

Calomel and its Critics

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ABSTRACT

Physicians of the 18th and 19th century sought a treatment to cure all diseases known to man.¹ The advances made by physics, chemistry, and anatomy led medical scientists to propose radical new theories to treat disease.² These theories led doctors to prescribe harmful medicaments such as the purgative calomel to treat nearly every ailment. Not all physicians subscribed to these new dangerous treatment protocols. While the most prolific writers of the day preached calomel as a cure-all, there were those in the shadows of medicine who chastised them for liberally prescribing this poisonous compound.³ Despite the significant amount of evidence against calomel since its introduction to medicine, it took until the mid 20th century for the medical community to unanimously realize calomel's lethal properties. At the height of its popularity in the late 18th and early 19th centuries many respected physicians believed that it could cure disease. Nevertheless, there were doctors who disagreed with the general consensus that calomel was therapeutically beneficial. These critics of calomel were the pioneers of evidence-based medicine, and by approaching medicine scientifically they found that calomel was more harmful than beneficial in treating disease.

Calomel is a simple compound insoluble in both fat and water, and composed of mercury and chlorine atoms (Hg_2Cl_2). Calomel was named for its black color (Calomelous is Greek for kalo = beautiful, and melos = black).⁴ The Greek philosopher Democritus was the first to describe a substance resembling calomel in a manuscript written circa 400 BC. The Arabs in 1200 AD rediscovered Democritus's manuscript and began using the substance to treat syphilis.⁵ Paracelsus, a sixteenth century Swiss physician and chemist, was the first to employ calomel as a therapeutic cathartic in Europe.⁶ Paracelsus is credited as being the first medicinal chemist, and his work with simple ionic compounds initiated a shift in medicine from plant-based medicines to synthetically derived medicinal compounds.⁷

Paracelsus and physicians after him were attracted to calomel because of its ability to rid the body of black bile. The removal of black bile was, at the time of Paracelsus, medically necessary because it was one of the four humors that made up the humorist theory of disease.⁸ Humorist theory, which was originally proposed by Hippocrates in the 4th century BC, espoused that disease was an imbalance of the four humors, consisting of black bile, yellow bile (urine), blood and phlegm. Correcting this imbalance or dyscrasia (Greek for "bad mixture") was believed to cure disease. Calomel was used to rid the body of black bile and restore the equilibrium of humors.⁹ For over 2 millennia,ⁱ humorism remained the fundamental model of disease in Western medicine.¹⁰

At the time of Paracelsus, many were skeptical of using calomel as a diuretic or purgative. Mercury had been used medicinally since the time of antiquity, and its toxicity was well understood.¹¹ Classically, mercury's distinguishing side effect is salivation followed by its more serious toxic effects including tooth loss, weakness, dementia, and eventually death.¹²

ⁱ In 1878 Louis Pasteur proposed the germ theory of disease, abolishing humorism. The germ theory of disease stipulates that microscopic pathogenic organism cause disease.⁹

While Paracelsus cautioned against the use of calomel, he stressed that calomel should be used as a treatment of last resort. He viewed calomel similar to the way modern physicians view chemotherapy, and recognized that its narrow therapeutic window and its toxic properties often superseded its beneficial effects to living organisms.¹³

Despite Paracelsus's caution, 18th and 19th English and American physicians would make calomel into one of the most infamous medical treatments of that time. Calomel's arrival to England was announced in the 1618 London pharmacopeia.¹⁴ The inclusion of calomel in this highly respected master book of medicines encouraged physicians to employ it as a purgative. At this time, mercurials were becoming more popular among Western practitioners to treat syphilis, cholera, and other diseases that failed to respond to less toxic treatments. Calomel became the mercurial of choice because it was tasteless and therefore, could be given orally. Calomel caused salivation in high doses given over an extended period of time, leading many to believe the drug was relatively harmless.¹⁵ The desirable purgative and diuretic effects of calomel caused patients to lose significant amounts of fluid resulting in severe (life threatening) dehydration. When combined with bloodletting, as was the norm, many died of hypovolemic shock brought on by this "heroic" treatment protocol.¹⁶

One of the leading medical authorities of the 18th century was William Cullen (1710-1790). Cullen was a brilliant physician who researched human physiology, was knowledgeable of humorism, well versed in classical physics, and lectured on chemistry at the University of Edinburg. Drawing from this knowledge base, he developed nosology, a system of classifying disease. From Nosology, Cullen developed his theory of nervous energy based on his observation that fevers are the result of dyscrasia caused by "nervous energy" that triggers the pulse to beat rapidly.¹⁷ Cullen believed that treating patients with bloodletting and purgatives reduced the amount of nervous energy in the body, and therefore would cure the fever. Cullen's

purgative of choice for removing black bile was calomel for its rapid and powerful results.¹⁸

