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The Death of Sodium Pentothal: The Rise and Fall of an Anesthetic Turned Lethal

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ABSTRACT

For nearly a century, sodium pentothal was the undisputed king of anesthetics. Anesthesiologists were not, however, the sole consumers of pentothal, as psychiatrists used it to treat acute anxiety during psychoanalysis. The associated drug-induced inhibitions were attractive not only to psychotherapists, but also to a new generation of policing and Cold War espionage searching for the elusive truth serum. Cameo appearances of pentothal in media, film, and popular culture propagated the anesthetic's negative public image. While legal challenges to the admissibility of pentothal-induced confessions and congressional investigations of clandestine truth serum programs may have tainted the popular anesthetic, it was pentothal's widespread adaptation as part of the lethal injection cocktail that finally killed the king of anesthetics as pharmaceutical companies around the world refused to manufacture what had been transformed into a largely unprofitable drug, associated with capital punishment.

KEYWORDS: Sodium Pentothal, Truth Serum, Lethal Injection, Anesthesia, Psychotherapy

Drug choices are not always determined by the medical profession in isolation. Decisions made in hospitals are often the consequence of politics, social taboos, public pressure, and pharmaco-economic calculations rather than solely based on the most prescient medical advice. Once a manufactured drug reaches the public market, there is little control over the nefarious uses of a drug in ways not approved by regulators. While the opioid epidemic is certainly the most well-known instance of drug misuse and its harmful impact on society, there are other drugs with similar clashes between the pharmaceutical industry and the public. The rise and fall of sodium pentothal, one of the most widely used anesthetics during the twentieth century, is the story of how social taboos, Cold War myths, and popular media defeated a revolutionary drug.

Sodium pentothal became the darling anesthetic that ushered hundreds of millions of Americans into surgery over 70 years, popularized by its rapid onset, limited nausea, and rapid post-operative recovery. Its use during and after World War II revolutionized the field of anesthesiology and was part of a successful treatment program for war neuroses, which took advantage of drug-reduced inhibitions to conduct psychoanalysis. These same benefits, however, made sodium pentothal attractive to criminologists and espionage agencies as a "truth serum" that could remove inhibitions and uncover hidden and repressed information. Pentothal's rapid onset and universal success also made it an ideal first component of lethal injections in correctional facilities across the country.

The alternative uses of sodium pentothal came about as a consequence of what Jack Pressman referred to as a "therapeutic niche," where physicians gradually adopt a drug or therapy to fill a clinical void: "The extent to which a treatment flourishes is directly dependent upon the specific features of the day's clinical landscape. In the long haul, visibility is a matter of ecology, not virtue."[1] Pressman's theory, used to explain the 1940s popularization of lobotomies in psychiatric asylums, can also be applied to the adaptation of sodium pentothal to areas of psychotherapy and lethal injection in addition to its prescribed use as an anesthetic. David S. Jones expounded on Pressman's theory by suggesting that therapeutic niche construction could be altered by either the changing nature of that niche or by the introduction of a therapeutic alternative where there previously was none.[2] By the end of the twentieth century, drug-induced psychoanalysis and lethal injection were faced with growing popular opposition and the availability and popularity of sodium pentothal as an anesthetic was in sharp decline. Coupled with the introduction of propofol, a new anesthetic alternative, sodium pentothal's therapeutic niche was entirely transformed, leaving no room for the once-king of anesthetics.

It was ultimately sodium pentothal's adaptation for uses outside the realm of anesthesia that ushered in its downfall. For the half a century between 1940 and 1990, sodium pentothal occupied a near monopoly of the therapeutic niche of short-acting induction anesthetic. As there was no other alternative, the drug could indeed reign as king, despite the growing criticism and media-propagated public suspicion surrounding psychoanalysis, the truth serum, and lethal injection. Once propofol was introduced during the 1990s as a viable competitor for this niche, all the negative associations coalesced to bring about sodium pentothal's demise. The creation of new functions for sodium pentothal ultimately affected the drug's capacity to serve in its original function as a rapid induction anesthesia.

Film, television, and media popularized the notion of sodium pentothal as a truth serum and as a lethal drug, making it the target of protests against the excesses of espionage and police interrogation as well as the anti-capital punishment movement. As the

1 Jack Pressman, *Last Resort: Psychosurgery and the Limits of Medicine* (Cambridge: Cambridge University Press, 1998), 14.

2 David S. Jones, "Therapeutic Evolution or Revolution? Metaphors and Their Consequences," in *Therapeutic Revolutions: Pharmaceuticals and Social Change in the Twentieth Century*, ed. Jeremy Greene, Flurin Condrau, and Elizabeth Watkins (Chicago: University of Chicago Press, 2016), 273-276.

general public came to associate the near universal anesthetic more readily with terms like truth serum and lethal injection than with surgery, the rise of similar alternatives such as propofol began to gradually supplant pentothal, despite several potentially harmful repercussions. Rather than solely a pharmacological debate, the phasing out of pentothal was an example of the struggle between science and imagery.[3]

Despite sodium pentothal's long history as a revolutionary and effective anesthetic, its imagery as a truth serum and lethal injection ultimately displaced its medical significance. Although sodium pentothal had once transformed medical care and continues to be an effective anesthesia, it has subsequently become the pariah of pharmaceuticals. By the beginning of the twenty-first century, not only was sodium pentothal no longer the king of anesthetics, but also it was not even available for purchase in the US. The king was dead, a victim of popular paranoia, mass media, non-prescribed uses of medication, and the introduction of a comparable untainted alternative.

A NEW AGE OF ANESTHESIA

In every region of the world, there are historical traditions of therapeutic agents that produce hypnotic or sedative states. Alcoholic beverages such as beer or wine are the most prevalent, while opium, hemp, qat, and other narcotic plants are popular in more limited geographic areas, but with limited degrees of effectiveness. Pain from even the simplest surgical procedure was feared by patients almost as much as the prospect of death on the operating table. Some early anesthetics produced successful and predictable results such as an herbal concoction that brought about unconsciousness, first introduced by Japanese surgeon Seishu Hanaoka in 1804, or the Chinese use of acupuncture to ease surgical pain that can be traced back for centuries. Horace Wells, a Connecticut dentist, and Joseph Priestley, an English clergyman and chemist, were among the first to record the usage of nitrous oxide, commonly known as "laughing gas," that still remains the oldest inhaled anesthetic.[4]

Centuries of discovery and experimentation culminated in the first public demonstration of the utility of diethyl ether as a general anesthetic during a surgical procedure in 1846. Ether had been discovered centuries earlier, but had been marketed primarily as a pain reliever. On 16 October 1846 in Boston's Massachusetts General Hospital,

3 John Vincent, "Science and Imagery in the 'War on Old Age,'" *Ageing and Society* 27 (2007): 941-942, 941-961. Similar to sodium pentothal's negative public image and its impact on management of care, the war on old age and the militarized imagery of biological aging has led to an entire self-portrayed field of pseudo-medicine promising anti-aging miracles. Militarized medical terms in general, such as the fight against cancer, have succeeded in portraying terminal illnesses and the process of aging itself as ultimately treatable, regardless of whether these terms reflect medical reality.

4 Rafael A. Ortega and Christine Mai, "History of Anesthesia," in *Essential Clinical Anesthesia*, ed. Charles Vacanti (Cambridge: Cambridge University Press, 2011), 1, 1-6. Sir Humphry Davy coined the term laughing gas after observing nitrous oxide's ability to trigger uncontrollable laughter. I. Russell Weinstein, "Horace Wells and Nitrous Oxide," *JAMA* 194 (1965): 1391. Although Joseph Priestley may have worked with nitrous oxide, he did not study its properties. Humphry Davy (of Davy's safety lamp for mining fame) studied its properties and even suggested that it might be used to relieve the pain of surgery. However, he never tried it for this purpose. The first person to use nitrous oxide for painful medical procedures was Hartford, Connecticut dentist Horace Wells (1845).

William T.G. Morton, a dentist, performed an operation to remove a vascular tumor from Edward Gilbert Abbott, after using ether to sedate the patient in front of a large audience in the hospital's amphitheater which was later named "The Ether Dome."[5] Morton's procedure transformed the field of surgery by heralding a new era of pain-free operations and sparking new excitement into the field of anesthesia. Even as ether spread in its popularity as a general anesthetic, alternatives in England, such as chloroform, were used widely. The search for the ideal inhaled anesthetic met many roadblocks as compounds were found to be pungent, impotent, and flammable, forcing chemists to look for additional alternatives.[6]

For almost a century after its introduction in the 1840s, ether was the principal anesthetic used for surgical operations. Although safe, it had a pungent odor that left most patients nauseated, but more importantly, it was flammable. As equipment powered by electricity became common, including lighting, ether presented an explosive hazard in the operating theater. The surgical community was actively seeking an alternative anesthetic, particularly an induction anesthetic that might more predictably and rapidly sedate the patient. The first clinical introduction of barbiturates, a class of sedative drugs derived from barbituric acid, did not occur until 1904 when diethyl-barbituric acid, also known as barbital, was approved for use in treating psychiatric and neurological disorders. This revolutionary advance in pharmacology presented psychotherapists with a sedative that exhibited relatively low levels of toxicity. Barbital sedated patients who were suffering from what were then termed neuroses and psychoses, facilitating psychotherapeutic treatment while bypassing the patients' emotional repression. This early generation of barbiturates was also used to treat sleeping disorders and epileptic seizures (anti-convulsant effects). Over the course of the twentieth century, chemists synthesized more than 2,500 barbiturates and successfully employed 50 variations clinically.[7]

Ernest Volwiler, a chief chemist and a lifelong employee at Abbott Laboratories, together with a young scientist named Donalee L. Tabern, experimented with barbituric

5 Ortega and Mai, "History of Anesthesia," 2-4. The first use of modern anesthesia is attributed to Crawford Long of Jefferson, Georgia. However, he did not publish his results until 1849, and that too in a local journal. In many ways, his accomplishment has been eclipsed by that of Morton who was the first to publicly demonstrate the use of ether. K. Frank Boland, "Crawford W. Long, the Discoverer of Anesthesia," *Southern Medical Journal* 15 (1922): 920, 919-923. William T.G. Morton is often referred to as Dr. Morton. However, he never had the distinction of graduating from dental or medical school. During the demonstration, he was attending courses at Harvard Medical School. Many years later, he was given an honorary MD from a medical school in Baltimore, a school that no longer exists.

