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Mengele in America: Human Experimentation and the Walter Reed Connection

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ABSTRACT: Human experimentation performed on unsuspecting patients in the United States over a period of 70 years is reviewed. The pioneering heroism of Dr. Walter Reed and his associates have stood as a hallmark for ethical medical practice.

KEY WORDS: arachnoiditis, adhesive arachnoiditis, biosorb, BMP, cages, ethics, fusion, human experimentation, meningitis, myelography, myodil, Pantopaque, plutonium, Walter Reed

"Those who forget history are doomed to repeat it." —George Santayana

I. INTRODUCTION

The dark side of medicine was not just a unique phenomena that occurred only in Europe and Asia during the years of World War II involving the likes of aberrant physicians such as Josef Mengele (Auschwitz concentration camp), Shiro Ishii (Japanese Unit 731), Fukajiro Ishiyama (Kyushu University Imperial Hospital), Sigmund Rasher (Dachau concentration camp), and Hiroshi Iwanabi (Dublon Island, Truk). We now know that the United States also had its medical dark side during that period of time and that the shadow of this has re-emerged in the 21st century.

The "ethical standard" regarding human experimentation was set well before Nuremberg by the heroic legacy of Army Major Walter Reed (1845–1902) and his associates. Both the Walter Reed Army Medical Center and the newly created Walter Reed National Military Medical Center in Bethesda, Maryland, have rightfully honored the memory of this physician and his team, who postulated and then confirmed the theory that yellow fever was transmitted by a particular mosquitospecies rather than by direct contact with clothing or bedding soiled by bodily fluids (fomites).

During Major Reed's leadership of the U.S. Army Yellow Fever Commission in Cuba, this organization's pioneering work served as an important impetus in creating the emerging fields of epidemiology and biomedicine and were of great importance in allowing the resumption and successful completion of work on the Panama Canal (1904–1914) by the United States.[1]

The Yellow Fever Commission conducted many of its dramatic experiments at Camp Lazear, so named in November 1900 in honor of Major Reed's assistant and friend Dr. Jesse Lazear, who had suffered a martyr's death 2 months earlier from yellow

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fever as a direct consequence of his having volunteered himself as a human subject to be bitten by infected mosquitoes, along with his other colleagues. In addition to Dr. Lazer, a nurse, Clara Maass, also died from the results of her self-inflicted affliction.

In 1942, Army personnel being admitted to the Walter Reed Hospital in Bethesda, Maryland, and other military hospitals for disabling back and leg pain were the first individuals ever to undergo full-column lumbar myelography (6–12 cc) using a new radiographic oil ester dye which had been trademarked as "Pantopaque."2 Pantopaque, and its companion oil-based myelographic dye Myodil (used mainly in Europe), then were employed routinely on a continuing basis on many thousands of servicemen (and subsequently on many thousands of civilians) throughout the world. It has been estimated that at the height of its popularity, 450,000 Pantopaque myelograms were being performed in the United States each year (and an equal number of Myodil studies in other countries).

Initially, the use of Pantopaque (Fig. 1) was limited to small amounts (less than 3 cc) specifically for the purpose of locating spinal obstructions (i.e., spinal tumors) by introducing it into the cisterna magna at the base of the brain and allowing this hyperbaric substance to migrate down the spinal canal.

The first full-column use of large amounts of Pantopaque (usually approximately ≥12 cc) to identify lumbar herniated discs represented a quantum leap in its indications for use. Because Pantopaque was highly viscous—unlike subsequent water-soluble contrast agents—not infrequently it produced false-positive dye column defects (Fig. 2), which often were misinterpreted as being caused by herniated discs, for which open surgical discectomy (or repeat discectomy) then was performed.

