Profiles in Medical Courage: Evidence-Based Medicine and Archie Cochrane

"Medicine is a science of uncertainty and an art of probability."
-Sir William Osler

Abstract

Archibald (Archie) Cochrane is often credited with being the inspiration for evidence-based medicine. His influential 1971 book, "Effectiveness and Efficiency", strongly criticized the lack of reliable evidence behind many common healthcare practices. His call for a collection of systematic reviews led to the creation of The Cochrane Collaboration, named in honor of him. Archie Cochrane's life was a tortuous one, which included psychoanalysis, service in two wars, and studies of pneumoconiosis, tuberculosis and healthcare delivery. In this profile of medical courage we explore not only his thoughts on healthcare but his extraordinary background that shaped his ideas.

Early Life

Archie Cochrane was born in 1909 in Galashiels, Scotland, a cloth manufacturing town 30 miles south of Edinburgh. His family was wealthy mill owners that instilled in Archie the principles of self-reliance and accomplishment. This was important since his father died in the First World War when Archie was 8. However, Archie was financially secure since as the first born, he inherited a private income.

By all accounts, he was a bright student. After attending preparatory school at Rhos-on-Sea in Wales, Archie won a scholarship to Uppingham School in Rutland, England, where he became a school prefect and a member of the rugby team. In 1927, he won a scholarship to King's College Cambridge, where he graduated in 1930 with honors in natural sciences. His inheritance enabled him to continue studying, and during 1931 he worked on tissue culture at the Strangeways Laboratory at Cambridge and later in Toronto. However, he soon tired of what he concluded was trivial research and abandoned basic studies.

Psychoanalysis

At about this time he became anxious about his sexual development. He had developed anejaculation, a condition where he was unable to ejaculate. This led him to seek medical help but he received little sympathy from the British doctors. However, he found the doctors at the Kaiser Wilhelm Institute in Berlin were willing to take his problem seriously. Between 1931 and 1934 he underwent psychoanalysis with Freud's leading lay analyst, Theodor Reik. The psychoanalysis began initially in Berlin, but like Freud, Reik was a Jew. Archie followed Reik first to Vienna and later The Hague as Reik fled from Hitler. Archie did some medical studies in Vienna and Leiden during this time, and published his first paper (Elie Metchinikoff and his theory of an 'instinct de la mort'). Unfortunately, the psychoanalysis did not cure his condition which plagued him for the rest of his life. However, his sojourn in Europe instilled in him a hatred of fascism and a

skeptical attitude not only of psychoanalysis, but or all theories which had not been validated by testing. Later in his life, Cochrane condemned the entire field of psychiatry for “using a large number of therapies whose effectiveness has not been proven” and for being “basically inefficient” (1).

Spanish Civil War

Disenchanted, he returned to London in 1934 and continued his studies as a clinical medical student at University College Hospital. His experiences in Europe, his hatred of fascism, and his sense of social justice led him to joint the Socialist Medical Association. In 1936, this group of doctors, medical students and nurses met in London to consider ways of sending medical help to Republicans fighting fascism in the Spanish Civil War. This was viewed by Archie as important since the addition of Spain as a fascist ally to Germany and Italy would likely result in the fall of France and England to fascist aggression. The Socialists decided to send doctors, nurses and medical students to Spain to assist the Republicans and Archie abandoned his studies in order to serve as a volunteer.

Figure 1. Panel A. Archie Cochrane as a medical student. Panel B. As a volunteer in the Spanish Civil War with a “flourishing red beard” (From Cardiff University Library, Cochrane Archive, University Hospital Llandough).

He served at Grañén near Huesca on the Aragon front and the siege of Madrid. Although not qualified as a physician, he served in an ambulance unit as well as performing duties such as triage in the hospital. During this time Archie had contact with the Communists that made up much of the Republican army. Like many intellectuals of that period, Archie had been attracted by Marx during his undergraduate studies. However, his experience in Spain turned him against communism, but he remained a man of the left throughout his life. After about a year all British medical students were ordered to return home to qualify. Archie had grown sick of the war and was happy to comply.

World War II

He resumed his clinical studies at University College Hospital in 1937, and qualified in 1938. Until the outbreak of the Second World War he worked first as a house physician at the West London Hospital and then as a research assistant University College Hospital. At the beginning of World War II, he enlisted in the Royal Army Medical Corps and served first in Egypt and then as a medical officer in “D” Battalion Layforce, a commando unit. The one military action in which he was involved ended disastrously in Crete when the British troops surrendered and Archie was taken as a prisoner of war (POW).