6 Ortega and Mai, "History of Anesthesia," 4-5. By the 1970s, some of these options such as isoflurane, desflurane, and sevoflurane had been further developed, made safer for public use, and today constitute the most prevalent inhalation anesthetics.

7 Francisco Lopez-Munoz, Ronaldo Ucha-Udabe, and Cecilio Alamo, "The History of Barbiturates a Century after Their Clinical Introduction," *Neuropsychiatric Disease and Treatment* 1 (2005): 330, 329-331. There are several hypotheses about the origin of the term "barbiturate," originally coined by Adolf von Baeyer in 1864. Two are pure happenstance that Baeyer named the compound after his friend Barbara or that he celebrated his discovery at a neighborhood tavern where artillery officers frequenting the establishment were celebrating their patron St. Barbara. Another theory claims that Baeyer was inspired by the "barbed" crystals of the ureic compound, thus forming "barb(ara)" and "urea."

acid derivatives producing an alcohol-sodium combination known as Nembutal, an improved sedative, by 1923. The barbiturate was first tested at the University of Wisconsin before being used for clinical tests at the Mayo Clinic's Department of Anesthesia run by John Silas Lundy. By the end of 1930, Lundy administered Nembutal in over 2,000 cases, including his wife, the clinic's co-founder Charles H. Mayo, and the ex-heavyweight boxing champion Jack Dempsey. In most cases the anesthetic was administered orally while intravenous delivery was used only in emergencies. The barbiturate sedated the patient and unless the procedure was extremely short, something else (ether, chloroform, or later agents such as halothane) would be needed to maintain the anesthesia over the course of a longer surgical procedure. Although Nembutal was revolutionary in the time it took patients to fall asleep and recover post-surgery without nausea, there was continued research to bring initial onset to under twenty minutes.[8]

The team of Volwiler and Tabern continued their research work on intravenous anesthetics by preparing and testing 200 different compounds similar to Nembutal. One of these compounds, a sulphur analogue of Nembutal, demonstrated near-instantaneous onset and a quick post-operative recovery estimated at less than half an hour. The new sulphur-based compound which would be renamed sodium pentothal was sent again to Lundy, known by then as the "Warrior against Pain," who tested it on 700 patients.[9] Rather than take twenty minutes to take effect, the patients injected with pentothal were asleep before they could count to 20! Medical journals praised the discovery in no uncertain terms, describing sodium pentothal as "one of the most valuable advances in the science of anesthesia that has been made in recent times."[10] Specifically highlighted in the literature were the short-acting properties of pentothal when compared with other barbiturates like Nembutal and sodium amytal which take up to seventy-two hours to be excreted by the kidneys, thereby unnecessarily prolonging the anesthetic effect. Sodium pentothal, on the other hand, is excreted in less than twelve hours when sedating a patient for a major surgery, without lingering levels of toxicity following the operation inherent in other barbiturates.[11] Sodium pentothal was used mainly as an induction anesthetic, which could only be given intravenously and which would render the patient unconscious for up to 3-5 minutes, depending on the dose. Once the patient was asleep under the effect of sodium pentothal, the patient would be

8 Herman Kogan, *The Long White Line: The Story of Abbott Laboratories* (New York: Random House, 1963), 126-128; Sarah Bartlett Churchwell, *The Many Lives of Marilyn Monroe* (New York: Metropolitan Books, 2005). Marilyn Monroe overdosed on Nembutal, marketed as the sleeping pill pentobarbital in 1962.

9 "Folklore of Anesthesia," *British Medical Bulletin* 4 (1946): 150–151.

10 Barnett Mallinson, "Pentothal Sodium in Intravenous Anaesthesia," *The Lancet* 230 (1937): 1070, 1070-1073.

11 Carroll H. Long and Alton Ochsner, "Intravenous Pentothal Sodium Anesthesia: A Review of the Literature," *Surgery* 11 (1942): 590, 590-592; Mallinson, "Pentothal Sodium in Intravenous Anesthesia." Even though pentothal is excreted in less than twelve hours, the concentration of the drug in the brain declines very rapidly after initial dosage, thus allowing the patient to wake up relatively quickly – in as little as three to five minutes. The drug is fat soluble so it goes to organs with high fat and high blood flow (brain). Within minutes it equilibrates with other stores of fat (adipose tissue) which have low blood flow, thus lowering the concentration and allowing the patient to wake up.

further sedated with other inhaled anesthetics such as ether, halothane, or other vapors, and often accompanied by nitrous oxide. Sodium pentothal was a great advance in anesthetics considering that the alternative was falling asleep gradually by inhaling ether. The pungent odor of ether was dreaded by patients, and most suffered significant post-surgical nausea and vomiting. What ether achieved in two to five minutes, sodium pentothal could do in less than a minute, and the process was very pleasant for the patient.

The only time that sodium pentothal could serve as the total anesthetic would be for extremely short procedures. Its earliest adopters were eye surgeons who discovered the benefits of operating without being encumbered by unwieldy face masks to anesthetize patients. Dentists and oral surgeons similarly used sodium pentothal to replace the less reliable nitrous oxide, while oncologists used the rapid-onset sodium pentothal for quick biopsies of very ill patients who lacked the strength to withstand longer-lasting anesthetics. Sodium pentothal was adapted early in some of the most-performed operations such as Caesarian births, tonsillectomies, cataract removals, thyroidectomies, and urologic and neurologic surgeries. Between 1934 and 1955, intravenous anesthetics were used an estimated three million times, with 94 percent sodium pentothal. By the 1960s, the truth of the following statement was self-evident: "To know intravenous anesthesia is to know *Pentothal*."[12]

WWII presented a complicated historical pathway of popularized pentothal usage. On the one hand, Lundy argued in a 1945 medical review that sodium pentothal "has been one of the outstanding advances in modern military surgery," citing a drop in mortality rates and the ability to conduct emergent surgery on the battlefield, thus saving the lives of countless servicemen. On the other hand, during the Japanese attack on Pearl Harbor, sodium pentothal was used extensively to devastating effect as many of the patients were severely ill with hypovolemia, anemia, and sepsis, resulting in the death of an undocumented number of servicemen and women. Rather than using sodium pentothal for its intended purposes as an induction anesthetic, inexperienced hands were using it for longer procedures, placing the patient at risk. It is rumored that more patients died due to misuse of sodium pentothal than the injuries that were being treated surgically. The improper dosing and administration of sodium pentothal, which although superior to most induction anesthetic alternatives was a sophisticated and complex drug, highlighted the need to train a new generation of anesthesiologists in the pharmacology, physiology, and science of this and other new anesthetics. Sodium pentothal survived this complicated paradox during WWII and actually pointed out the need for a new and more sophisticated era of anesthesiology.[13] The critique of

12 Sheryl Ault and Abbott Laboratories, *A Promise for Life: The Story of Abbott* (2013), 112-113; Francisco López-Muñoz, Ronaldo Ucha-Udabe, and Cecilio Alamo, "The History of Barbiturates A Century After Their Clinical Introduction," *Neuropsychiatric Disease and Treatment* 1 (2005): 329-343.

13 S. R. Charles Adams, H. John Lundy, and H. Thomas Seldon, "Ten Years of Pentothal Sodium Intravenous Anesthesia an Evaluation of Its Past, Present and Future," *Anesthesiology* 6 (1945): 242-243; John A. Crowhurst, "The Legacy of the Anaesthesia 'Events' at Pearl Harbor, 7th December 1941," *Journal of Military and Veterans Health* 24 (2016): 52, 52-57; John Crowhurst, "The Historical Significance of Anaesthesia Events at Pearl Harbor," *Anaesthesia and Intensive Care* 42 Suppl (2014): 21.

pentothal's performance at Pearl Harbor was contained within the field of medicine rather than as fodder for public condemnation, thus prolonging the anesthetic's life and prominence in the field.

