Pulmonary Disease in History and Biography

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This is to acknowledge that Dr. Pitcher has not disclosed any financial interests or other relationships with commercial concerns related directly or indirectly to this program. Dr. Pitcher will not be discussing off-label uses in his presentation.

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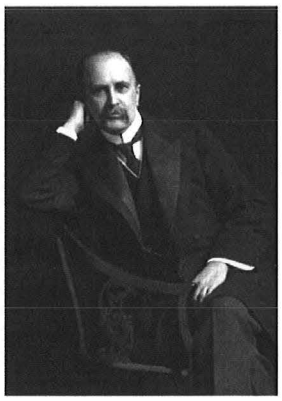
Dr. Pitcher's primary interests are pulmonary physiology, pulmonary infections, obstructive lung disease, lung cancer, pulmonary embolism, general critical care, critical care pharmacology, graduate medical education, quality improvement, and medical administration.

Introduction:

In this presentation I have set out to weave a narrative that draws upon examples of pulmonary disease in the lives of several notable individuals to illustrate the effects of these disorders on their lives and perhaps even the course of history. All of which is intended to provide a backdrop for discussing how medicine was practiced in the past and perhaps providing lessons for the present.

The list of famous people who suffered or died from diseases of the chest is long indeed; most of us know of examples. Smoking-related diseases account for many in the modern era. Lung cancer claimed the lives of Desi Arnaz, Jack Benny, Yul Brenner, Chuck Connors, Gary Cooper, Walt Disney, Arthur Godfrey ("smoke 'em [Chesterfield cigarettes] by the carton"), Betty Grable, Robert Mitchum, Ayn Rand, Ed Sullivan, and John Wayne to name just a few [1]. COPD felled many as well including John Huston, R.J. Reynolds and his grandson (of the R.J. Reynolds Tobacco Co.), and Dick York (the first Darrin Stephens on *Bewitched)* [1].

Though the ill of effects of smoking seem obvious to us now, this was not always the case. Indeed, one of the paragons of medicine, Sir William Osler, was himself a long-time smoker. He thought it to be a generally harmless habit in moderation and even spoke of its benefit: "The effects of habitual use are very varied. In the large majority of persons the habit in moderation is harmless, to many it is beneficial"[2].



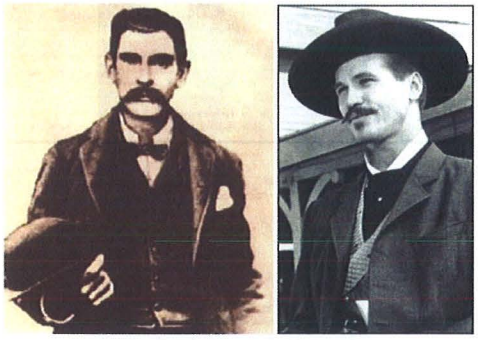
Prior to modern times, however, other pulmonary diseases dominated the picture, especially infections such as pneumonia, influenza, and tuberculosis. Osler died of *Hemophilus influenzae* pneumonia and empyema, which he diagnosed himself and predicated its fatal outcome; "Archie [Mallock], you lunatic, I've been watching this case for two months and I'm sorry I shall not see the post-mortem…" [3]. William Harrison was the first American president to die in office. He gave the longest inaugural address in history and served the shortest term. He delivered his address in cold, wet weather without coat or hat and then died on his 32nd day in office of pneumonia [4]. James Buchanan and Herbert Hoover died of pneumonia; Martin van Buren of influenza. Pneumonia

ultimately claimed its share of civil war combatants, including Generals Robert E. Lee, William Tecumseh Sherman, and Stonewall Jackson (whom we will come back to in more detail).

Tuberculosis has felled the mighty and wealthy (Henry Clay, Jay Gould), and the lowly outlaw (Doc Holliday, Bob Younger) [5]. TB seems to have been particularly unkind to authors and poets (O. Henry, John Keats, D.H. Lawrence, Henry David Thoreau, Walt Whitman) to the extent that it was almost romanticized, referred to as the "muse of literature" [6]. Though he recovered and lived a long life thereafter, Oral Roberts claimed to have been moved to his calling by God during a worship service with a healing evangelist he had sought at age 16 when he developed an advanced case of tuberculosis; "Then I heard that voice I've heard many times since: 'Son, I am going to heal you, and you are to take my healing power to your generation. You are to build me a university and build it on my authority and the Holy Spirit.'" He died at the age of 91 of pneumonia [7].

Doc Holliday: Tuberculosis

Doc Holliday has occupied a conspicuous place in popular culture, having been portrayed in movies (Kirk Douglas, *Gunfight at the OK Corral*, 1957) and especially Val Kilmer's iconic role in *Tombstone* [8]. But it is unlikely that Doc would ever have found himself at the side of Wyatt Earp in Tombstone's OK Corral, blazing away with his pistol and fatally shot-gunning Tom McLaury of the Clanton gang if it had not been for his tuberculosis.

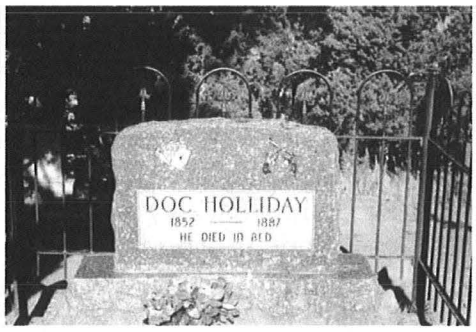


John Henry ("Doc") Holliday was born and raised in Georgia. He trained as a dentist in Pennsylvania and returned to practice in Georgia. However, he developed tuberculosis which he likely contracted from either his mother or step-brother who both died of the disease [9]. He was thought to have an advanced case. The common story is that he moved west on the advice of physicians to seek better climate [10], though there is some evidence that problems in his professional and personal life (possible illegitimate children, definite drinking and gambling) may have contributed to his decision to leave [11].

Interestingly, the first stop he made on his way westward was in Dallas, where he arrived in 1873 at the end of the train line. If, indeed, he had left Georgia to find a better climate, it is hard to see that Dallas was any different or certainly any better; it had just been closed for a month the previous spring for yellow fever [11]. He established his dental practice with a family friend, Dr. John Seegar, in an office at 56 Elm Street [11, 12]. The site no longer exists (though likely would have been near the site of the present Lew Sterret building). Elm street at the time ran all the way to the river, which frequently flooded downtown Dallas. The river was later dredged and re-routed and the Elm, Main and Commerce were brought together at Dealy Plaza with construction of the triple underpass in 1936 [13].

Holliday's tenure in Dallas marked his first gun fight on New Year's Day, 1875 (both parties missed each other, were arrested, fined and released). He sustained himself largely through dealing Faro rather than through dentistry. His original practice having folded in 1874, he moved to a new office above the Dallas County Bank on the corner of Main and Lamar [11, 12]. He spent time in the surrounding towns of Dennison and Fort Griffith Flat. Following his fatal shooting of a soldier from Fort Richardson in Jacksboro, he moved on west [11].