Figure 2. Archie Cochrane as a POW with his identity card (From Cardiff University Library, Cochrane Archive, University Hospital Llandough).

Shortly after his capture in June 1941, he was sent to a POW camp at Slonica in Greece where he conducted his “first, worst and most successful clinical trial” (2). The camp was a run-down, overcrowded army barracks, infested with bed bugs. The diet was minimal-breakfast: unsweetened "ersatz" coffee; midday: a bowl of vegetable soup; evening: two slices of plain bread- in all, about 400 to 500 calories. Archie was appointed chief medical officer by the Germans, not because of his medical abilities, but because of his time in Germany he spoke fluent German. He also became the senior British officer in charge of 8000 demoralized, hungry British prisoners of war.

In August an epidemic of jaundice accompanied by edema began and rapidly progressed. The German doctors claimed that the edema was due to the sun and not to starvation. Archie was also afflicted with severe jaundice and pitting edema above the knees. He decided that something must be done, and that he was the only one who could do it. He hypothesized, incorrectly as it turns out, that the prisoners were suffering from “wet beriberi" due to a vitamin deficiency. Archie bought some yeast on the black market and recruited 20 young prisoners and divided them between two wards. Each man in one ward received two spoonfuls of yeast daily. Those in the other ward received one tablet of vitamin C. By the fourth day there was a conclusive difference in the edema. Archie asked the members of each ward whether they felt better, the same, or worse. Nine out of ten in the "yeast" ward felt better; none in the other.

Archie showed the results to the Germans and asked for yeast and more food. They said, as usual, that they would see what they could do. However, a young German doctor pointed out that the results were incontrovertible and they could be prosecuted for war crimes unless that did something. This led to the unexpected, the Germans actually produced the yeast and the epidemic was quashed. On reflection, Archie realized the edema was not wet beriberi. Furthermore, his trial numbers were too small, the time too short, and the outcome measurements poor. Yet the treatment worked. Archie later speculated that the small amount of protein in the yeast raised the plasma proteins sufficiently to correct fluid imbalance that led to the edema (2).

Archie’s second experience in POW life at Elsterhorst, Germany was very different. He was assigned to the medical section where there were two other British doctors, who had been captured at Dunkirk. All the POWs with tuberculosis (most of whom were far advanced) of all nationalities, were herded together behind the wire. Archie knew a certain amount about tuberculosis and offered to take over that section of the medical work. Conditions were in many ways not too bad. Through Red Cross parcels there was sufficient food. Archie was able to 'screen' patients and do sputum 'smears' but radiographs were very limited. He could give patients bed rest, pneumothorax, and pneumoperitoneum. There was a French physiologist, an expert in 'adhesion-section', and thoracoplasty was a possibility. This tuberculosis work took up only a small part of Archie’s time. He realized that the rest of efforts must be devoted to "care" as the chance of a cure among these cases was minimal.

He would later state that “I remember at that time reading one of those propaganda pamphlets, considered suitable for POW medical officers about ‘clinical freedom and democracy’. I found it impossible to understand. I had considerable freedom of choice of therapy: my trouble was that I did not know which to use and when. I would gladly have sacrificed my freedom for a little knowledge. I had never heard of ‘randomized controlled trials’, but I knew that there was no real evidence that anything we had to offer had any effect on tuberculosis, and I was afraid that I shortened the lives of some of my friends by unnecessary intervention” (1).

Post-War Studies

After the War, Archie continued his studies. He studied preventive medicine at the London School of Hygiene and Tropical Medicine. There he was greatly influenced by Austin Bradford Hill's teaching on randomized clinical trials and acknowledged Bradford Hill's influence for the rest of his life. In 1947, Archie won a Rockefeller Scholarship and went to the Henry Phipps Clinic in Philadelphia, where he became interested in x-ray studies of pulmonary tuberculosis and developed what became a lifelong interest in observer error.

Academic Career

After returning from Philadelphia in 1948, Archie began his academic career at the recently formed Medical Research Council's Pneumoconiosis Research Unit in Penarth, near Cardiff in South Wales. He initially conducted groundbreaking comparative studies of dust levels in the coal mines of South Wales. Two years later, he launched the Rhondda Fach study to investigate the etiology of progressive massive fibrosis and worked at the Pneumoconiosis Research Unit for over a decade. His main interests were the x-ray classification of coal workers' pneumoconiosis and the relationship between x-ray categories, dust exposure, and disability. His interest in this field continued for the rest of his life, as reflected in the completion during 1974 to 1986 of twenty year and thirty year follow-up studies of the population of the Rhondda Fach (3-6).