Lundy received regular correspondence from hospitals around the country seeking his recommendation for the use of sodium pentothal. In 1946 for example, Richard Crowell from Mercy Hospital in Michigan wrote to Lundy asking for a "humble request to aid us in settling the question as to whether or not we should use sodium pentothal for Oral Surgery in Mercy Hospital, Benton Harbor. . .There have been reported to us many glowing reports of the use of this drug in Oral Surgery, and we are wondering whether we are justified in continuing to permit its general use among Oral Surgeons. . ." Lundy's responses were almost always hesitant, reminding correspondents that anesthesia administration was a complicated procedure that required intubation, correct dosage, and monitoring.[14] Lundy's conservative medical advice may have been necessary during the 1940s as sodium pentothal was a relatively new anesthetic and was dangerous to the patient if not used properly or in the correct dose. By 1950, however, his caution was no longer as necessary because anesthesia departments across the US became familiar with the drug's contraindications and specifics.[15]

As part of a worldwide marketing campaign, Abbott Laboratories launched a postcard promotional program mailing cards from over 70 countries to surgeons and anesthesiologists in the United States, Canada, Europe, and South America. The front of each postcard featured photographs of scenery, archeology, culture, or iconic imagery from the country of origin, with a local stamp. The written side of the card referenced the exotic locale, extolling the virtues and ubiquitous presence of sodium pentothal even in remote regions of the world. For example, a postcard sent to a doctor in Toronto from Brasilia, Brazil's then new and modern capital city, read, "Dear Doctor. Yesterday only waist-high grasses of a trackless savanna stood here. Today sky scrapers thrust upward in one of the world's most advanced concepts of city planning. And as you would expect in Brasilia's ultramodern hospital operating rooms, PENTOTHAL (Thiopental) is an anesthetic of choice. Abbott." Other more remote locations included Polcirkeln, Sweden in 1958, Ruanda-Urundi in 1959, the Maldives in 1962, and the Pacific Island of Hebrides in 1966.[16]

Between 1954 and 1968, approximately 170 different postcards in multiple languages were shipped as part of an era of medical mail advertisements to over 220,000 physicians. R. J. Dubourdieu, Abbott's product advertising manager, envisioned this campaign as part of a concerted effort to maintain pentothal's dominant market share

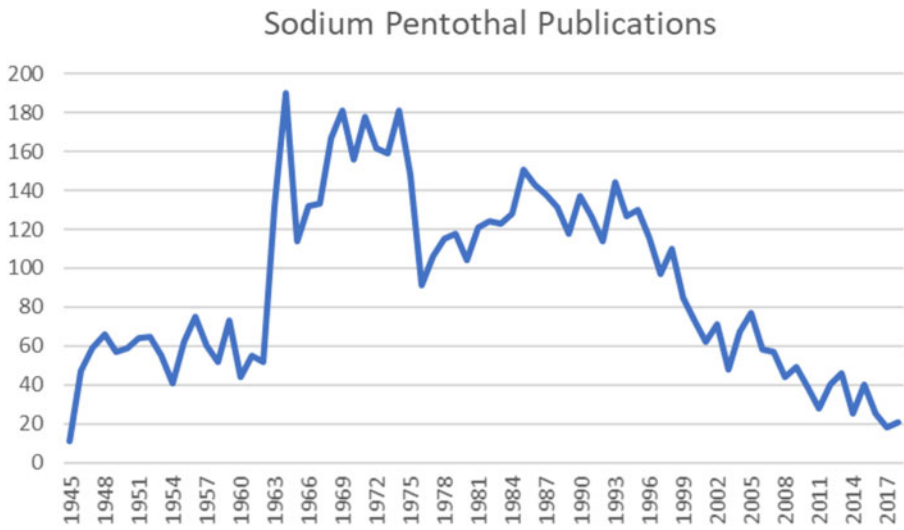
14 Richard Crowell to John Lundy, 14 October 1946; Lundy to Crowell, 1 November 1946. Lundy warned Crowell against using sodium pentothal without following the appropriate procedures required. MHU-0616: John Silas Lundy Papers, folders "Inquiries re: Drugs, Dosage, Technic, Correspondence May 1, 1946-December 31, 1946," and "Inquiries re: Drugs, Dosage, Technic, Correspondence 1947." By permission of Mayo Foundation for Medical Education and Research. Courtesy of the W. Bruce Fye Center for the History of Medicine, Mayo Clinic, Rochester, Minnesota.

15 Kogan, *Long White Line*, 170-171.

16 David Lai, *Pentothol Postcards* (West New York, NJ: M. Batty, 2005), 59-60, 137-138, 61-62, 75-76, 83-84.

in the anesthetic industry. 1954 marked both the expiration of the sodium pentothal patent and the emergence of other short-acting barbiturates, thereby exerting pressure on pentothal's universality.[17]

Sodium pentothal became the anesthetic of choice for the entire field of anesthesiology for all forms of surgery, from dental and outpatient to cardiac and inpatient.[18] During the 1960s and 1970s, the number of papers published in the medical literature dealing with various aspects of sodium pentothal increased exponentially.



In 1985, John Alfred Lee, one of the United Kingdom's best-known anesthetist clinicians and researchers, observed that although alternative intravenous agents had been discovered since 1935, he saw no advantage relative to sodium pentothal. "During the nearly 50 years that I have been using this drug, it has never let me down, and I must have either given or supervised the administration of many thousands of doses. Like most anesthetists, I have sometimes given too much or not enough, but I have never seen a single untoward result. . .Pentothal sodium, thiopentone – truly a milestone in clinical anesthesia."[19]

ALTERNATIVE USES OF SODIUM PENTOTHAL

In 1931, a London-based physician named J. Stephen Horsley began experimenting with pentothal and other barbiturates, noting how patients relaxed inhibitions, were

17 Ibid., 3-9; Daniel Friedman, "The Story Behind Pentathol (Sic) Sodium Cards by Abbott," *Barr's Post Card News* 567 (1993): 1, 38-39.

18 National Library of Medicine, "Anesthesia and Sedation in the Dental Office. National Institutes of Health Consensus Development Conference Statement," *National Institutes of Health Consensus Development Conference Consensus Statement* 5, no. 10 (1985).

19 J. Alfred Lee, "The Origins of Three Important Changes in Anaesthetic Practice," in *Anaesthesia: Essays on Its History*, ed. Joseph Rupreht (Berlin: Springer Berlin Heidelberg, 1985), 157-158, 155-160.

unable to refuse answer to even intimate questions, and afterwards had little recollection of the interrogation that transpired. Horsley's "narco-analysis" was utilized to treat WWII civilians and military personnel suffering from wartime stress.[20] For example, during the evacuation of Dunkirk and later during the London blitz, men and women were given intravenous doses of pentothal and other oral doses of Nembutal, reducing them to a semi-sleepy state and freeing them from overwhelming feelings of fear, anger, and frustration.[21]

Traumatic battle experiences have long been known to lead to debilitating symptoms of anxiety. For instance, those who experienced a long duration of dive-bombing or air raids might have instinctively searched for cover at the sound of a passing truck or other loud noises. Before post-traumatic stress disorder (PTSD) emerged as the most common term to describe the general nervous and mental conditions suffered by soldiers in modern-day warfare, these symptoms were referred to during World War I as shell-shock and during World War II as war neuroses. Psychiatrists observed that acute anxiety could be exacerbated by unconscious emotions of fear, survivor guilt, or an innate need to protect oneself by psychological avoiding the memories of a distressing experience. The post-stuporous state brought on by intravenous sodium pentothal tended to reduce the inhibitions of a patient, allowing psychotherapists to probe deeply into a patient's mind and to uncover memories and specific details of the episode causing these feelings of anxiety. Sodium pentothal interviews became a staple of postwar psychiatric investigations, with experts documenting hundreds of individual cases of successful treatment during the 1940s.[22]

Pioneering work on war neuroses was conducted by Roy Grinker and John Spiegel, both psychiatrists who served during the Allied Tunisian Campaign between January and May 1943. The two were stationed in Algiers, around 150 miles behind the front lines, where they conducted the treatment and study of psychiatric casualties. After the end of WWII in Europe, Grinker and Spiegel co-published two volumes on their study of war neuroses, specifically highlighting the role sodium pentothal played in their experimental treatment.[23] In one case outlined by Grinker, a 20-year-old infantry platoon sergeant narrowly survived a massive artillery bombardment during the 1943 Battle of Sedjenane by seeking cover in a foxhole under two corpses belonging to fellow platoon members. Once safely in a bivouac area, he was diagnosed with "acute anxiety, persistent tremor, great restlessness, loss of appetite, and insomnia with battle dreams." After a series of pentothal interviews and therapy during which the soldier relived his experience and confronted his anxiety, the nightmares subsided and he returned to noncombatant duty. In other instances, pentothal therapy uncovered repressed memories that had been the cause of severe depression, allowing therapists to work through complex

20 Dominic Streatfeild, *Brainwash: The Secret History of Mind Control* (London: Hodder & Stoughton, 2006), 32-33. William Sargant was among the first to use pentothal in this fashion in June 1940 while working at Belmont Hospital.