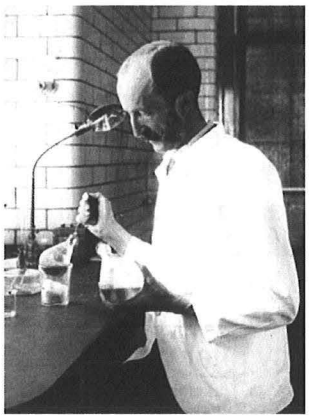
Ultimately he befriended Wyatt Earp (whom he had met for the first time in Fort Griffith) and though plagued with his tuberculosis throughout, he went on to his more famous exploits in Kansas, Arizona, and Colorado. In May, 1873, he went to Glenwood Springs, Colorado for the "cure" in the local sulfur springs that the Ute Indians believed to have curative power. Although popular legend suggests that he entered a sanatorium there, he in fact checked into the Hotel Glenwood (shown below) and continued dealing Faro until he became bedbound. Perhaps hedging his bets, he befriended a Catholic priest and a Presbyterian minister. Unlike the movie depiction (the loyal Wyatt Earp at his bedside), he died alone in his bed, boots off, but gun and knife on the nightstand, on November 8, 1887 [11]. The average life expectancy after diagnosis of TB at the time was 15 to 25 years; Doc Holliday had created a legend of himself in his 15 or so years.



The advice Doc Holliday received to move westward for his TB was a common one based upon the theory of climatic therapy for consumption (or phthisis). Much was written about which locales and climates best favored healing, but common advice was that "Dryness, equability, and purity of the atmosphere are

essential elements of a favorable climate" [14]. Moving to better climates had been heeded by legions of luminaries over time, including Cicero who took a long voyage to Greece and Egypt; Keats who went to Rome; and Shelley who fled to Venice [6]. Osler himself had written that "for more than two centuries the cleared-headed members of the profession have known that an open-air life sometimes cures a case of phthisis" [15]. In some cases, this meant simply moving to another location. However, taken together with notions about diet, exercise, and what was referred to in part as rest therapy, climatic therapy provided the basis for the development of sanatoria, most of which focused on TB. Spas for the wealthy became fashionable in the Bavarian alps, southern France, and in England [6, 15].

In the United States, the development of the sanatorium at Saranac Lake in the Adirondacks of northern New York by Edward Livingstone Trudeau set the mold for American sanatoria. Trudeau was the first president of National Association for the Study and Prevention of Tuberculosis, founded in 1904 and now known as the American Lung Association. The American Sanatorium Association was founded the next year and was renamed in his honor; The American Trudeau Society later became the American Thoracic Society. Its highest honor is the Trudeau Award.



Trudeau contracted tuberculosis while working as a physician in New York City. His condition deteriorated to the point he could no longer work. He decided that if he was dying, then he would attempt to live life to the fullest and most enjoyable extent he could. To him, this meant getting out in the wilds to fish and hunt. He went the Adirondacks for this purpose (and not for its putative climatic benefits). He shot a deer on his first day from a litter mounted on a boat. After a time he returned to New York, feeling that his symptoms and condition improved. After several cycles of improvement and decline, he decided to move to Saranac Lake permanently. For a time he also practiced medicine for the small local population, but then founded the Adirondack Cottage Sanatorium in 1884 at Saranac Lake where he worked for almost forty years before dying himself of TB. His son and grandson both served as directors [16]; his great-grandson Garry created *Doonesbury*.

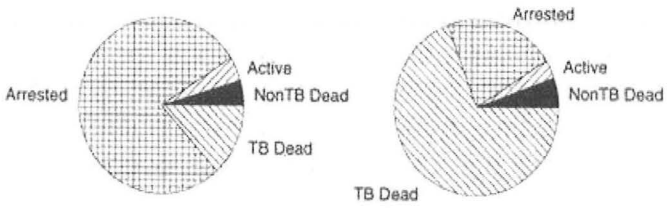

Unlike European institutions that catered largely to the rich, Trudeau was keen to provide treatment opportunities for the lower socioeconomic classes. The initial grounds contained a limited number of cottages and first patients were two sisters who had been factory workers in New York City. The Sanatorium was expanded to become a sprawling complex through Trudeau's considerable fund-raising skills. Numerous similar facilities sprang up in the area, constituting the major economic engine for the region for several decades [6, 15, 16]. One of the most famous of Saranac Lake patients was Robert Louis Stevenson, whose later use of cocaine (occasionally prescribed for TB) has been credited with his shift in literary style that produced *The Strange Case of Dr. Jekyll and Mr. Hyde*.

The therapeutic approach was largely based upon Dr. Hermann Brehmer's experience with the "rest cure", focusing largely on bed rest and graded expansion of limited exercise [17, 18]. Trudeau was also guided by Koch's work and established his own lab where he learned to stain and culture TB. He conducted animal experiments and wrote expansively. He developed theories of the effects of rest therapy, which presaged more modern understanding of the role of innate and acquired immunity on the course of the disease.


Sanatoria spread throughout the country. One of the largest in Texas was built on 1000 acres near San Angelo [19]. It included 662 patient beds in thirty five buildings. Indeed, it became its own town (Sanatorium, TX). In a 1916 directory of institutions compiled by the National Association for the Study and Prevention of Tuberculosis, the Woodlawn Hospital in Dallas (which preceded Parkland Hospital) was identified as having 62 beds for TB sanatorium care at $1 per day ("charity cases received").

The effectiveness of sanatoria is debatable. Isolation of cases likely limited the spread of disease, though improved sanitation and living conditions in urban areas likely had greater effect. Other more cynical reasons for their popularity were the economic and professional benefits to the physicians who ran them, as well as providing an option for referring physicians to be shed of hopeless cases by sending them away.

There is some evidence that climatic and rest therapy had some benefit, at least to causing the disease to be slowed or arrested. However, this seemed to accrue only to those who presented with minimal disease as compared to those with far advanced disease, who overwhelmingly succumbed [20]. The figure below shows the outcome at 15 years for patients treated in one sanatorium.