Despite his advocacy for its use, he cautioned that calomel should be prescribed at the minimally effective dose.¹⁹ Benjamin Rush, Cullen's protégé, ignored Cullen's warnings, and went on to advocate for the calomel to be prescribed in excessive "heroic" doses to treat disease.²⁰

Benjamin Rush was a gifted, driven, and respected physician who worked tirelessly for his patients. He was a philosopher, a great thinker and was held in the highest esteem. He signed the Declaration of Independence and is considered one of the founding fathers of the United States. He believed that he was destined for greatness and spent every minute of his life working to better humanity.²¹ Unfortunately, despite his genius, he valued theory over observation. As a result, his therapies tended to cause harm and sometimes even led to the early demise of his patients. Over time, he trained many doctors to do the same.²²

Benjamin Rush was educated at the Edinburgh School of Medicine in Scotland. He matriculated in 1766 and graduated in 1768. He wrote his thesis on the anatomy of the colon. His early study of the colon would later play a role in his uniform treatment of disease known as "depletion therapy".²³ Depletion therapy was based on Rush's belief that all diseases were caused by too much friction between the blood, its vessels, and the blockage of black bile in the intestines. Rush therefore bled all of his patients excessively and prescribed what he called "heroic" doses of calomel.²⁴ Utilizing excessive purges and generous bloodletting, he is believed to have killed thousands during the yellow fever epidemic in Philadelphia of 1793. This episode cemented his status as a controversial figure in medicine. Following two more epidemics of yellow fever in the late 1790's, Rush's reputation as a healer began to decline. To some he was regarded as a heroic healer for staying in the city and treating every ill person who came to his door. To others he was "the mortal angel of death", as they believed he killed more people than he healed.²⁵ William Cobbett, a harsh critic of Rush, claimed that Rush's depletion therapy was

“one of those great discoveries which are made from time to time for the depopulation of the earth”.²⁶ Rush was so enraged; he sued Cobbett in civil court for defamation of character and won.

The treatments of Cullen and Rush inspired a fear of physicians through the 18th and 19th century. Charles Churchill captures this fear of doctors in his poem, *Night*.

The surest road to health, say what they will,
Is never to suppose we shall be ill.
Most of those evils we poor mortals know,
From doctors and imagination flow.

-Charles Churchill (British poet lived from 1731-1764), taken from his poem *Night*.²⁷

Despite the lawsuit, Rush devoutly believed that his treatment worked. He believed that bleeding and calomel cured disease. Further, he convinced himself beyond reasonable doubt that his patients were dying of their disease, not his treatment. However, none of his writings showed any empirical evidence that his treatments were effective. He believed in his therapy with a religious zeal. His excessive bloodletting and heroic purges with calomel were so extreme that his patients died before they showed signs of mercury poisoning, leading him to believe that people were dying of the disease instead of prescription cure.²⁸

The work of Rush and Cullen led Samuel Hahnemann to found the Homeopathic School of Medicine. In 1796, Hahnemann wrote that he first conceived the fundamental theories of homeopathic medicine while translating Cullen’s book, *A Treatise of The Materia Medica*. In its simplest terms, Homeopathy is based on the premise *similia similibus curentur* (like cures like) and is distinct from allopathic medicine in its theory and practice.²⁹ He expressed his views on Rush’s favorite treatment of bloodletting and calomel in his manifesto *Samuel Hahnemann's Organon of Homœopathic Medicine*.

“Among chronic diseases we must still, alas!, reckon those so commonly met with, artificially produced in allopathic treatment by the prolonged use of violent heroic medicines in large and increasing doses, by the abuse of calomel...shedding streams of blood...whereby the vital energy is sometimes weakened to an unmerciful extent”.³⁰

Hahnemann’s theory spread throughout Europe, chasing the work of Cullen and Rush. Most physicians were inclined to trust Cullen and Rush because they were more respected than Hahnemann. However, the growing mistrust of Allopathic medicine’s violent treatments led some physicians to train as homeopaths.³¹ While homeopathic medicine is still practiced today, its theories and treatments have been repeatedly proven to be ineffective.³² Not all the early critique of calomel came from the homeopaths. Some of the allopathic physicians also saw signs that calomel was ineffective.

William Buchan, MD, was one of those who silently voiced his opposition to Rush’s depletion theory. As a noted student of math and botany, Buchan published a medical textbook in 1799. His book cautioned against the use of mercury, citing the fact that many of those who worked in mercury mines rarely survived for more than 4 years. Furthermore, Buchan warned against the use of calomel and advocated its use only in the case of worms and syphilis. These observations and prescriptions by Buchan clearly oppose Rush's depletion theory. Unlike Rush, who was exercising a priestly authority, Buchan was more of a scientist. He realized there was no universal treatment for disease and instead, painstakingly described a specific treatment for every fever and every disease known at the time.³³ Despite the superiority of Buchan’s work, he lacked the influence of Rush, and failed to effectively spread his superior medical doctrine.