Despite whether a herniated disc actually was found during surgery after myelography, most patients initially experienced postoperative improvement; however, within a few months many patients were again disabled, and repeat Pantopaque myelography

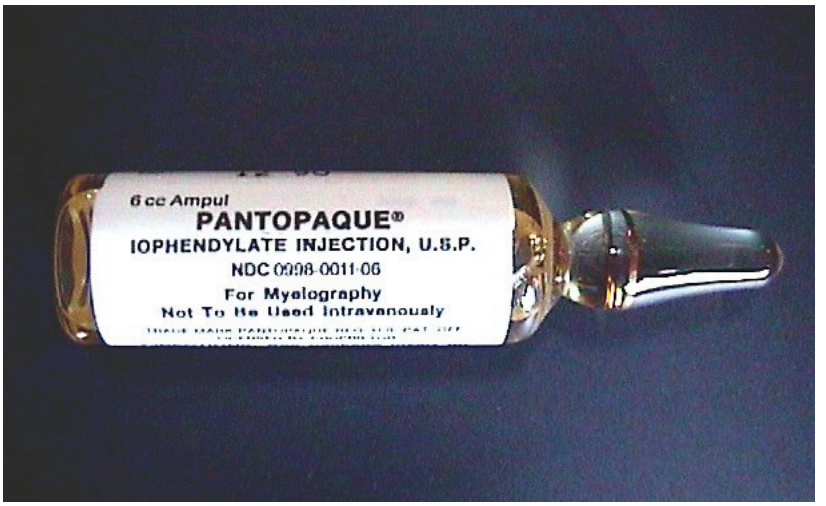

FIGURE 1. This is a 6-cc vial of Pantopaque (lot # 2 INAF), which was manufactured by Alcon Corporation in Puerto Rico. The expiration date listed is 1990.

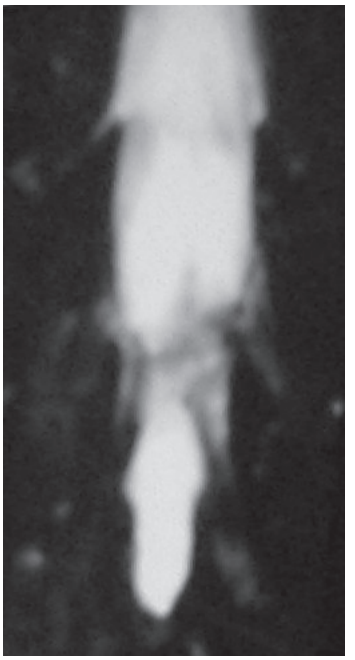

FIGURE 2. A postoperative Pantopaque myelogram showing what was thought to be a recurrent disc herniation but was actually a focal area of adhesive arachnoiditis secondary to a local inflammatory process.

frequently continued to demonstrate dye column abnormalities, for which additional discectomies were attempted, often finding no recurrent disc herniation. Additional Pantopaque myelography and additional spinal surgeries generally followed, continually adding to the patient's constant pain, progressive disability, and sometimes death.

Little did the Walter Reed patients suspect that that Pantopaque was actually a toxic material that produced a progressive chemical meningitis. The end result of this progressive meningeal inflammatory process became known as "adhesive arachnoiditis."[2]

How Pantopaque, which never had been shown to be safe or effective in humans, came to be used for routine full-column myelography in thousands of servicemen in the early 1940s is no longer a mystery. Pantopaque was pressed into clinical use despite the fact that its use was inconsistent with existing American Medical Association guidelines as well as the US Food and Drug Administration (FDA) requirements. Remarkably, Pantopaque, the use of which had serious adverse effects on public health throughout the world, was never banned from use in the United States. It did, however, ultimately "fall intodisuse" sometime in the 1980s.

II. THE PLUTONIUM EXPERIMENTS

US Army Colonel Stafford Warren, MD, was, in 1942, not only a military officer directly involved in the Manhattan Atomic Energy Program but was also, at the same

time, a faculty member in the Department of Radiology at the University of Rochester in New York, where he had been working for a number of years on the development of myelographic substances.

Warren subsequently became a primary participant in a clandestine project to create a new medical facility that was connected, via an underground tunnel, with the Strong Memorial Hospital, which was across the street. The purpose of this secret facility was to determine the then-unknown effects of plutonium on the human body. Rather than asking for volunteers (of which there was an inexhaustible supply during wartime), Warren and his associates chose the course of injecting plutonium into unsuspecting hospitalized patients without their knowledge or consent.