21 Kogan, *Long White Line*, 175-176.

22 Roy R. Grinker and John P. Spiegel, *War Neuroses* (Philadelphia: Blakiston, 1945), 16-17, 22.

23 Roy R. Grinker and John P. Spiegel, *War Neuroses in North Africa: The Tunisian Campaign, January-May 1943* (New York: Josiah Macy, Jr. Foundation, 1943).

emotional responses on the path to postwar mental recovery. For example, a 20-year-old WWII hospital engineer had been suffering from tremendous anxiety and guilt after he shot a German soldier his own age. The episode remained hidden from his team of hospital therapists until pentothal treatment revealed the details and allowed the patient to address the root causes of his depression and produced a full recovery.[24]

Sodium pentothal-enabled narcoanalysis remained in use for over half a century. Experts continued to use "the sodium pentothal hypnosis interview" to treat episodes of acute war neuroses suffered by service men and women returning from the battlefield. For example, during the 1990s, a twenty-five-year-old active duty US army soldier checked into the hospital with a constant throbbing pain in his right hand. With no visible external injuries or other physical causes, the patient was referred to a group of pain management specialists. Using sodium pentothal and hypnotherapy, it was discovered that the chronic pain in the patient's right arm was a symptom of repressed emotions emanating from a traumatic tour of duty in Somalia as the pilot of a Cobra helicopter. After four sessions with the team, the soldier regained full and painless function of his right hand and was able to return to duty.[25]

Grinker and Spiegel's pioneering work in narcoanalysis was not met with unanimous approbation. A growing number of critics questioned both the morality of the drug-induced therapy sessions and the veracity of the recollections. Psychiatrists Martin Gerson and Victor Victoroff observed in a 1948 study that although barbiturate narcoanalysis "has been successful for the revelation of deception, validity of information garnered by this method is not so decisive that it should be admissible in court without further investigation and substantiation. The doctor cannot tell when the suspect's recollections turn into fantasy, cannot positively state whether he is stimulating deep narcosis and actually maintaining his lies, and cannot, without social investigation, determine which of contrary stories told under narcoanalysis is true."[26] Whether sodium pentothal narcoanalysis produced verifiable recollections or whether drug-induced testimony was mere fantasy, this marked the first of many uses of the drug that varied from its initial release as a surgical anesthetic.

TRUTH SERUM

Not all uses of narcoanalysis were intended for the altruistic purposes of treating war neuroses. The search for a magical drug that could break down barriers to the human

24 Grinker and Spiegel, *War Neuroses*, 18-19, 28-29, 32-35. In addition to recovering memories that might have been lost due to trauma or a concussion, pentothal therapy was also observed to "heal" ailments such as hearing loss that were induced by psychological trauma rather than the rupture of membranes in the ear. Similarly, pentothal therapy managed to reverse psychologically-induced paralysis resulting from war neuroses.

25 Eric P. Simon and Lynn F. Dahl, "The Sodium Pentothal Hypnosis Interview with Follow-up Treatment for Complex Regional Pain Syndrome," *Journal of Pain and Symptom Management* 18 (1999): 132-136.

26 Martin J. Gerson and Victor M. Victoroff, "Experimental Investigation into the Validity of Confessions Obtained under Sodium Amytal Narcosis," *Journal of Clinical and Experimental Psychopathology* 9 (1948): 374.

mind began during the 1920s when it was discovered that certain sedatives could induce patients to divulge information that would have otherwise been highly guarded.[27]

According to English law, drug-induced statements, or confessions made by an accused person involuntarily or against his will, could not be admissible in court. Similar limitations did not exist in US law during the 1940s, leading to the controversial 1946 case of William Heirens of Cook County, Illinois who was arrested in an attempted burglary. Heirens, a 17-year-old, was injected with sodium pentothal and under a drug-induced interrogation and four days of torture confessed to three murders and more than five hundred burglaries. Roy Grinker was one of the two physicians administering sodium pentothal to Heirens.[28] Heirens was popularly known as the "Lipstick Killer" for the haunting lines written in red lipstick on the wall of one of the murder victims: "For heaven's sake catch me before I kill more. I cannot control myself." Throughout his 65-year prison sentence and until his death in 2012, Heirens maintained his innocence, claiming that the confessions were coerced and retrieved unwillingly by the use of sodium pentothal in the interrogation.[29]

The Heirens case captured the public imagination and sympathy for the tragic victims of murder. The public horror was matched in later years by the ensuing doubts as to the legality of his interrogation and the admissibility in court of confessions obtained through sodium pentothal coercion. Police departments across the country barred the use of sodium pentothal or any analogous truth serum in investigations. In 1956, for example, the US Air Force issued a clear statement banning pentothal: "To eliminate any misunderstanding in the use of truth serum during the conduct of any administrative, aircraft accident, or other investigation, the following policy is announced: The use of truth serum or other hypnotic drugs is prohibited in any USAF investigation or inquiry. This policy is to be disseminated to all commanders."[30]

Cold War dynamics and the real and imagined pervasiveness of Soviet and Eastern Bloc intelligence capabilities created mass hysteria related to mind control methods and the elusive truth serum in particular.[31] Despite scientific evidence to the contrary, both government officials and the general public believed that Soviet control over the metaphorical "Iron Curtain" was a product of medically-induced brainwashing that was accomplished by using a secretive substance that allowed unwilling and untraceable probes into the human mind. Sodium pentothal, in particular, was well-documented for its use in the WWII treatment of war neuroses and during police investigations.[32]

27 "'Truth' Drugs in Interrogation – Central Intelligence Agency," https://www.cia.gov/static/a56eb9be08868b6e14c6ff838ae77087/Truth-Drugs-in-Interrogation.pdf; Robert House, "The Use of Scopolamine in Criminology," *American Journal of Police Science* 2 (1931): 328-336; Alison Winter, "The Making of 'Truth Serum,'" *Bulletin of the History of Medicine* 79 (2005): 501, 500-533.

28 "Drug-Induced Statements," *Lancet* 250: 6482 (1947): 763.

29 Douglas Martin, "William Heirens, the 'Lipstick Killer,' Dies at 83," *New York Times*, 7 March 2012.

30 F.B. Winch, 1956 Police Administration Staff Management, September 19, 1956. US Air Force Commands, Activities, and Organizations: Continental Air Command/Office of the Inspector General. RG 0342, Box 2, National Archives, College Park, MD.

31 "Stranger Than Fiction," Science History Institute, 2 December 2015, https://www.sciencehistory.org/distillations/magazine/stranger-than-fiction.

32 Streatfeild, *Brainwash*, 20-21.

In response to the fear of brainwasing in Eastern Europe, the CIA began Operation Bluebird, sanctioned in April 1950, as a training program to prepare US servicemen to withstand mind-control techniques. In August 1951, the program was renamed Operation Artichoke and transformed into an offensive program to develop drug-based interrogation and mind control techniques through induced amnesia, the use of hypnosis, forced morphine addiction and withdrawal, along with other drugs such as sodium pentothal. The central question driving these CIA experiments was if "we can get control of an individual to the point where he will do our bidding against his will and even against fundamental laws of nature, such as self-preservation." More specifically, the CIA wanted to know whether "an individual of [redacted] descent be made to perform an act of attempted assasination involuntarily under the influence of ARTICHOKE?" These early conjectures reflected the popular imagination of the 1950s, which was further encapsulated in Richard Condon's 1959 novel, *The Manchurian Candidate*, in which a US soldier is hypotized by Communist forces and returns home as an obedient assassin.[33] In April 1953, the program was renamed yet again to Operation MKUltra, a notorious codename that has come to symbolize an era of CIA clandestine operations. Sodium pentothal was used extensively, along with hypnosis, in overseas interrogations and experimentation as part of operation Artichoke and continued to be closely associated with the evolving program. With few concrete results emerging from the early years of the program, by 1964 the CIA had curtailed the extent of the program and halted its activities entirely by 1973.

The details of MKUltra remained classified until the 1970s, when a congressional inquiry was launched in response to what was perceived by lawmakers as a general abuse of power and influence by the intelligence services. MKUltra was first brought to public attention in 1975 by the Congressional Church Committee and the Rockefeller Commission (President Gerald Ford's Commission on CIA activities within the United States). During a subsequent 1977 congressional investigation, the CIA was accused of violating statutes and guidelines established for the field of behavioral research in their abuse of patients and prisoners during experimentation and interogation.[34]

In his opening remarks to the Senate in 1977, the chairman of the Health Subcommitte, Senator Ted Kennedy, detailed the earlier revelations that precipitated this congressional investigation:

> Some 2 years ago, the Senate Health Subcommittee heard chilling testimony about the human experimentation activities of the Central Intelligence Agency. The Deputy Director of the CIA revealed that over 30 universities and institutions were involved in an "extensive testing and experimentation" program

33 ARTICHOKE Report. 22 January 1954, https://nsarchive.files.wordpress.com/2010/04/project-artichoke-22-january-1954.pdf; Richard Condon, *The Manchurian Candidate* (New York: McGraw-Hill, 1959).

34 Streatfeild, *Brainwash*, 26-27; "Project MKULTRA, The CIA's Program of Research in Behavioral Modification," Joint Hearing before the Select Committee on Intelligence and the Subcommittee on Health and Scientific Research of the Committee on Human Resources United States Senate. Ninety-Fifth Congress, First Session (3 August 1977). Washington, DC: U.S. Government Printing Office, 1977.