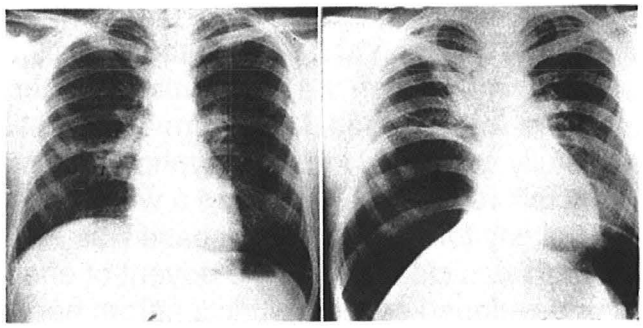


Minimal TB Far Advanced TB

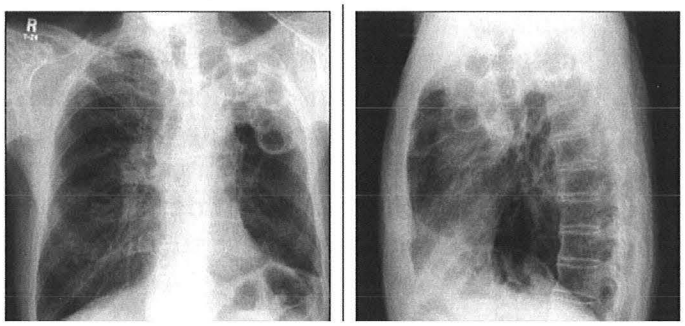
In fact, it became apparent that sanatorium therapy alone failed in patients who developed cavitation, which carried a five-year mortality of 85% [18, 21, 22]. This led to the institution of so-called "collapse therapy" in 1885, initially using artificial pneumothorax. One formulation of the pathophysiologic rationale is as follows: "The first consideration is the attempt to lessen toxic absorption, and this is done by slowing the circulation and lessening the movements of the lung. Healing of the tuberculosis takes place either resolution, or by fibrosis and calcification, but it is a known biological fact that healing does not occur until the toxicity of the lesion has been abated" [18]. The object was to effect cavity closure.

Artificial pneumothorax was indicated for patients with smear-positive disease with cavitation. Ideal candidates were those with unilateral, upper lobe disease with thin walled ("soft") cavities and minimal fibrosis or pleural disease. Complications included spontaneous resolution of pneumothorax, empyema, and pleural adhesions requiring thoracoscopic lysis [18]. It is very difficult to find hard data on outcome, but reported outcomes suggest some benefit over historical results of rest therapy alone. In any event, Thearle reported in 1935 that its use increased from only 3-5% of cases to 50-75% over the preceding decade [22].

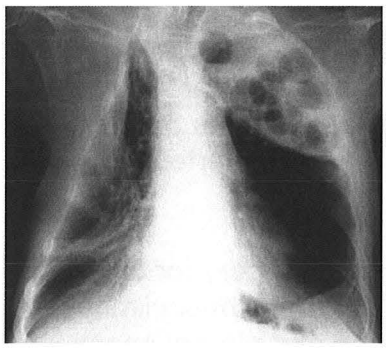
A variation on this approach was artificial pneumoperitoneum, which was popularized by Banyai [21, 23]. Phrenic nerve interruption by either "crush" or avulsion ("exairesis"), which was performed via a cervical approach, was used alone or more commonly as an adjunctive measure. These were designed primarily to target lower zone cavities, but were also employed for bilateral disease.



Plombage, another form of collapse therapy, involved placement of foreign bodies within the pleura or extra-pleural chest wall. The most frequent application used Lucite spheres to fill the space and collapse the lung. This produced rather dramatic-appearing chest imaging [24].



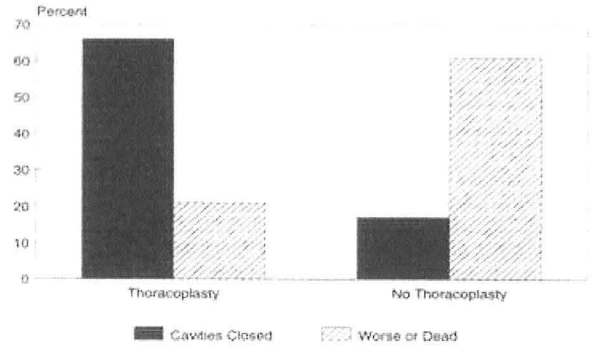
The most dramatic form of collapse therapy was thoracoplasty, first performed by Dr. George Fowler in 1893 [25]. This was generally done in patients with smear positive cavitary disease, especially with unilateral, upper lobe disease. The procedure involved resection of contiguous ribs, usually ribs 1 through 6 or 7, which allowed the upper chest wall to be pushed into the thorax, thus collapsing the upper lobe and hopefully obliterating the cavity [26]. The procedure was fairly morbid with evidence of shock and significant blood loss, so that it was usually done in 2-3 stages.



Immediate mortality was said to be in the range of 6-9% [27, 28]. However, in the language typical of the day, this was the "surgical" mortality; if "medical" deaths

were included, mortality was more in the range of 14-18% [28, 29]. Other short term complications included infection and venous thrombosis.
The procedure was disfiguring, though the preserved shoulder girdle helped mask this when the patient was dressed. Long term complications in those whose TB was successfully controlled included kyphoscolisosis and restrictive hypercapnic respiratory failure [30, 31]. I followed a woman for many years that had undergone thoracoplasty for her TB. Her disease was felt to have stabilized for several years and then was cleared with the advent of effective antimicrobial therapy. However, she developed severe restriction from her procedure and later kyphoscoliosis, ultimately requiring tracheostomy and home ventilation. She lived a cheerful and fairly active life for over decade on ventilation.

Literature from the period suggested that thoracoplasty was remarkably successful, and perhaps in comparison to rest therapy it was an improvement. The figure below shows outcome for patients with cavitary disease who were recommended for thoracoplasty and either accepted or refused the procedure. This suggested that the surgery did frequently lead to cavity closure and perhaps improved mortality [32]. This may represent an effect on bacillary burden as smear positive sputum in cavity disease contains several logs greater bacilli than non-cavitary disease, with 10^5-10^7 vs. 10^3-10^5 colony forming units per ml of sputum respectively [33]. Reduction in bacillus burden could theoretically tip the scales in favor of innate and acquired immunity in such cases.



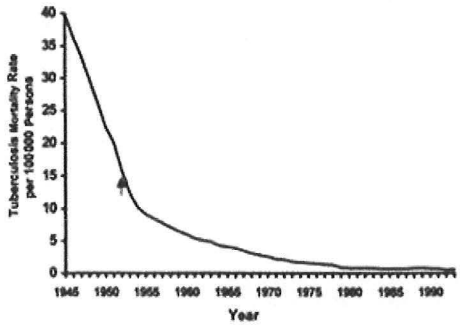
Clinical outcomes for thoracoplasty were reported to be very high, with some series reporting that disease was arrested or improved in 55-74% of cases [27-29, 34]. Cure was claimed in as many as 35-40% of these. There were patients who were clinically improved and converted to negative smears, but only in about 4% of cases [28].

For the most part resection lung surgery for tuberculosis was largely avoided due to very high operative mortality, anesthesia limitations, and severe morbidity including bronchial dehiscence and pleural space infection due to residual infection. The advent of effective chemotherapy (see below) led to rapid and dramatic decline in the use of collapse therapy, but interestingly for a time produced a substantial increase in resectional surgery [35]. This was largely

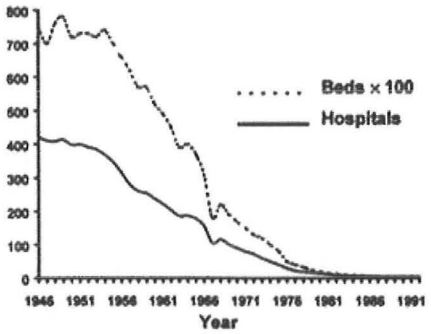
confined to cases refractory to medical therapy. Thoracoplasty is now almost never used in the United States and most other countries [36, 37], though it is still employed to some extent in others [38]. Resectional surgery for TB is currently rarely used for the vast majority of patients, though it is still used in specialized referral centers with expertise in managing multi-drug resistant (MDR) tuberculosis [36, 37, 39, 40]. Plombage has also been used for MDR-TB [41].