At the end of World War II, this secret Rochester facility was completely destroyed. The US government then kept its presence secret for more than 50 years. This effort was terminated during the Carter administration, when Secretary of the Department of Energy Hazel O'Leary officially acknowledged what was referred to, at the time, as "America's nuclear shame." O'Leary was the first government official to acknowledge the existence of this program, to provide official apologies, and to initiate some restitution to the few remaining plutonium injection survivors. The documentation of these events has been well chronicled by Eileen Welsome in her book, *The Plutonium Files: America's Secret Medical Experiments in the Cold War*.[3]

III. THE PANTOPAQUE EXPERIMENTS

In May 1944, Warren and his Rochester associates personally received US Patent 2,348,231 for their discovery of Pantopaque. Before this, Warren had begun to provide Pantopaque for use at military hospitals. It has since been suggested that Warren and his associates were not, at that time, actually aware of the serious dangers associated with the use of Pantopaque. However, this theory is directly contradicted by Warren's contemporary neurosurgical colleague at the University of Rochester, William Van Wagenen, who in 1942 presented a paper before the Harvey Cushing Society clearly implicating Pantopaque as being the cause of a "chemical meningitis" in the spine.[4–5] Van Wagenen, who then became the first president of the Harvey Cushing Society (now the American Association of Neurological Surgeons), also reported a series of his personal patients in whom Pantopaque was identified as being the cause of inflammatory "space displacing masses" within the spinal canal.

The extensive disability and related deaths created throughout the world as a result of the toxic chemical meningitis caused by the myelographic agents Pantopaque and Myodil has been researched extensively by regulatory and medical consultant Suzanne Parisian, MD, and reviewed in her March 2002 expert report.[6]

The failure of the medical community to make this information better known to physicians has directly resulted in the continual occurrence of cases of chemical meningitis now caused by ill-advised epidural steroid injections containing other similarly toxic materials.[6]

IV. THE BIOSORB EXPERIMENTS

Between the years 2002 and 2004, 35 patients hospitalized at the Walter Reed Medical Center underwent multilevel (up to level 5) lumbar interbody fusions using a Medtronic (Minneapolis, MN) interbody implant composed of potentially biodegradable material trademarked as the Telemon Hydrosorb fusion device (Fig. 3). This was used in association with Medtronic's recombinant human bone morphogenic protein marketed as InFuse. In 2002, InFuse was approved by the FDA for very limited and restricted clinical use. Not only was the Walter Reed Medical Center's use of InFuse "off label," the Telemon Hydrosorb device had not been approved by the FDA for use in humans. These experimental surgeries were in clear violation of the post–World War II Nuremberg Code, the related Declaration of Helsinki, as well as the subsequent regulations issued by the US Department of Health and Human Services governing all federally funded research in the United States, and they seem to have been performed without the knowledge or approval of the Walter Reed Medical Center or its Human Subjects Research Review Committee.

The US Army orthopedic surgeons involved in these Walter Reed procedures were David Polly, Jr., and Timothy Kuklo, who, in addition to being full-time duty Army officers, at that time also were paid consultants and traveling ambassadors for the Medtronic organization. In the March 2004 issue of *Neurosurgical Focus*, Polly and Kuklo[7] reported on their series of patients who had undergone operation at Walter Reed Medical Center and compared it to a similar series of patients in whom Medtronic-manufactured PEEK interbody implants were used (also with Medtronic's InFuse) as a comparison study group. However, in 2001, on the basis of an initial trial of similar biodegradable

