 1920: A Public Health Nightmare and the First Challenge to Medical Ethics," *Essays in History*, 2000, *42*. www.etext.virginia.edu/journals/EH/EH42/Jabbour42.html. Accessed 18, Apr. 2006.
[78] Lederer, 1984, p.384.
[79] Lederer, 1984, p.386.

> experimental syphilis has been carried out with strains isolated from chancres or mucous patches, and the clinical potentialities of these strains are entirely unknown."[80]

In addition to Wile's cutting edge research, his decision to use live patients was a thoughtful one. The explanation he offered suggests he both learned from past experiments and was cognizant of the limitations of current methods: "It seemed to me that the lack of success of previous observers might be due to the small number of organisms present [obtained from other methods]…Moreover, it seemed possible that the organisms from a living subject would be more likely to infect than those taken at autopsy."[81] Furthermore, Wile's work followed a pattern similar to the high standards used today: he minimized the number of human subjects used to only involve six, he minimized the pain induced as he applied local anesthetic, and he substituted animal models as soon as possible. Finally, in repeating the protocol of Forster and Tomasczewski's experiment, Wile demonstrated repeatability, one of the fundamental principles of credible scientific work. His results even improved the status of the data, demonstrating once again, he was a true scientist motivated by the altruistic and immediate idea of a curative treatment for one of the country's largest health concerns. Although his contemporary supporters were scarce, Matthew A. Reasoner, a practicing army doctor investigator of syphilis, published in *JAMA* in 1916 and recognized the legitimacy of Wile's work. He wrote, "It is desired to take this opportunity of expressing an appreciation of the great value of Dr. Wile's work along this particular line."[82]

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[80] Nichols, 1914, p.363.

[81] Wile, 1916, p.200.

[82] Lederer, 1984, p.396.

## VI. CONCLUSION

Wile's experiment clearly raises significant bioethical concerns. One of the most unsatisfying aspects of analyzing an ethical dispute is the elusiveness of a single correct answer. In light of such, this paper has explored Wile's experiment from the perspectives of 1916 medical research defenders, antivivisectionists, and American citizens of both the early twentieth and twenty-first centuries. This paper suggests that Wile's work is best served by exploring his contribution to the evolution of the AMA's *The Principles of Medical Ethics*, what his work says about the mentality of the early twentieth century research community, and how his work testifies to the effectiveness and practicality of the scientific method. The exploration of these historical insights therefore supplants the quest for that elusive, single answer.