Not surprisingly, the development of effective chemotherapy for tuberculosis radically altered the management of TB. Streptomycin (SM) was first introduced in 1945 and was the subject of the first randomized clinical trial (comparing streptomycin to rest therapy) conducted by the Medical Research Council [42]. The results are shown below.

Para-aminosalicylic acid (PAS) was soon used in combination with SM and isoniazid (INH) was introduced in 1952 [43]. The mortality and especially the incidence of TB in the United States dropped dramatically thereafter [17].



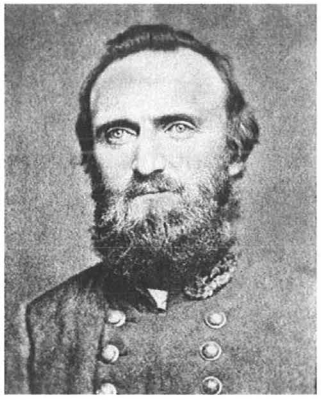
Other studies from Hong Kong and Madras demonstrated that bed rest and hospitalization (i.e. sanatorium care) had no added benefit over chemotherapy alone [44, 45]. As a consequence TB beds and hospitals declined rapidly over the following decade or so, essentially eliminating TB sanatoria [17].



The advent of anti-tuberculosis therapy dramatically changed the face of chest medicine. The Trudeau Sanatorium became the Trudeau Institute and still operates as a research facility focusing on immunology. Lung doctors went from being "phthisiologitsts" to "pulmonologists". The former American Sanatorium Association is now the American Thoracic Society; the title of its journal was changed from the *Journal of Tuberculosis* to the *American Review of Respiratory Disease* in 1955. Trailers offering TB screening X-rays went the way of the dinosaur and the Easter Seals campaign now advocates for people with disabilities rather than TB.

Stonewall Jackson: Pneumonia

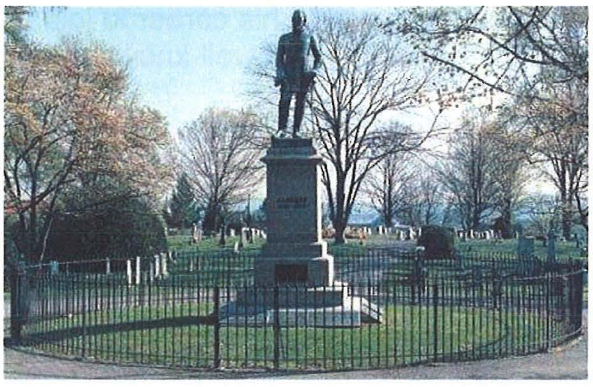
General Thomas Jonathan "Stonewall" Jackson was a devout Christian, one of many West Point graduates to provide leadership on both sides of the Civil War conflict, and arguably one of Robert E. Lee's most important generals and confidants. On May 2, 1863, Jackson's troops executed a remarkable flanking action of Hooker's federal ranks leading to the confederate victory at the Battle of Chancellorsville [46]. Presaging other "lead from the front generals" such as George Patton, Jackson declared, "The danger is over! The enemy is routed," and was soon riding out ahead of his pickets and skirmishers. A single shot from one of the troops of the 18th North Carolina was followed by a barrage of "friendly fire" from the same unit, believing the approaching riders were federal officers. Jackson took three .57 caliber bullets, two to the left arm and one to the right hand [47].

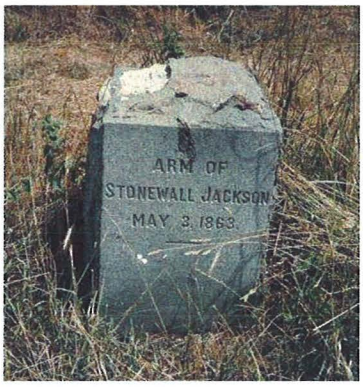


He was taken to the field hospital at the Melzi Chancellor house, where he was attended by Dr. Hunter Holmes McGuire, a graduate of the University of Pennsylvania's medical school prior to the war. McGuire's description of Jackson suggests he was suffering from shock: "His suffering at this time was intense; his hands were cold, his skin clammy, his face pale, and his lips compressed and bloodless" [48]. Several surgeons present all concurred that amputation of the left arm was needed. McGuire felt the patient's pulse was strong enough for the surgery and the use of chloroform; he recommended this course to Jackson who replied, "Do for me whatever you think best."

The arm was amputated just below the shoulder with minimal loss of blood. The unit chaplain took it upon himself to see that the revered general's arm received its own proper burial at the chaplain's family cemetery at the Elwood house near Chancellorsville. The site is still marked by a stone marker [49], separated from Jackson's ultimate burial site at Lexington, Virginia. Jackson seemed to recover promptly from the surgery and was taken from the field hospital to a home owned by the Chandler family at Guiney's Station 24 miles away, where he was joined by his wife. McGuire accompanied to provide continued, one-on-one care. He had become all but pain free and was taking nourishment.

However, on May 7 (five days after his wounding), Jackson developed right-sided chest pain, nausea, and fever. Dr. McGuire later reported, from notes taken at the time, "An examination disclosed pleura-pneumonia on the right side". He attributed this possibly to a fall that the general had sustained when his litter-bearers had stumbled the night of his initial injury, leading to "contusion of the lung, with extravasation of blood in his chest…and then inflammation ensued" [48]. He was treated with cupping (hot glasses were inverted and applied to affected areas to draw blood away from the diseased site), mercury, antimony, and opiates. Despite, or perhaps exacerbated by, his care Jackson succumbed and died on May 10, 1863. His last words were reported by his family to be "Let us cross over the river and rest under the shade of trees."





Jackson's death had profound effects on the morale of the confederacy. Lee was devastated, as poignantly portrayed in Jeff Shaara's *Gods and Generals* [50]. President Davis, perhaps somewhat desperate to credit the southern success of

Jackson's victory at Chancellorsville, wired Lee to say that "the nation has reverently united with you in giving praise to God for the success with which He has crowned your arms" [46]. However, upon learning of Jackson's wounding, Lee had said, "Victory is dearly bought which deprives us of the services of General Jackson." Lee had sent word to Jackson saying, "Could I have directed events, I would have chosen for the good of the country to be disabled in your stead." And later he famously said, "He has lost his left arm, but I have lost my right arm" [48]. Many have speculated as to how events at Gettysburg (and perhaps even the war) might have unfolded had Jackson not been replaced by Longstreet. Perhaps the sentiment was best expressed in the benediction at the unveiling of one of Jackson's monuments, "And Thou knowest O Lord, that when Thou didst decide that the Confederacy should not succeed, Thou hadst first to remove Thy servant, Stonewall Jackson."