> which included covert drug tests on unwitting citizens "at all social levels, high and low, native Americans and foreign.". . .The intelligence community of this Nation, which requires a shroud of secrecy in order to operate, has a very sacred trust from the American people. The CIA's program of human experimentation of the fifties and sixties violated that trust. It was violated again on the day the bulk of the agency's records were destroyed in 1973. It is violated each time a responsible official refuses to recollect the details of the program. The best safeguard against abuses in the future is a complete public accounting of the abuses of the past.[35]

A GROWING CRITIQUE

Pressman's therapeutic niche theory explains that a medication or procedure can become irrelevant when either replaced by a more effective alternative or when the niche itself falls out of favor in the medical and public communities. Even before propofol entered the anesthetic field as an alternative to sodium pentothal, the psychiatric community began to question the efficacy of narcoanalysis as a standard of treatment. Scientific trials during the second half of the twentieth century continued to question the efficacy of using sodium pentothal and other barbiturates as part of a psychiatric treatment program. Although recovering the debilitating memories that had caused serious health and lifestyle issues for WWII-era soldiers suffering from war neuroses evidently produced admirable results, the success of the war neuroses studies during the 1940s could not be replicated in other venues. For instance, there was no empirical evidence that pentothal or other chemical interventions used in the process of recovering memory therapy improved the long-term outcomes for participating patients. The repressed memories purportedly regained with the assistance of barbiturates, often had never actually occurred, were the product of leading questions by a therapist, and were not corroborated with independent evidence. Falsely recovered memories of committing child abuse or having been the victim of child molestation have at times led to a deleterious impact on patients who were forced to suffer incarceration or mental anguish for an event that never occurred.[36] According to the conclusions of a 1993 study, medically-enhanced therapy sessions produced no better results than the placebo alternative and if anything could cause harm to the patient: "Barbiturate-facilitated interviews intended to uncover memories of childhood sexual abuse may be worse than useless, because they may encourage patients' beliefs in completely mythical events."[37] In other words, the "truth" induced by sodium pentothal in patients could not be trusted.

35 "Project MKULTRA," 7-8.

36 J. T. Stocks, "Recovered Memory Therapy: A Dubious Practice Technique," *Social Work* 43 (1998): 423-424.

37 August Piper, Jr., "'Truth Serum' and 'Recovered Memories' of Sexual Abuse: A Review of the Evidence," *Journal of Psychiatry and Law* 21 (1993): 447-471, 465.

Doubts about narcoanalysis were not limited to the medical community but were also expressed by the legal community who challenged the admissibility of medically-facilitated testimony. In a landmark 1994 court case, Gary Ramona, a father from California, successfully sued Western Medical Center in Anaheim, California, and received a $500,000 settlement after two psychotherapists used barbiturates to "recover" his daughter's repressed memories of sexual abuse by her father over a period of ten years. Gary's daughter had initially sought therapy for an eating disorder and was led to believe after medically-administered therapy sessions that her condition was a result of sexual abuse of which she had no previous recollection. Gary Ramona's wife demanded a divorce, he lost his job, and he suffered public humiliation and shame stemming from the reports of the psychotherapists. In the aftermath of the Ramona case, the American Medical Association called for "external validation" in order to authenticate the patient's trauma history.[38] Most experts concluded that while a patient under truth serum might exhibit decreased inhibitions, the recalled memories were as much a consequence of the interrogator who might have unwittingly or intentionally provided leading questions in order to elicit the drug-induced answers sought after, especially as the patient was not entirely cognizant during the narcoanalysis.[39]

Despite the absence of evidence that sodium pentothal produced verifiable testimony, US intelligence agents continued to advocate its use in post-9/11 interrogations. For example, in April 2002, William Webster, a former director of the CIA and FBI, urged the Pentagon to administer truth serum, and sodium pentothal in particular, to al-Qaeda prisoners in order to obtain vital intelligence, to prevent a future terrorist attack, and "for the protection of the country."[40] Webster was not alone in advocating for the use of sodium pentothal during the Global War on Terror. Following the 2008 terror attacks in Mumbai, Indian police detained Azam Amir Kasab, the sole surviving terrorist, and opted to uncover plot details through the use of narcoanalysis. He was injected with sodium pentothal in an effort to glean details about his Pakistani upbringing, pieces of information that served to flame tensions between India and Pakistan following the terror attacks. Kasab was eventually hanged, after being sentenced on a preponderance of evidence that did not rely solely on his unwitting testimony while under the influence of sodium pentothal.[41]

The use of sodium pentothal during terrorist investigations became a subject of intense public debate in 2012 during the trial of James Holmes, who was accused of killing 12 people in an Aurora, Colorado movie theater. Judge William Sylvester of Colorado ruled that narcoanalysis using sodium pentothal or another short-acting

38 Ralph Slovenko, "The Duty of Therapists to Third Parties," *Journal of Psychiatry and Law* 23 (1995): 392-395. This AMA ruling was particularly controversial as traditional psychotherapy did not seek objective or corroborating evidence to substantiate a patient's trauma history. The American Psychiatric Association agreed that when recovering lost memories in particular, when the therapy affects not only the patient but also the subject of the repressed memory, there should be due diligence.

39 "The Truth About Truth Serum," *Los Angeles Times*, 5 November 2001.

40 "Use of Truth Serum Urged," *Chicago Tribune*, 26 April 2002.

41 Rahul Bedi, "Mumbai Attacks: Terror Suspect to Be Injected with Truth Drug," *Telegraph*, 3 December 2008.

barbiturate could be conducted in order to determine Holmes's sanity during the crime. The legal and medical merits of the "narcoanalytic interview" were contested by experts. William Shepherd, the chair of the criminal justice section of the American Bar Association, argued that administering the truth serum would be a violation of the accused's Fifth Amendment rights to remain silent. Steven Hodge, a professor of psychiatry at Columbia University, questioned the efficacy of such an interview, citing the absence of sufficient evidence supporting the veracity of narcoanalysis.[42] Jurors eventually sentenced Holmes to life in prison after no unanimous decision could be reached regarding the death penalty. Although no confirmation or report was released regarding any narcoanalysis conducted of Holmes, the very public nature of this trial proved the final straw for the use of sodium pentothal either as part of the psychoanalytic therapeutic niche or as a truth serum admissible in court.

PENTOTHAL AND POPULAR MEDIA

The infamy of sodium pentothal as a truth serum was not limited to a small subset of medical professionals, legal minds, or politicians who debated the ethical dual use of one of the world's most successful anesthetics. Despite a growing body of literature and legal precedence demonstrating the futility of truth serum in interrogation, sodium pentothal became one of Hollywood's most popular pharmaceuticals, making cameos in film, television, novels, and at times serving as a central component of the plot. In the 1947 film *High Wall* starring Robert Taylor and Audrey Totter, Steven Kenet, a WWII veteran, returns home to find his unfaithful wife in bed with her boss Willard Whitcombe. When his wife is found murdered, suspicions fall on Kenet who has no memory of the murder night, a presumed consequence of a brain injury during the war. Kenet is given sodium pentothal and under narcoanalysis reveals that he did indeed faint on the night of the murder and did not kill his wife. When Whitcombe is injected with sodium pentothal, however, he confesses to the murder. The film ends with Whitcombe's declaration that he will seek legal counsel and have the sodium pentothal confession dismissed.[43] Although it was not a popular film, *High Wall* does address many issues surrounding sodium pentothal, including its use in treating postwar soldiers, the controversial use of the drug as a truth serum, and the legal challenges of court admissibility. Both during WWII and in the early postwar years, barbiturate narcoanalysis was used as part of the recommended treatment for severe cases of war neuroses.

The 1952 film *Big Jim McClain*, starring John Wayne and Nancy Olson, was a far more popular film that addressed the use of truth serum in the context of espionage. In one of the movie's climactic scenes, a Communist psychiatrist kidnaps an agent of the House Un-American Activities Committee who was in Hawaii tracking Communist Party activities, and accidentally kills him by using excessive amounts of sodium

42 Ed Pilkington, "Judge Approves Use of 'Truth Serum' on Accused Aurora Shooter James Holmes," *The Guardian*, 12 March 2013.

43 Curtis Bernhardt, *High Wall* (Metro-Goldwyn-Mayer Corp., 1948).

pentothal as a truth serum.[44] *Big Jim McClain* popularized the myth that Communists were wantonly using truth serum, while at the same time highlighting the very real dangers of incorrect dosage of sodium pentothal. Within the medical and legal community at this time there was growing opposition to the admissibility and veracity of barbiturate narcoanalysis in a criminal court case.

A more modern example of films using sodium pentothal as a central plot feature was the 2007 horror film *Hannibal Rising*, the fifth instalment of the Hannibal Lecter franchise starring Gaspard Ulliel as the title character, Lecter. The film begins with Lecter witnessing the loss of his family in Lithuania during WWII. As an adult studying in a French medical school a decade later, Lecter witnesses a condemned war criminal being given sodium pentothal to forcibly retrieve memories of his numerous war crimes. In a pivotal scene, Lecter injects himself with sodium pentothal, drawing out a flashback identifying his sister's murderers, a group of Lithuanian militiamen led by a Nazi collaborator. The entire movie plot follows Lector's hunt for the murderers, guided by memories retrieved through the use of sodium pentothal.[45] The appearance of sodium pentothal in *Hannibal Rising* was particularly ironic as by the time of the film's 2007 production it was clear that the anesthetic was ineffective in conducting psychoanalysis or recalling repressed memories. Hollywood's decades-old image of sodium pentothal as an effective truth serum remained unchanged by inconvenient medical facts, emphasizing the difficulty of modifying popular imagery with scientific evidence.