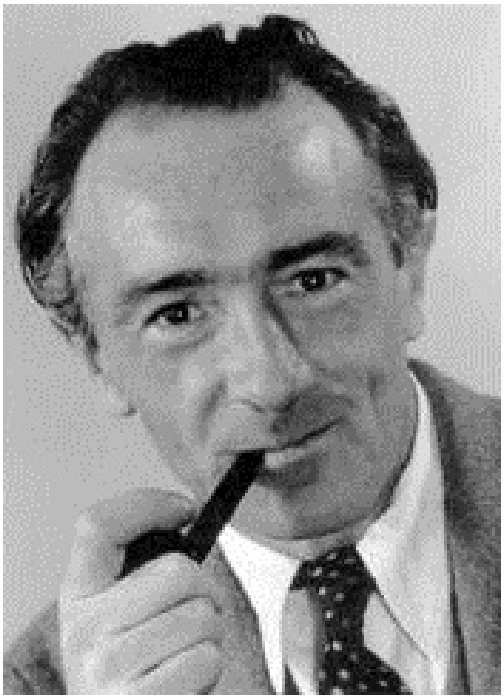

Figure 3. Archie Cochrane in 1949 (From Cardiff University Library, Cochrane Archive, University Hospital Llandough).

Archie's research achieved very high response rates in surveys and follow-up studies probably due to the team of disabled miners he formed to help maximize survey follow-up rates. This approach was new and revolutionary at the time. The quality of Archie's research was reflected in the decision by the Medical Research Council to invite him to establish and direct a new epidemiology unit based in Cardiff in 1960. Archie was appointed to the David Davies Chair of Tuberculosis and Diseases of the Chest at the Welsh National School of Medicine. Under Archie's direction, the Epidemiology Unit quickly established an international reputation for the quality of its surveys and studies of the natural history and etiology of a wide range of common diseases, including anemia, glaucoma, asthma, and gallbladder disease.

Archie is probably best remembered for his advocacy of randomized controlled trials. He always acknowledged influence of Bradford Hill in introducing him to the principles of using these studies to obtain unbiased estimates of the effects of healthcare interventions. He coordinated a wide variety of randomized trials to evaluate pharmaceutical, surgical and health service interventions. The trials with the most enduring and important implications for human health were those done in collaboration with Peter Elwood and included the first studies showing that aspirin could reduce the incidence of cardiovascular diseases (7)

His interest in health care delivery extended to a trial to determine where patients with an uncomplicated myocardial infarction should recover-either at home or in the hospital (8). After several unsuccessful attempts and over the protests of the cardiologists, Archie finally succeeded in receiving approval to start the trial. An interim analysis was planned and Archie gathered the hospital staff to present the results. He passed out a table and began by pointing out that none of the results were statistically significant. Archie went on to say, "Well gentlemen, it turns out that you were right and I was wrong. It is dangerous for patients to be cared for at home and they should be in the hospital." An immediate cry from the cardiologists went up that "You're killing people with your clinical trial" and they demanded that Archie stop the study. Archie let the commotion die and replied, "Well that's very interesting, gentlemen, because when I gave you the table of results, I swapped the columns around. It turns out that your hospitals are killing people and they should be at home. Would you like to close down the trial now; or should we wait until the best results?" Archie referred to the cardiologists' attitude as the "God complex" (8). By this he meant, no matter how complex the problem, the person has an overwhelming belief that they are infallibly right in their solution.

An invitation from the Nuffield Provincial Hospitals Trusts to prepare the 1971 Rock Carling Lecture provided Archie with an opportunity to speak on controlled clinical trials. The book that resulted from the lecture, "Effectiveness and efficiency: random reflections on health services" (1), promptly became influential. He emphasized three themes in the book: 1. the importance of using randomized trials to identify which health service interventions are effective; 2. the relevance of assessing the costs or efficiency of the options available; and 3. the importance of equitable access to effective treatments.

Recognition and Later Years

In the year the book was published, 1972, Archie became the first president of the new Faculty of Community Medicine of the Royal College of Physicians (subsequently Faculty of Public Health). He received an honorary doctorate from the University of York the following year; was Dunham Lecturer at Harvard in 1974; became an honorary fellow of the American Epidemiological Association in 1975; and, in 1977, he received an honorary doctorate from Rochester University and became an honorary fellow of the International Epidemiological Association.