Pneumonia may be the "old man's friend" as Osler has said, but certainly is no friend to the young. In the pre-antibiotic era, the mortality of untreated pneumococcal disease was 30-35% in adults; the advent of penicillin significantly reduced mortality to 5-8% [51]. However, lower respiratory tract infections (including TB) continue to account for a significant percentage of global mortality, representing the 3rd leading cause of death in poor-middle income countries, and the 4th in higher income countries [52].

Jackson's death from pneumonia illustrates several points. The fact that he was wounded by his own men is certainly ironic and tragic; but so-called "friendly fire" has long been part of warfare, most especially as weaponry allowed combatants to engage each other at a distance rather than hand-to-hand. Though data do not seem to exist on the incidence of friendly fire in the civil war, it was likely not a common cause of injury or death. Interestingly, as modern warfare has evolved, especially in the U.S. military, overall battlefield fatalities have been dramatically reduced. However, friendly fire deaths have actually increased proportionally. In the first Persian Gulf War, 24% of American fatalities were caused by allied combatants (largely reflecting the low denominator, 148 total deaths) [53]. The death of Pat Tillman (the NFL linebacker who gave up his career to join the Army) in Afghanistan to friendly fire is perhaps the most well-known example.

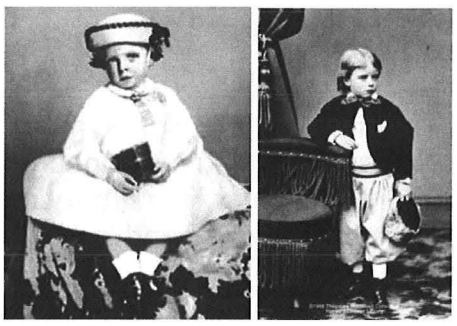
It is not unusual that Jackson should have died of an infection rather than as a direct result of either his injury or his amputation. Indeed, infection and non-combat injuries have caused more casualties and loss of combat-ready-time than direct battle injuries in the U.S. military from the American Revolution to the present wars in Iraq and Afghanistan [54]. Despite the state of medicine during the civil war, Jackson actually proved that one had a better chance of surviving his amputation than his pneumonia. As noted above, the mortality for pneumococcal pneumonia pre-antibiotics was 30-35% [51]. For the Union army, the mortality was 24% of 6,500 upper extremity amputations [48].

The First World War, fought between 1914 and 1918, was one of the bloodiest conflicts, with so many young men dying that they came to represent the "Lost Generation". There were an estimated 8.6 million fatalities; 3.5 million Central Power soldiers died as compared to 5.1 million from the Allied armies [55]. There likely were at least 5 million civilian deaths. However, this pales in comparison to the 20 to 40 million who died from the influenza pandemic of 1918-1919 [56]. Indeed, influenza killed more American soldiers (62,000) than died in combat (48,000), in large part reflecting the late entry of the US into the war just as the influenza pandemic arose [55]. Indeed, the debilitating effects of influenza significantly impacted Woodrow Wilson's health and political effectiveness as the post-war world was being negotiated by the victor nations, potentially impacting America's role in the global politics and the political face of conditions leading to World War II and more modern conflicts in the Middle East [57, 58].

Teddy Roosevelt: Asthma

Theodore Roosevelt, Jr. is certainly one of the most recognizable political figures of the last century, his image one of four on Mount Rushmore. "Bully!" and "big-stick diplomacy", posed with the Roughriders on the top of San Juan Hill, his toothy smile with wire-rimmed glasses, the imperial presidency, and African safari all project the manly persona we know so well [59]. Not surprisingly, he came of tough stock, inheriting the sturdy Dutch character of Klaes Martenszen van Rosenvelt, one of the earliest settlers of New Amsterdam who arrived in 1649. He was born into the wealthy and privileged New York Roosevelt family in 1858, weighing a robust 8 ½ pounds[60].

Yet this is not the way his early life started at all. In his autobiography, he wrote: "I was a sickly, delicate boy, suffered much from asthma, and frequently had to be taken away on trips to find a place I could breathe. One of my memories is of my father walking up and down the room with me in his arms at night when I was a very small person, and of sitting up in bed gasping, with my father and mother trying to help me. I went very little to school. I never went to the public schools, as my own children later did" [61]. One of his family described him as the "great home-boy" of the family, extremely frail, undersized, nervous and timid. Early photos of him show him dressed in frilly, feminine attire. His nickname in the family was Teedie.

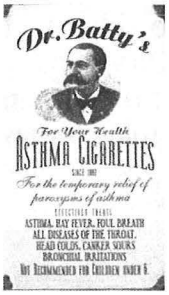


His asthma attacks began at about age three. He would have sudden onset of terrifying dyspnea, fighting to take in a breath. Coughing and wheezing were characteristic. His attacks were often nocturnal, would begin unexpectedly, often last for days, but would be interspersed with normal periods [62]. There was no apparent seasonal variation, nor were any obvious allergens identified [63].

The suddenness and severity of his spells came to shape the family dynamics, causing abrupt changes in travel plans and sudden trips to potentially more favorable climate or location. His attacks would "hardly have three or four days' complete exemption and keep us constantly uneasy and on the stretch" [63]. Although he briefly attempted to attend a small private school near his home, he didn't tolerate this and ultimately was tutored entirely at home until entering Harvard much later. His parents largely confined him to the life of an invalid, paralleling in many ways the habits of his loving, but neurasthenic mother [62].

The treatments attempted were typical of the times. His parents would hold him and walk endlessly about his room. They would rouse the servants to bring the coach to take long rides to catch the open air. His father would occasionally have the young boy smoke one his cigars. One of his physicians applied some form of electrical shocks to his head and abdomen. Strong black coffee seemed to help, which makes sense given that caffeine is a xanthine just as is theophyline, inhibiting cyclic AMP and causing bronchodilation.

Other treatments of the day included emetics, purges, enemas, cold baths, alcohol, and laudanum. By 1917 the AMA had at least dismissed alcohol as having no scientific basis for use in therapeutics. Ironically, driven by the immense revenue potential for "medicinal alcohol" that physicians could reap prescribing alcohol under one of the few exemptions to the Volstead Act during Prohibition, the AMA reversed itself in 1922 and determined that alcohol had significant value in treating 27 different conditions including asthma [64].



Smoking a variety of things was also used: cigars, marijuana, and a variety of "asthma cigarettes". These cigarettes often contained dried jimsom weed (*Datura stramonium*), a poisonous plant. However, its primary contents were the anti-cholinergic alkaloids atropine, scopolamine, and hyoscyamine which might well have provided bronchodilation [65].