Sodium pentothal was used not only as the fearful memory-inducing drug of horror films, but was also fodder for comedy in countless films and television shows. For example, in the 2007 film *Meet the Fockers*, Robert De Niro's character injects his son-in-law, played by Ben Stiller, with a vial of sodium pentothal leading to a farcical public confession in front of friends and relatives about a secret sexual lust for his mother-in-law.[46] Similar to its 2007 cameo in *Hannibal Rising*, the inaccurate portrayal of sodium pentothal as a truth serum is less important than the comical value of using the drug's popular image, a seemingly inescapable association in popular consciousness.

There was evidently a degree of comedic value in sodium pentothal even when portrayed as a rapid onset anesthetic. For example, "The A-Team" was a popular NBC television series during the 1980s. The main characters were four members of a US Army Special Forces unit in Vietnam who were convicted of a "crime they didn't commit," escaped prison to live a life as soldiers of fortune helping the oppressed, and used sodium pentothal as comic relief during high octane action-adventure sequences. The character of B.A. Baracus, played by Mr. T (Laurence Tureaud), is a professional boxer who personifies the group's strength and brutality, yet is fearful of flying. During each episode where the A-Team is called upon to board an aircraft en route to a mission, Baracus voices his, now famous, catchphrase: "I ain't getting on no plane!" What follows is usually

44 Edward Ludwig, *Big Jim Mclain* (Warner Bros, 1952).

45 Peter Webber, *Hannibal Rising* (Momentum Pictures (UK), The Weinstein Company, Metro-Goldwyn-Mayer (US), 2007).

46 Jay Roach, *Meet the Fockers* (Universal Pictures and DreamWorks Pictures, 2004).

an amusing charade of ruses as the rest of the team tries to inject Baracus with sodium pentothal and drag him onto the plane in a sedated state. Whether they end up injecting Baracus with a syringe or feeding him tainted food with sodium pentothal, he ends up passing out and when he awakes in a state of confusion as to his whereabouts, the team always attributes his temporary amnesia to him having blacked out.[47] The producers of "A-Team" even managed to feature pentothal/truth serum as a key plot element during a 1986 episode, where a Soviet agent gives the A-Team a "variation of sodium pentothal [that's] not only truth serum but it can cause temporary amnesia. . .if you use too much it can act like laughing gas." This reference recycled some of the unsubstantiated Cold War themes related to Soviet truth serum, which culminated in a humorous escapade where an overdose of "spray sodium pentothal" sends the villainous main character into an uncontrollable fit of laughter as he divulges the secret conspiracy. This is another example of how popular comic relief does not always need to be grounded in scientific evidence to perpetuate the negative image of a popular drug.[48]

Beyond providing comic relief and playing an important role in movie plots, sodium pentothal was enshrined in the public media as a drug used by international spies, criminal detectives, homicidal psychopaths, and vigilante soldiers. The public image of sodium pentothal proved far more long-lasting and potent than the scientific and medical values of the anesthetic in the operating room. Although pentothal remained the dominant rapid onset anesthetic well into 1990s despite its growing negative image, the drug could not overcome its infamous association with lethal injections in the US.

LETHAL INJECTION

During the 1970s, Jay Chapman, the inventor of the lethal injection who was serving as medical examiner for the state of Oklahoma, was tasked by State legislator Bill Wiseman with finding a more "humane" way to kill prisoners other than the gallows, electric chair, or firing squad. In what became known as the Chapman Protocol, Chapman proposed a cocktail of three readily available drugs, with each administered in lethal and toxic doses. Sodium pentothal was the first of the three, ostensibly to provide a "painless" death and to paralyze the death row inmate by preventing spasms and resistance during the short process of execution for the benefit of those watching. In an interview conducted four decades later, Chapman admitted that he had little experience beyond pronouncing death and examining cadavers.[49]

According to the 2006 Human Rights Watch Report on lethal injection in the US, the general public prefers lethal injection to other methods of execution, such as electrocution, lethal gas, or hanging. The process of strapping the death row inmate to a gurney, inserting an intravenous line into a vein, and injecting drugs mimics a medical

47 Frank Lupo and Stephen J. Cannell, "The A - Team" (1983-1987).

48 "The A-Team is Coming, The A-Team is Coming," Season 4, Episode 14, Air Date 21 January 1986.

49 Max Kutner,"Meet A. Jay Chapman, 'Father of the Legal Injection,'" *Newsweek*, 1 May 2017; Deborah W. Denno, "The Lethal Injection Quandary: How Medicine Has Dismantled the Death Penalty," *Fordham Law Review* 76 (2007): 65-66, 49-128.

procedure and appears more humane than alternatives. Lethal injection has become the most prevalent form of execution in the US with all of the remaining thirty death penalty states, along with the federal government, adopting this method. Up until 2009, most states used a three-drug cocktail, starting off with sodium pentothal as an anesthetic to temporarily render the prisoner unconscious. To prevent the prisoner from coming out of the initial sodium pentothal stupor, pancuronium bromide was administered as a paralytic agent so that breathing would stop along with all possibility of movement that might suggest pain or discomfort. As the brain was slowly deprived of oxygen, a stiff dose of potassium was given to stop the heart even if the paralysis did not deprive the brain of oxygen and render the patient brain dead. The anesthetics and paralytic agents are necessary to achieve a deep level of unconsciousness because the potassium chloride, especially in high doses, can be excruciatingly painful as the drug passes like fire through the prisoner's veins before causing cardiac arrest. For nearly three decades, sodium pentothal was the only anesthetic used in lethal injections because of its rapid onset, especially when the prisoner was injected with five to twenty times the normal surgical dose, an amount that could itself be lethal. The pancuronium bromide was nevertheless administered to conceal the agony of a prisoner not sufficiently anesthetized.[50]

The AMA's Code of Medical Ethics prohibits doctors from assisting in capital punishment: "as a member of a profession dedicated to preserving life when there is hope of doing so, a physician must not participate in a legally authorized execution."[51] In several states, including California, it was exceedingly difficult to find trained anesthesiologists willing to expertly monitor sodium pentothal levels, leading to the unfortunate circumstances when the prisoner died in great pain from a botched lethal injection. Dozens of lawsuits have challenged the constitutionality of the lethal injection protocol, leading to periodic stays of execution as states considered alternatives to the three drug cocktails.[52]

The absence of medical professionals during the execution has led to numerous questionable decisions made independently by corrections officers, untrained in anesthetics. For instance, in 1990, the pharmacy director for the Louisiana State Penitentiary recounted a conversation with his equivalent at the Texas Department of Corrections about a recent dosage issue with anesthetics: "We were getting ready to hang up the phone, and I said, 'I have but just one question I need to ask you. Every other state I have spoken to is using 2 grams of sodium pentothal. Why are y'all using five?' And he started laughing and said, 'Well, you see, when we did our very first execution, the only thing I had on hand was a 5-gram vial. And rather than do the paperwork on wasting 3 grams, we just gave all five.'"[53]

50 Human Rights Watch, *So Long as They Die: Lethal Injections in the United States* (Human Rights Watch, 2006), 1-3.

51 American Medical Association, "Ethical Opinion E-2.06: Capital punishment," in *Code of Medical Ethics of the American Medical Association*, 2006-2007 (Chicago, IL: American Medical Association; 2006), 19-20.

52 Human Rights Watch, *So Long as They Die*, 4-8.

53 Testimony of Donald Courts, Special Hearing, Louisiana v. Code, Case No. 138,860, 18 March 2003, Vol. II, p. 58-59. Also cited in Ibid., 17.

Botched executions and unnecessarily inflicted pain have occurred as a result of insufficient medical insight into execution methods and the absence of medical review of lethal injection protocols across the country.[54] In the landmark 2008 case of *Ralph Baze and Thomas Bowling v. John D. Rees, Commissioner, Kentucky's Department of Corrections et al*, the US Supreme Court upheld the constitutionality of the three cocktail lethal injection method that featured sodium pentothal. The plaintiffs, Blaze and Bowling, were each convicted of a double murder and sentenced to death, but each claimed that the lethal injection would violate their Eighth Amendment protection from "cruel and unusual punishment." While the justices deliberated the case between September 2007 and April 2008, the Supreme Court stayed all executions across the country. The eventual decision ruled in favor of Kentucky's Department of Corrections.[55]

The *Baze v. Rees* decision, which precipitated the country's longest moratorium without a public execution, focused the spotlight on the use of sodium pentothal not as a superior anesthetic, but as an inseparable component of lethal injections in the US. Beginning with the first execution which took place 7 December 1982, sodium pentothal was used in an effort to provide a "painless execution." The still widely-used anesthetic, which was already known popularly as the truth serum, began now to be publicly associated with lethal injections.