Benjamin Rush survived the attacks on his credibility and continued to teach depletion theory at the College of Philadelphia Medical School (now a part of the University of

Pennsylvania). In 1799, when former President George Washington became ill with an acute respiratory illness, Rush's use of calomel and bloodletting killed him before the disease could.³⁴ As a gifted lecturer and prolific writer, his theory of medicine spread across the United States and Western Europe. He influenced over 3,000 students at the College of Philadelphia Medical School over the course of his 40 years of teaching. His students and writings are responsible for the infamous heroic age of medicine where patients were bled and purged with a ferocity and horror never seen before in medicine.³⁵ In the year 1813, at the age of 67, Rush became ill and had his personal physician treat him with his own prescription of heavy doses of calomel and bloodletting. As with all of his other patients, he is believed to have died from his treatment rather than the disease.³⁶ His friend and fellow founding father Thomas Jefferson wrote a eulogy that lamented Rush's contribution to medicine.

“For classic learning I have become a zealous advocate; and in this, as in his theory of bleeding and mercury, I was ever opposed to my friend Rush, whom I greatly loved; but who has done much harm, in the sincerest persuasion that he was preserving life and happiness all around him.”³⁷

The death of Benjamin Rush would not end the excessive use of calomel. Having trained an entire generation of American doctors, his legacy of depletion theory lasted through the mid 19th century.

The heroic age of medicine was characterized by daring purges and the excessive use of calomel, the dose of which was increased by Rush's protégés. The heroic age began to fade as physicians in Europe began to write about the dangers of bloodletting and prescribing calomel.³⁸ This was highlighted by the books written by Dr. George Sigmud in 1840 and Dr. Haberson in 1860, which emphasized the harmful effects of calomel.^{39,40} In the United States, the Union Surgeon General, William A. Hammond noticed that soldiers seemed to be dying after being

treated with calomel. In 1863, he performed one of the first empirical studies on the effectiveness of calomel in treating illness. He found that patients treated with calomel died at a greater frequency than those who received no treatment. Following his study, he banned calomel from being used to treat soldiers in the Union army.⁴¹ Despite this, many physicians still believed that calomel could cure disease and chose to ignore its lethal properties.

In 1879, Louis Pasteur performed several experiments that proved disease was caused by microorganisms.⁴² Pasteur's experiments put an end to the theory of humorism and effectively dismissed the need to purge and bleed disease away. Despite mounting evidence that calomel should be removed from pharmacies, papers were published through the late 1890's promoting its use.⁴³ It took a fundamental change in the way that American medical students were educated to end the American doctor's love affair with the beautiful black powder, calomel.

In the late 19th century, Andrew Taylor Still and William Henry Welch transformed American medical education with the goal of teaching medical students evidence-based medicine. Dr. Still founded Osteopathic Medicine in 1892 because he rejected the obsessions of traditional allopathic physicians with harmful drugs like calomel.⁴⁴

While Still formed a new school of medicine, it was William Welch, M.D. who transformed American medicine to such an extent that he is considered a father of modern medicine in the United States. He was one of the founders of the Johns Hopkins School of Medicine. The school opened in 1893, and established vigorous medical education standards that promoted the scientific basis of medicine. To do this, Welch also required applicants to John's Hopkins to hold a bachelors degree in a physical science and to be fluent in Greek and Latin. The Johns Hopkins model laid the foundation for the groundbreaking medical education reforms of the early twentieth century.⁴⁵

Although the new standards in medical education changed the way physicians thought about disease, older physicians and those who studied at substandard medical schools continued to use calomel to treat illness into the early 20th century. The last mention of calomel was in the 1967 US Dispensatory.⁴⁶ Today, it can still be found in some third world countries being prescribed by believers in alternative medicine. Cases of calomel poisoning, while rare, still occur.⁴⁷

Even at the height of its use, calomel was known to have lethal side effects and no evidence of therapeutic benefit. It was known to be toxic since its discovery, and yet it became one of the most popular drugs of the 19th century. Calomel, however, clearly had been shown to do far more harm than good. Surprisingly it continued to be used even when the evidence indicated that the harm it caused far outweighed any potential benefits. Few commonly used drugs in history have been used so indiscriminately as calomel, and with such lethal consequences. However, the thought of doing nothing to treat an illness can be more terrifying for a physician than attempting a dangerous heroic cure. Although modern pharmaceuticals can do serious harm, they are prescribed because their benefits outweigh their harmful effects. The legacy of calomel should serve as a cautionary tale to remind doctors and patients alike that our treatments should always have a strong foundation in evidence-based research; and that sometimes, the best treatment may be to do nothing at all.

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