Although climate therapy was applied more often to tuberculosis, it was also felt that asthma was influenced as well. Roosevelt's physicians suggested travel and time spent in the outdoors. Being of the privileged class allowed the family to travel to the mountains, especially the Adirondacks up-state, but also to the European Alps at Lake Como. They traveled down the Nile in style while visiting Egypt. None of this appeared to help and sudden attacks occurred during their travels, often necessitating abrupt changes in plans.

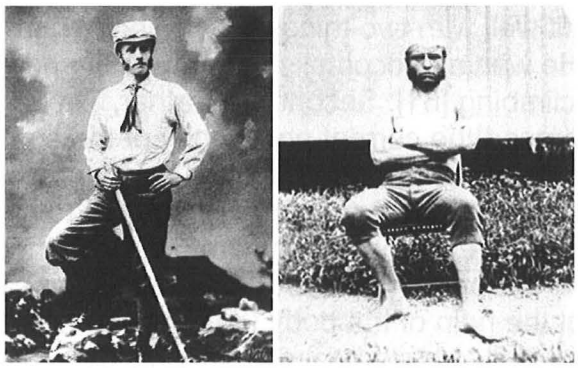
Medical opinion of the day also held that asthma had an important emotional component. Strong emotions such as anger were to be avoided. The Roosevelt's consulted Dr. Alphonso Rockwell, the partner of Dr. George Beard, who had become an expert on neurasthenia with his book *American Nervousness*. Rockwell ascribed young Teedie's ailments to the "handicap of the riches" as well as "excessive upper class refinement" and the "wretchedness of extreme civilization." Teedie would, in fact, seem worse when his father left home to travel for his work and he tended to use his illness for secondary gain. Outdoor exposure and exercise were recommended [62].

As it happened, this fit well with two things. First, Teddy had come to thoroughly enjoy the outdoors. He was an accomplished naturalist and enjoyed riding, hunting, hiking, and climbing [61]. Second, his father, Theodore, Sr., was a robust man who embraced the current philosophy of the so-called "muscular Christians" who had given rise to Young Men's Christian Associations. Clean living, body building, and competitive exercise were felt to have strong health and religious influence. When Teedie was 12 years old, his father is said to have come to him and, addressing him as Theodore, said: "You have the mind, but not the body, and without the help of the body the mind cannot go as far as it should." He was instructed to build himself up by his own effort [63]. He took this advice to heart and soon began to work with weights on the piazza, later crediting his father for his ultimate development and success [61].

Roosevelt claimed that his father was the most important and influential person in his life. However, there was one negative aspect of this relationship (unrelated to his health) which may have shaped his future as well. The young Roosevelt had grown up during the civil war, having been imbued with tales of the martial exploits of his mother's family through the generations. Young Roosevelt was mesmerized by the uniformed soldiers he saw. He watched Lincoln's funeral procession with his brother from an upstairs window of their mansion. But Roosevelt was apparently deeply ashamed that his father, while serving the Union cause in a civilian capacity, had paid two others to serve in his stead in the army (a common practice of the day). It is thought that contributed in some measure to Teddy's later militaristic ways, including his fierce determination to serve in the cavalry of the Spanish-American war that propelled him to further fame on San Juan Hill [63].

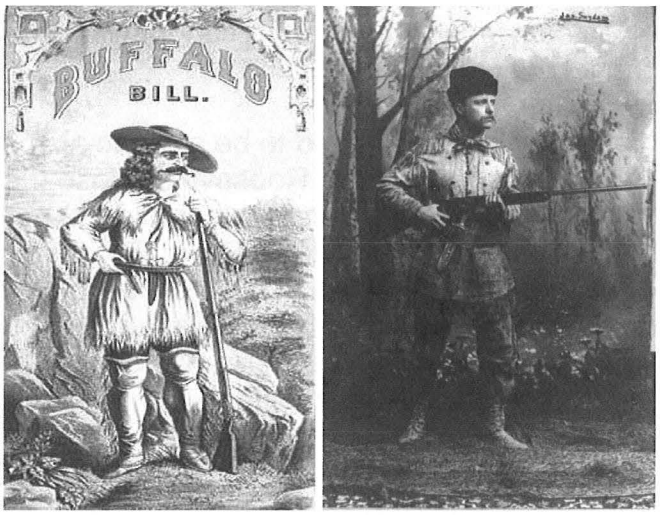
There was one particular incident from his boyhood that he recalled in his autobiography that further pushed his drive to strengthen his body and overcome his physical ailments. He encountered two boys on a stage coach who were about his own age. "They found that I was a foreordained and predestined victim, and industriously proceeded to make life miserable for me. The worst feature was that when I finally tried to fight them I discovered that either one singly could not only handle me with easy contempt, but handle me so as not to hurt me much and yet prevent my doing any damage whatever in return" [61, 63]. The humiliation caused him, with the hearty approval of his father, to take up boxing.

His physical condition gradually improved, as did his asthma, whether causally related or through just the natural course of his disease. Before leaving for college he travelled in Europe, hiking extensively and climbing the Matterhorn. At Harvard he was an avid boxer and rower. His pursuit of robust, active outdoor life, though born of his desire to overcome his asthma, dominated much of his adult life; the first thing he did upon leaving the presidency was to go on an extended big-game safari in Africa [59, 60].



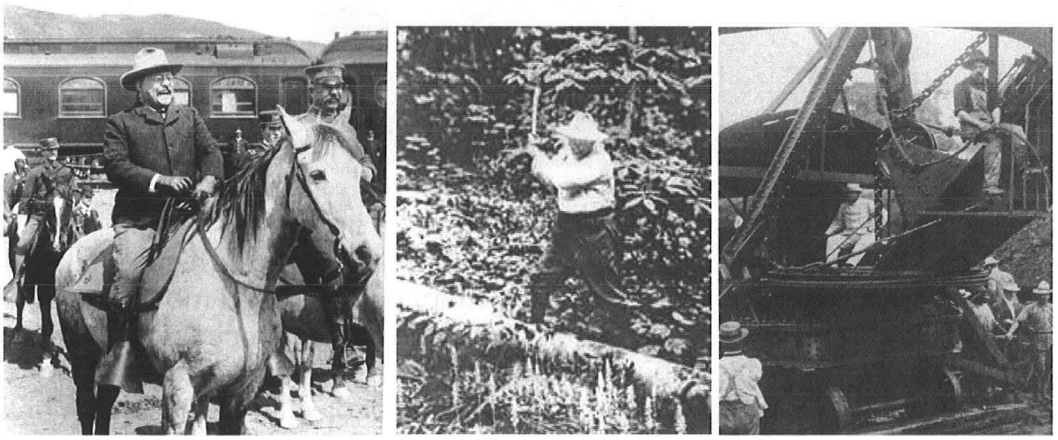
Asthma was not the only aspect of TR's life that drove him to project a robust, manly image. Roosevelt was elected to the New York state assembly and arrived in Albany in January, 1882. His squeaky, nasal voice and his upper class mannerisms, Saville Row tailoring and furnishings with long-tailed coats and gold-capped cane clearly made an unwanted initial impression amongst the other rough and tumble politicians. When first entering the assembly it was asked, "Who's the dude?" He was variously referred to as "weakling", "punkin-lily", "Jane-Dandy", and perhaps worst (for the times especially) "Oscar Wilde" with a not-so-veiled reference to his sexual orientation [60]. This was entirely unacceptable for politics and especially for men of the times; being seen as effeminate was a death sentence for a politician [66]. Roosevelt set out to change that image. What followed was one the most complete public relations makeovers perhaps even to date. In many ways, Roosevelt set the pattern for future politicians, presidents in particular.