In 2004, Abbott Laboratories spun off the company's hospital products division, Hospira, which became the world's largest producer of generic injectable pharmaceuticals. Along with many other popular drugs, Hospira assumed responsibility for manufacturing sodium pentothal. In addition to the growing public controversy regarding the anesthetic's use in the legal injection cocktail, Hospira was faced with a Food and Drug Administration (FDA) investigation in April 2010 when drugs made in the company's pharmaceutical plant in Rocky Mount, North Carolina were discovered to have been contaminated. Hospira was forced to abandon the production of sodium pentothal, leaving no other US company with FDA approval to manufacture the anesthetic used by all 32 states (at the time) where capital punishment was legal.[56] Hospira had tried to circulate a letter to prison officials across the country with a request to desist from using sodium pentothal in lethal executions: "Hospira provides these products because they improve or save lives and markets them solely for use as indicated on the product labeling. As such, we do not support the use of any of our products in capital punishment procedures."[57] Despite these protestations, there was no conceivable way that Hospira could prevent prisons from using their product in execution. The

54 Denno, "The Lethal Injection Quandary," 49-50.

55 Ralph Baze and Thomas C. Bowling, Petitioners v. John D. Rees, Commissioner, Kentucky Department of Corrections, 19 July 2007, Capital Case No. 07-5439, Supreme Court of the United States. Courts have interpreted Eight Amendment protection to include execution techniques that pose a substantial risk of harm.

56 Jeffrey Stern, "The Execution of Clayton Lockett," *Atlantic Monthly* 315 (2015): 70.

57 Hospira to Ohio Department of Corrections, 31 March 2010, Death Penalty Information Center.

company was brought to the realization that any profits it made from the sale of sodium pentothal were not worth the public outcry against Hospira and the potential lawsuits that might emanate from its sale.[58] Indeed Hospira's profit from sodium pentothal was "little more than a revenue rounding error" for the world's largest manufacturer of generic injectable drugs. In 2009, for example, sodium pentothal generated only $6 million in US sales which was less than 0.25% of Hospira's total sales that year.[59] The cessation of sodium pentothal production also meant that the drug would no longer be available to anesthesiologists who were now either forced to procure their supplies from abroad or rely on alternative anesthetics.

In June 2010, correctional facilities in Georgia, Arkansas, and California placed orders for the import of sodium pentothal from Mehdi Alavi, a London-based businessman who sold drugs through Dream Pharma, a UK-based international wholesale pharmaceutical distributor. After a formal complaint to the UK government submitted by Maya Foa, an anti-death-penalty advocate, all exports of sodium pentothal to the US were declared illegal. The anesthetic that had once revolutionized the surgical world was now seen as nothing more than a tool of lethal executions and could no longer be exported by European pharmaceuticals who were beholden to the continent's prohibition on capital punishment.[60]

Similar legal and public relations campaigns were leveled against Sandoz, a unit of Novartis AG, whose sodium pentothal products ultimately ended up in the US prison system. Clive Stafford Smith, the head of Reprieve, a UK nonprofit group lobbying against the death penalty, filed a lawsuit in London challenging Sandoz's pentothal shipments to the US, ultimately resulting in the UK decision to ban the drug's export to the US for use in the country's correctional facilities. In response to an accusatory letter sent by Reprieve, Jeff George, then serving as the head of Sandoz, claimed to have been unaware of the issue, emphasizing sodium pentothal's continued importance in treating certain kinds of epilepsy and blaming the distribution practices of third parties for the unapproved sales to the US prison system.[61]

Hospira made one last effort to transfer the production of pentothal abroad, thereby continuing to sell the drug in the US without needing to manufacture it domestically. In a statement released in January 2011, Hospira admitted that this plan too would need to be withdrawn in light of public and legal pressure:

> Hospira had intended to produce Pentothal at its Italian plant. In the last month, we've had ongoing dialogue with the Italian authorities concerning the use of Pentothal in capital punishment procedures in the United States – a use Hospira has never condoned. Italy's intent is that we control the product all the way to the ultimate end user to prevent use in capital punishment. . .we

58 Ty Alper, "The United States Execution Drug Shortage: A Consequence of Our Values," *Brown Journal of World Affairs* 21 (2014): 27.

59 Nathan Koppel, "Drug Halt Hinders Executions In the U.S.," *Wall Street Journal*, 22 January 2011.

60 Stern, "The Execution of Clayton Lockett"; "Death Penalty Opposition: EU Set to Ban Export of Drug Used in US Executions," *Der Spiegel*, 12 December 2011.

61 Koppel, "Drug Halt Hinders Executions in the U.S."

> could not prevent the drug from being diverted to departments of corrections for use in capital punishment procedures. Based on this understanding, we cannot take the risk that we will be held liable by the Italian authorities if the product is diverted for use in capital punishment. Exposing our employees or facilities to liability is not a risk we are prepared to take. Given the issues surrounding the product, including the government's requirements and challenges bringing the drug back to market, Hospira has decided to exit the market. We regret that issues outside of our control forced Hospira's decision to exit the market, and that our many hospital customers who use the drug for its well-established medical benefits will not be able to obtain the product from Hospira.[62]

With no domestic sodium pentothal manufacture approved by the FDA and a complete ban on imports from European pharmaceuticals, US correctional services began importing the drug from a small Indian firm called Kayem Pharmaceuticals. Shipments of sodium pentothal were documented to have been sent to the correctional services of both Nebraska and South Dakota in December 2010 and February 2011, respectively. In an ironic and unfortunate twist of fate, earlier attempts to purchase sodium pentothal from a British firm Dream Pharma resulted in the tortuous death of three prisoners as a result of defective anesthetic and led to a delay in the execution of Nebraska inmate Carey Dean Moore until the drug could be purchased from a more reliable pharmaceutical source. Moore's execution ended up being delayed until 14 August 2018 when the Nebraska State Penitentiary carried out its first capital punishment since 1997. It was also the first time in the US that lethal execution replaced sodium pentothal with fentanyl, an opioid used as pain medication.[63] When word reached Kayem that the sodium pentothal was indeed being used for executions, all future sales were put on hold. Rather than continue the fruitless search for new sodium pentothal manufacturers, the Oklahoma Correctional Facilities broke ranks and chose to use an alternative barbiturate, pentobarbital sodium, which had previously been used as a short-term therapy for insomnia and was readily available from European manufacturers.[64] Pentobarbital proved a short-lived solution as Lundbeck, the Danish international pharmaceutical company, announced restrictions on its export of the drug sold under the trade name Nembutal, following revelations that it was being use for lethal injection in the US. Staffan Schiuberg, the president of Lundbeck, voiced his opposition in an open letter to Ohio prison officials: "We recognize that we cannot control how licensed health care professionals use this or any pharmaceutical product. Nevertheless, we urge you to

62 Statement from Hospira Regarding its halt of production of Pentothal (sodium thiopental), 21 January 2011.

63 "US Death Row Injection Comes from Mumbai Firm," *Times of India*, 5 April 2011; "Cabdriver Killer Carey Dean Moore Recounted How He Got to Death Row," *Omaha World Herald*, 14 April 2018.

64 Stern, "The Execution of Clayton Lockett."

discontinue the use of Nembutal in the execution of prisoners in your state because it contradicts everything we are in business to do – provide therapies that improve people's lives."[65] Schiuberg's announcement introduced an ironic notion of morality in the pharmaceutical industry by collectively punishing the majority of physicians using Nembutal medicinally because of the misuse by a minority for executions.

Lundbeck's decision was followed by dozens of other global companies voluntarily taking similar steps to prevent US correctional facilities from purchasing execution-related drugs through their facilities.[66] Taken in isolation, the cultural associations and legal entanglements surrounding sodium pentothal as a truth serum and as a component of the lethal injection cocktail would not have been enough to sign the death warrant of sodium pentothal in the operating room. But coupled with the discovery and popularization of an alternative anesthetic during the 1980s and 1990s, sodium pentothal gradually began to lose its therapeutic niche and began its precipitous fall from grace.

THE DECLINE OF SODIUM PENTOTHAL

When Hospira and pharmaceutical companies in Europe and India announced a virtual embargo on sodium pentothal exports to the US as a safeguard against lethal injections using the drug, the decision was met with protest by the medical community. The American Society of Anesthesiologists issued a clear statement against the decisions, highlighting the fact that the scarcity of sodium pentothal in the operating room would lead to the death of patients who would be forced to use less efficacious anesthetics, a consequence of anti-capital punishment advocacy:

> Sodium thiopental is an important and medically necessary anesthetic agent that has been used for years to induce anesthesia in patients undergoing surgical procedures. Although its use has decreased in recent years due to the introduction of newer medications, such as propofol, sodium thiopental is still considered a first-line anesthetic in many cases including those involving geriatric, neurologic, cardiovascular and obstetric patients, for whom the side effects of other medications could lead to serious complications. The ASA certainly does not condone the use of sodium thiopental for capital punishment, but we also do not condone using the issue as the basis to place undue burdens on the distribution of this critical drug to the

65 "Lundbeck Overhauls Pentobarbital Distribution Program to Restrict Misuse," H. Lundbeck A/S, 1 January 2011. Staffan Schiuberg, president of Lundbeck Inc. to Gary C. Mohr, director of the Department of Rehabilitation and Correction at Columbus, OH, 26 January 2011, Death Penalty Information Center. Ironically, Nembutal is used by Dignitas, a Swiss company that promotes "sensible euthanasia," or assisted suicide. The patient is given 15 grams of Nembutal by mouth, administered by a nurse who comes around the next morning to confirm that the individual is indeed dead. Richard Griffith and Cassam Tengnah, "Assisted Suicide: Increased Support for a Change in the Law," *British Journal of Community Nursing* 14 (2013): 359, 356-362.