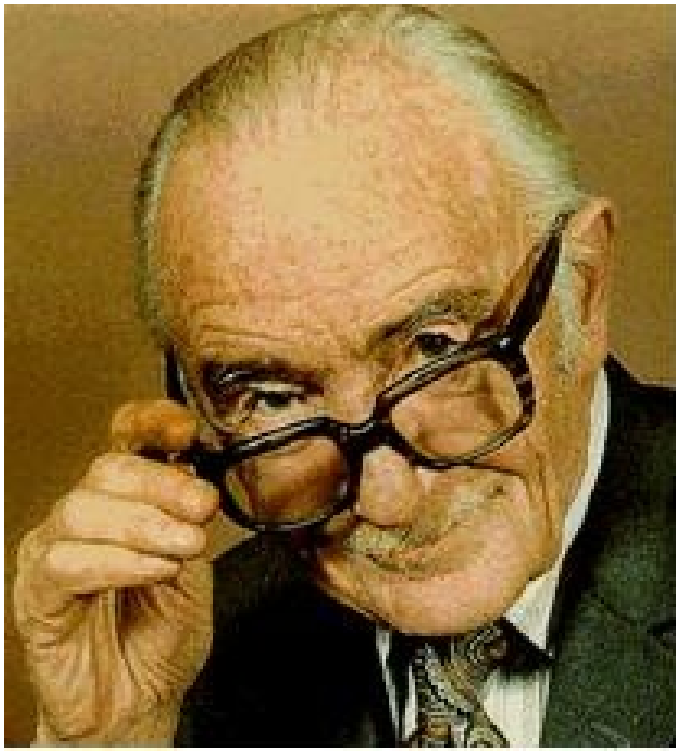

Figure 4. Archie Cochrane after retirement (From Cardiff University Library, Cochrane Archive, University Hospital Llandough).

Now with time to reflect, Archie followed up his criticism of the medical profession in 1979 by stating, “It is surely a great criticism of our profession that we have not organized a critical summary, by specialty or subspecialty, adapted periodically, of all relevant randomized controlled trials” (9). In particular he challenged the obstetric profession for not having used the randomized controlled trial design to ascertain whether interventions related to pregnancy and childbirth were effective. He awarded the “wooden spoon” to obstetrics but the “silver spoon” to phtisiology (the study of tuberculosis) because of his mentor’s, Sir Austin Bradford Hill’s, landmark trials on the use of streptomycin (9). A few years after his death, Archie’s challenge led Iain Chalmers, an obstetrician, and his co-workers to create the Oxford Database of Perinatal Trials (10). Based on this database of controlled clinical trials, it was quickly realized that, to keep up with the rapid developments in the fields of perinatology and neonatology, the published reviews required timely updates. This realization formed the

basis for the Cochrane Collaboration, which was established in the early 1990s, and had the aim of helping make well-informed decisions about health care (11). Thousands of volunteers are now involved in preparing and maintaining systematic reviews of randomized trials and other evidence within this international, non-profit organization. Cochrane Reviews are published electronically in The Cochrane Database of Systematic Reviews, the principal element of The Cochrane Library.

Legacy

Archie Cochrane died of cancer in 1988 after a long illness. His life has been described in an autobiography written with the assistance of Max Blythe (12). He did not found the Cochrane Collaboration as commonly believed, although he undoubtedly would be honored to have it named after him. Archie would be delighted with the Collaboration's 10 principles: 1. collaboration; 2. building on the enthusiasm of individuals; 3. avoiding duplication; 4. minimizing bias; 5. keeping up to date; 6. striving for relevance; 7. promoting access; 8. ensuring quality; 9. continuity; and 10. enabling wide participation. Undoubtedly, if he were alive today, he would have awarded the Collaboration his silver spoon.

Some have questioned whether the Cochrane Collaboration and evidence-based medicine are a threat to physician autonomy. The Lancet has decried evidence-based medicine as an internal threat to the autonomy of the physician (13). Similar fears were expressed by Feinstein and Horwitz (14) in their critique of evidence-based medicine, calling it, "A new form of dogmatic authoritarianism may . . . be revived in modern medicine, but the pronouncements will come from Cochranian Oxford rather than Galenic Rome" (14). However, Hill (15) dismisses these fears and adds the comment that physician autonomy would have been the last of Cochrane's concerns. I disagree. Archie would have been very concerned. He would have recognized those with the God complex who cite studies that lack scientific rigor as evidence based medicine. Furthermore, he would have abhorred that this is used by some to advance their own biases or conflicts of interest. Archie would undoubtedly have viewed these authoritarian and intolerant views of medical practice as disturbing as the lack of evidence and awarded them the wooden spoon.

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