Roosevelt invested in a ranch in Montana where he immersed himself in ranching and hunting. Though he became quite well-known for his exploits during his time as "Ranchman Teddy", he actually managed to spend more time in his mansion in New York than on the ranch. He wrote several successful (and self-promoting) books about his experiences. A photo in one work draws rather shamelessly on the image of Buffalo Bill Cody. Indeed, with the exception of the hat, side-by-side comparison with another famous photo of Buffalo Bill shows Roosevelt wearing the same fringed buckskins and moccasins with a large knife thrust in his belt and his rifle [66]. Indeed, Roosevelt even "stole" the Rough-rider theme from Cody, who had advertised his Wild West Show and "Congress of Rough Riders". Ironically, Cody later borrowed back from Roosevelt, including members of Roosevelt's Rough Riders in his show following the conclusion of the Spanish-American War.



During his presidency, Roosevelt made good use of the "photo-op". He encouraged photographers to capture his many outdoor activities, especially on horseback. He was shown chopping wood and clearing brush long before Reagan or George Bush did so on their ranches. He found opportunity to get himself photographed operating one of the huge steam-driven excavators during

an inspection trip to review the construction of the Panama Canal. It wasn't just that Roosevelt was open to reporters and photographers; he carefully cultivated what was captured for public viewing. For example, although he frequently enjoyed playing tennis, he would never allow a photo of himself in his tennis whites. He wrote, "You never saw a photograph of me playing tennis. I'm careful about that. Photographs on horseback, yes. Tennis, no" [66].



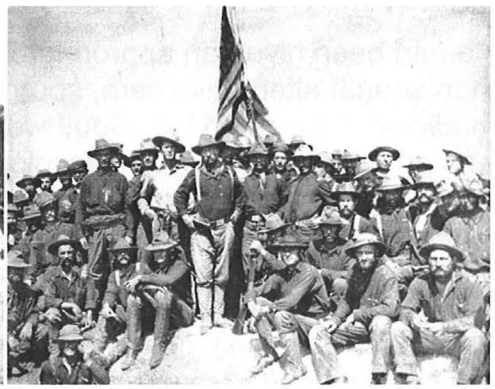
Perhaps nothing established the Roosevelt public image as vividly as did the Spanish-American War and Teddy's "Rough Riders." At the time of the USS Maine explosion in Havana harbor, which ultimately propelled the US into war with Spain, Roosevelt was serving as Assistant Secretary of the Navy. He was convinced that the explosion was caused by Spanish terrorism and pushed hard for war, quickly sending word to Dewey to be prepared to take action against Manila. Roosevelt was consumed with preparation for war and would soon lobby to be allowed to form a new cavalry unit.

His wife fell ill at this time with what proved to be a pelvic abscess, interrupting his plans. The family physician as well as Roosevelt's close friend, Leonard Wood (then serving as assistant physician to the president) both recommended conservative treatment. When she failed to improve, Roosevelt brought in William Osler, who recommended surgery. Teddy chose to continue take the advice of Wood over Osler. However, he finally relented and his wife rapidly recovered following surgery, leaving Roosevelt now unencumbered to pursue his martial ambitions over his marital obligations [67].

He was appointed Lieutenant Colonel of the 1st Volunteer Cavalry. The unit was commanded by his long-time friend, Colonel Leonard Wood. Wood was a Harvard trained surgeon who joined the army and served in the Apache War campaign against Geronimo where he distinguished himself as much or more for his military leadership than for his surgical skill, ultimately receiving the Medal of Honor. Wood would later serve as Military Governor of Cuba and in the Philippines. Fort Leonard Wood in Missouri is named for him.

Even though Wood was in command, the unit was quickly dubbed Roosevelt's Rough Riders. Roosevelt arrived in San Antonio where the unit organized and trained, fitted with his new uniform he had made by Brooks Brothers. The Menger Hotel, next to the Alamo, served as Teddy's primary recruitment site (the hotel's bar is worth stopping in even today, left largely as it was then with plenty of TR memorabilia).

The Rough Riders ultimately embarked for Cuba from Tampa, but owing to limited transport space, they were forced to leave most of their horses. A famous painting of the charge of San Juan heights by Frederic Remington accurately shows only Teddy on horse, the men all afoot. Once in Cuba, Roosevelt courted the Hearst reporter Richard Harding Davis. Wood had been assigned higher command and so Roosevelt was brevetted to Colonel and did, in fact, lead the famous charge. Following the successful assaults at Guasimas and San Juan Heights, Roosevelt became an instant hero in the press back home [67].



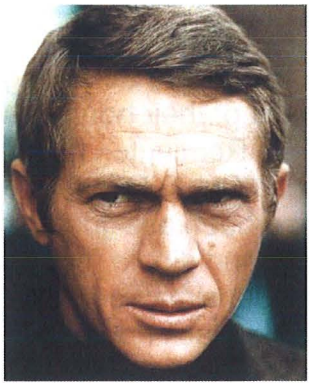
Despite all of the fame he achieved through the press, TR was convinced that he should receive the Congressional Medal of Honor for his exploits. He lobbied aggressively for the award. Indeed, in his later autobiography he includes an extensive appendix with all the nominations and citations on his behalf [61]. However, the military leadership in Washington felt he was far too self-promoting and would not forward the recommendation of his immediate commander. He did ultimately receive the Medal of Honor, but not until it was presented to his family

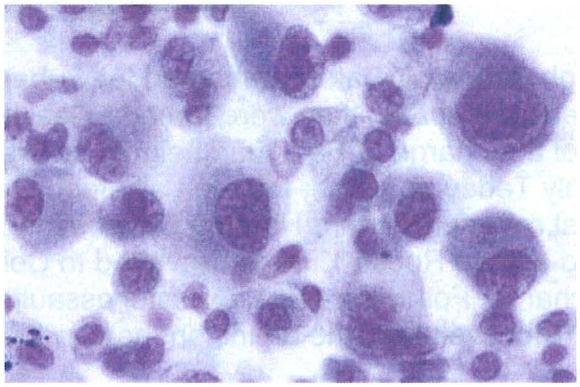
by President Bill Clinton in 2001. Ironically, one of his sons, Theodore D. Roosevelt, Jr., also received the Medal of Honor as well for his actions as a Major General who insisted on "leading from the front" during the initial assault on the beaches of Normandy; his was awarded in 1944 [68].