66 Alper, "The United States Execution Drug Shortage."

> United States. *It is an unfortunate irony that many more lives will be lost or put in jeopardy as a result of not having the drug available for its legitimate medical use.*[67]

Legal challenges related to the pain and comfort of executions thereby indirectly caused a patient safety issue by removing an effective anesthetic in response to its misuse as part of the lethal injection cocktail. The problem was ultimately not with the anesthetic itself but with capital punishment more generally.

For the past decade, sodium pentothal has not been available in the US and is gradually being replaced in other Western nations by propofol. Even attempts to import it for teaching purposes have been unsuccessful. As an example, Sukumar Desai at Harvard Medical School worked with officers at the FDA, but was informed that he would have to become an official company importing a drug into the US and complete several hundred pages of paperwork, something the FDA officials suggested was totally beyond the capabilities of one individual. The banned importation of sodium pentothal was also upheld in 2016 when a shipment of the drug was detained by the FDA, en route to the Texas Department of Criminal Justice. The FDA cited the absence of clinical trials substantiating pentothal's use for lethal injection, while the State of Texas argued that the drug's detention was a legal violation of a state's right to choose the manner of public execution. Furthermore, there was a serious concern about mislabeling occurring in drugs, particularly pentothal, manufactured abroad without proper oversight.[68] Coupled with the unavailability of pentothal on the open markets was the discovery and gradual adoption of an anesthetic alternative.

In the late 1980s, a new intravenous anesthetic named propofol was introduced with great marketing efforts during a period of time in medicine when there was a preference for outpatient surgeries. Propofol's principal benefit was that it allowed patients to wake up clearer headed, thus making it a drug of choice for outpatients who were to be sent home shortly after surgery. It also had mild anti-nausea properties, another selling point. Although patients complained of pain at the injection site, there were no major medical roadblocks barring propofol's adoption by anesthesiologists.[69] Initially expensive, its price came down after the period of exclusive rights of the initial manufacturer.

Since the introduction of propofol during the 1980s, numerous studies have compared the effectiveness and benefits of sodium pentothal to propofol. Most of the studies found little or no significant statistical differences between the performance of either anesthetic. Randomized and double-blind clinical trials comparing the anesthetics similarly produced results with few differences between the options available.[70]

67 "ASA Statement on Sodium Thiopental's Removal from the Market," 21 January 2011, emphasis by the authors.

68 The FDA's Admissibility Determination for Sodium Thiopental Entry – Texas Department of Criminal Justice, 20 April 2017.

69 Rajinder Mirakhur, "Induction Characteristics of Propofol in Children: Comparison with Thiopentone," *Anaesthesia* 43 (1988): 593-594, 593-598.

70 Hyunsook Hong, Seokyung Hahn, Yunhee Choi, "Evaluation of Propofol in Comparison with Other General Anesthetics for Surgery in Children Younger Than 3 Years: A Systematic Review and Meta-Analysis," *Journal of Korean Medical Science* 34 (2019): 2, 1-15; Oktay Ozge Canbek, Derya Ipekcoglu, Okan Oktay Menges, Murat Ilhan Atagun, Nesrin Karamustafaloglu, Ozlem Zekiye Cetinkaya, Mehmet

Not all the studies were inconclusive. In fact, many found flaws in propofol when compared with a pentothal alternative. For instance, one study found that propofol slightly delayed logical memory function 24 hours after surgery.[71] Other studies have concluded that pentothal possesses some relatively minor advantages when compared with propofol.[72] Propofol also presented a litany of risks, different but of equal significance to the early risks presented by incorrect sodium pentothal dosage during WWII. Propofol's risks include some addictive properties, along with potentially fatal complications emanating from the drug as a potent respiratory depressant. Michael Jackson's propofol overdose in 2009 also placed a tragic celebrity face on propofol, just as Marilyn Monroe's death from an overdose of Nembutal, a popular sleeping pill and precursor to sodium pentothal, cast scrutiny on the dangers of the anesthetic during the 1960s.[73] In essence, there were few medical effectiveness differences between propofol and sodium pentothal, and certainly not enough to warrant such a major transformation in the field of anesthesiology based on clinical decisions alone.

Surgeons and anesthesiologists continue to bemoan Hospira's ultimate decision to halt pentothal's production amid public critique and the negative imagery surrounding the drug. While propofol can serve as an alternative under most circumstances, there are certain high-risk situations where patient lives have been placed in jeopardy because of a social and political debate. For example, propofol's side-effects could lead to serious complications in elderly cardiovascular patients as well as following emergency caesarean sections where propofol could unnecessarily sedate the infant along with the mother.[74]

Were the pentothal vs. propofol debate to have taken place in isolation, without the influence of decades of negative associations surrounding sodium pentothal, the calculus made in the field of anesthesiology would have been dominated by Martin Pernick's "calculus of suffering," or the degree of risk proportional to the degree of pain relieved.[75] When weighing the effectiveness and appropriateness of either propofol or sodium pentothal, the clinical decision would be made according to clear clinical guidelines, rather than social sensitivities and policy decisions. Without the negative associations, it is likely that sodium pentothal would have still been available as an anesthetic of choice in the operating room, albeit within a therapeutic niche shared by propofol.

Cem Ilnem, "Comparison of Propofol, Etomidate, and Thiopental in Anesthesia for Electroconvulsive Therapy: A Randomized, Double-Blind Clinical Trial," *Journal of ECT* 31 (2015): 92-93, 91-97; B. Rozec, H. Floch, P. Berlivet, P. Michel, Y. Blanloeil, "Propofol Versus Thiopental by Target Controlled Infusion in Patients Undergoing Craniotomy," *Minerva Anestesiologica* 80 (2014): 761-763, 761-768.

71 P. J. Heath, T. W. Ogg, W. R. Gilks, "Recovery after Day-Case Anaesthesia: A 24-Hour Comparison of Recovery after Thiopentone or Propofol Anaesthesia," *Anaesthesia* 45 (1990): 356-359.

72 Massimiliano Nuzzi, Dario Delmonte, Barbara Barbini, Laura Pasin, Ornella Sottocorna, Giuseppina Maria Casiraghi, Cristina Colombo, Giovanni Landoni, Alberto Zangrillo, "Thiopental Is Better Than Propofol for Electroconvulsive Therapy," *Acta Bio Medica: Atenei Parmensis* 88 (2017): 450-451, 450-456.

73 Andrew Hartle and Surbhi Malhotra, "The Safety of Propofol," *British Medical Journal* 339; 7727 (2009): 928-929.

74 Nathan Koppel, "Execution Drug Halt Raises Ire of Doctors," *Wall Street Journal*, 25 January 2011.

75 Martin Pernick, "The Calculus of Suffering in Nineteenth-Century Surgery," *Hastings Center Report* 13 (1983): 26-36.

Marc Popovich, an anesthesiologist at the Cleveland Clinic observed that "for generations, clinical pharmacology in critical care centered on the idea that drugs were chosen for a certain condition or indication relative to their efficacy, pharmacodynamics, pharmacokinetics, bioavailability, or actions on distinct receptors." In other words, medications were often given because they were the most effective. In the new age of pharmaceuticals, profit analysis, and the erosion of predictable manufacturing by legal and popular culture challenges, medications are not always chosen for purely medical reasons.[76] Despite the fact that propofol was not remarkably superior to sodium pentothal, the decreasing availability of pentothal on the open market has been the determining factor for the default choice of available anesthetics. The lingering concern about anesthesia's reliance on propofol is that manufacturers have little economic incentive to produce the anesthetic, a generic drug with a relatively costly production and high liability, a consequence of propofol's use in the operating room. As a result, the drug choices made by anesthesiologists are often a consequence of the vicissitudes of pharmaceutical manufacturing, such as the recent shortage of propofol following an outbreak of hepatitis C following the inappropriate and unsanitary use of propofol manufactured by Teva Pharmaceuticals which was responsible for 40% of the US market share at the time. A lawsuit against Teva ultimately awarded $356 million to one male patient who developed hepatitis C, thus setting a dangerous precedent for high liability risk in respect of propofol manufacture. Similarly, Hospira, who had only recently phased out the manufacture of sodium pentothal, was faced with a 2010 crisis in a North Carolina manufacturing plant where propofol was produced. The plant was shut down and a recall of certain lots of propofol was issued, citing possible contamination.[77] Despite alarming and dangerous shortages of propofol, the default choice for most anesthesiologists in the US, the import or production of sodium pentothal remains curtailed by the legal, policy, and cultural public image of the disgraced anesthetic.

Once the king of anesthetics, sodium pentothal has given way to public pressure, nefarious non-surgical uses, and a stigma closely associated with the truth serum and lethal injection. Once readily available across the world, sodium pentothal is almost impossible to import into the US, leading to a story of the misappropriation of science and deleterious consequences of popular imagery, misinformed policy decisions, and the economics of the pharmaceutical industry.

76 Marc J. Popovich, "Bioavailability or Just Availability? How the National Propofol Shortage Example May Transform Tenets of Critical Care Management," *Critical Care Medicine* 40 (2012): 661-662.

77 Christopher Hvisdas, Andrea Lordan, Laura Pizzi, BrandiThoma, "US Propofol Drug Shortages: A Review of the Problem and Stakeholder Analysis," *American Health & Drug Benefits* 6 (2013): 171-175.