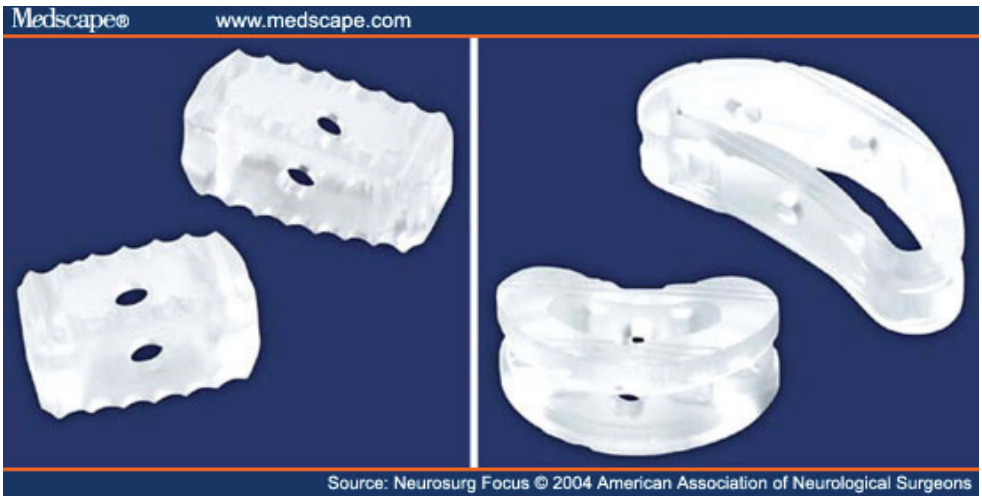

FIGURE 3. These represent different configurations of Hydrosorb implants intended for interbody fusion. Permission to use this illustration given by American Association of Neurological Surgeons. Originally published in Neurosurgical Focus (16)3, Article1, 2004 titled: Robbins MM,Vaccaro AR, Madigan,L: The use of bioabsorbable implants in spine surgery

lumbar interbody implants, European surgeons concluded that further in vivo animal experiments were essential before the clinical use of such devices was initiated.[8]

Historically, it seems that after 2004, the use of bioabsorbable interbody spinal implants "fell into disuse," much like Pantopaque and Myodil. In 2007, Mullender et al[9] experimentally performed Polly and Kuklo's fusion procedure on a series of goats (including the use of InFuse). They reported actual inhibition of the fusion process with the Hydrosorb (poly-lactic acid) implants.

In 2011, on the basis of an extensive review of the medical literature published in *The Spine Journal*, Carragee et al[10] found that the earlier studies of the use of Medtronic's InFuse had reflected "biased and corrupted research" that often had been published by physicians with serious conflicts of interest with the Medtronic organization. In none of 13 clinical trials (of more than 700 patients) carried out by surgeons with financial ties to Medtronic were significant adverse effects of InFuse disclosed. Other data provided by government regulators and other medical publications documented that up to 50% of patients treated with InFuse experienced significant complications and side effects, including bone osteolysis and ectopic bone growth, inflammatory reactions including radiculitis, graft subsidence and migration, infertility in men, and concerns regarding carcinogenesis.[11]

Contrary to this has been the experience of a single neurosurgeon spine specialist (the author), who, in a series of fusion cases extending from 1992 to 2010 and involving more than 700 patients, has utilized autologous bone marrow (rather than bioengineered substances) and locally harvested autologous bone for the purpose of enhancing bone fusion. Autologous bone marrow actually contains bone morphogenetic protein and is even better than bone morphogenetic protein because it also contains stem cells to further power the osteogenic process. Autologous bone marrow is readily available and very cost effective.

Is the cost of InFuse important? Presently, InFuse is estimated as being used in more than 1,000 fusion cases in the United States each year. In 2003, Medtronic, using an "analytical" approach, convinced the US Center for Medicare Services to approve the then new InFuse product and allow an add-on payment of $8,900 for each single-level spine fusion case performed in the United States. Since that time, InFuse has represented a significant component of Medtronic's revenue, estimated at roughly $700 to $800 million annually. Infuse has been a particularly high-margin revenue item for the Medtronic organization.[12–14]

V. MEDICAL ETHICS

This article discusses well-documented examples of human experimentation performed by American physicians over a period of 70 years as well as contrasting instances of medical heroism carried out by their colleagues. Although the motivations behind exploiting unsuspecting hospitalized patients may vary, the common factor here has been that of a desire to achieve personal gain at the expense of patients whose lives these physicians have sworn to protect. Remarkably, up until now, none of the American Mengeles has yet been held accountable for their betrayal of their chosen profession.

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