Theodore Roosevelt created one of the most robust and dynamic images of any modern politician. Though certainly other factors contributed, there is little doubt that his early experiences and his desire to overcome his asthma largely shaped the persona and legacy he ultimately developed.

Steve McQueen: Mesothelioma

Steve McQueen lived hard and died even harder of widely metastatic mesothelioma. He was diagnosed in late 1979 and initially underwent chemo-radiation at Cedars-Sinai Medical Center in Los Angeles. McQueen attempted to keep his condition secret from the public and his family; however, the National Enquirer broke the news of his illness in March, 1980 [69].



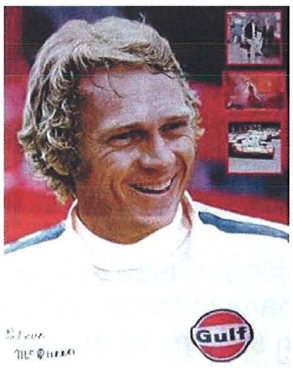


He had been given an appropriately grim prognosis, which he did not accept. He then sought alternative care, spurring a national discussion on non-traditional medicine. (Our own U. T. Southwestern faculty colleague, Dr. Eugene Frenkel, was quoted as head of the Oncology Division as saying, "While nutrition is an important part of managing cancer, seeking a magical or unusual cure is a serious risk") [70]. Dr. William D. Kelly, a dentist and orthodontist, had been black-listed by the American Cancer Society and his Texas license suspended for his controversial therapies. He treated McQueen in Mexico with oral pancreatic enzymes, coffee enemas, dietary manipulation, and various injectable cell preparations from sheep and cattle fetuses. The most memorable of his treatments was laetrile, made from apricot pits [71]. McQueen died in a Ciudad Juarez clinic across the border from El Paso the day following botched surgery for his cancer.

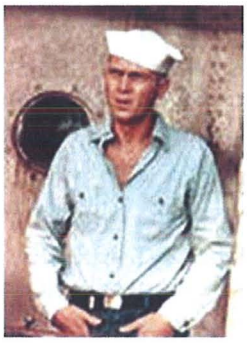
McQueen's saga not only produced a wide-ranging consideration of alternative medicine, but it awakened public interest in the relationship between asbestos and cancer, and mesothelioma in particular. There are dozens of web-sites

devoted to asbestos and mesothelioma, most of them by legal firms specializing in asbestos litigation. McQueen's story is mentioned in nearly all. Asbestos can produce fibrotic lung disease, benign pleural fibrosis and characteristic pleural plaques, and carcinoma of the lung (especially with concomitant smoking). However, the strongest association is with mesothelioma, which is nearly always fatal. Although there are some cases in which no exposure can be found, in the vast majority a significant exposure can be found [72]. Indeed, in legal matters, the diagnosis of mesothelioma is essentially de facto evidence of asbestos exposure; the trick is to find someone with deep pockets to pin liability on.

One of the greatest difficulties in asbestos related disease is establishing an exposure through the occupational history. McQueen's story is illustrative of this point. If we start with his primary occupation as an actor, there is little to suggest significant exposure; although several have pointed out that the insulation used for sound abatement in sound stages and studios often contain asbestos [70, 73]. If we take the history a little further and include his favorite hobby, race car driving, then we can expand the possibilities to include brake linings (though there is no evidence that McQueen did work on brakes) and the fire-retardant materials in racing suits and helmets [70, 73, 74]. However, most of these materials likely posed minimal risk as they are post-manufacturing products wherein the asbestos is embedded until significantly worn, damaged, or abatement efforts are attempted.



Exploring McQueen's pre-actor life is finally more compelling. When he was sixteen and drifting around the country on his own, he found himself in a bar in New York City with two characters named Ford and Tinker who plied him with drinks, convinced him to join the merchant marines with them, and provided him with falsified papers as an able-bodied seaman (they probably were working on "commission"). He shipped out on an old tanker, the *Alpha*, filled with molasses and bound for Cuba [70, 74, 75]. This holds promise for asbestos exposure.



The U.S. Navy had been using asbestos in its ships since the 1920's [76]. Following a devastating fire on board the luxury liner *SS Morro Castle* in 1934, there was an international effort to improve shipboard fire safety [77] which included the widespread use of asbestos, especially in holds, on pipes (which were extensive), and in boiler/engine rooms. Indeed, the federal government mandated that all U.S. ships built from the mid-1930's through the mid-1970's were made with extensive asbestos insulation. The massive ship-building during World War II produced extensive exposures for ship-yard workers and sailors (especially machinist mates and engine room workers).

Even though asbestos was no longer used in ship-building after the 1970's, exposures have persisted as many of these ships remained in service or importantly, workers involved in salvage of decommissioned ships have continued to have potential exposure. Indeed, the saga of the French aircraft carrier *Clemenceau* provides an interesting recent example. After long and glorious service, the French navy decided to outsource the scrapping of the old ship to India. Efforts by the Indian government and Greenpeace managed to get the "toxic ship" (as it was portrayed in the press) with its asbestos stopped prior to entry to the Suez Canal in 2006 [78]. The ship was forced back to France. It was not until 2009 that the arrangements were finally made for a firm in the U.K. to begin dismantling the ship.

So, it would seem plausible that McQueen's stint in the merchant marines might have provided his exposure. However, in keeping with our efforts to determine a good occupational history, we need to explore this further. It turns out that McQueen was hired as a deckhand on the *Alpha,* his primary duties including swabbing decks and hauling garbage for dumping overboard. It is unlikely that he

spent much time in areas of the ship with significant asbestos or did anything that would be problematic. Indeed, McQueen didn't take to life at sea and jumped ship at the first opportunity when the ship landed at its first port of call in the Dominican Republic [70, 74, 79].

McQueen was in the Marines from April, 1947 through April, 1950 (just before the start of the Korean War. He served in the 2nd Division Fleet Marine Force as a tank driver. He wasn't a particularly stellar marine, serving time in the brig early on for being AWOL. Of note, was that he spent a fairly lengthy time deployed in the Arctic (in the Aleutian Islands in some accounts, in Canada in a few others) where his unit was involved in practicing amphibious landings. This would have involved being aboard World War II era transport ships.

Indeed, in one frequently quoted escapade McQueen incurred the ire of an officer when he stole a case of beans. He had attempted to warm them by placing the cans (unopened) on the warm engine block of a vehicle. The officer was sprayed with beans as he was passing when the cans exploded, and McQueen was sentenced to 60 days in the brig [70, 73, 74, 79]. His time was reported to have been spent cleaning pipes in the holds of the transports. By one account his ex-wife, Barbara, reported that this included stripping asbestos off the pipes of the ship (though this story is somewhat suspect as it was not reported until more than 25 years after his death and in an interview with a noted asbestos attorney) [75]. Thus, it is at least plausible that McQueen's asbestos exposure as a veteran might have made his mesothelioma and death a service-connected condition.

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