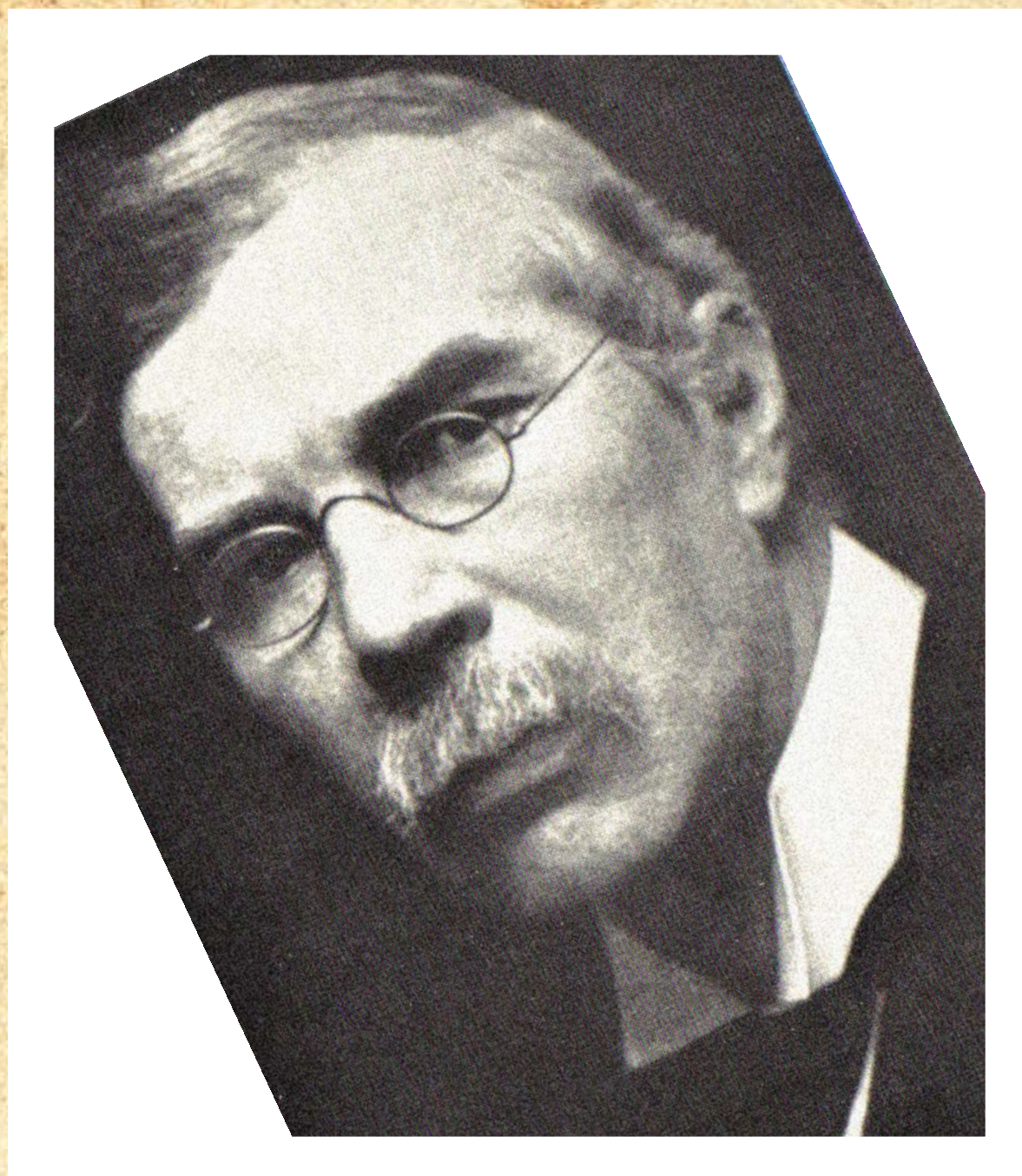


Typhoid Vaccine



Sir Almroth Edward Wright (1861-1947)

Britain's first Academic Immunologist
 A pioneer of Medical Laboratory Science

He was qualified in both Modern Languages and Medicine and commenced his professional life as a Physiologist. After working in Europe and Australia he returned to London. In 1889 he worked at the conjunct research laboratories of the Royal College of Physicians and Surgeons where his supervisor Dr German Sims Woodhead, then advisor on Pathology to the British Army, recommended him to the post of Professor of Pathology at the Royal Army Medical College based at Netley. He was appointed in 1892 as a civilian which led to some conflict with the other candidate David Bruce, a serving Officer who was appointed Assistant Professor.

An opinionated man, often aggressive when propounding his views and not always right, hence his nick-name "Sir Almost Right".

Typhoid Inoculation

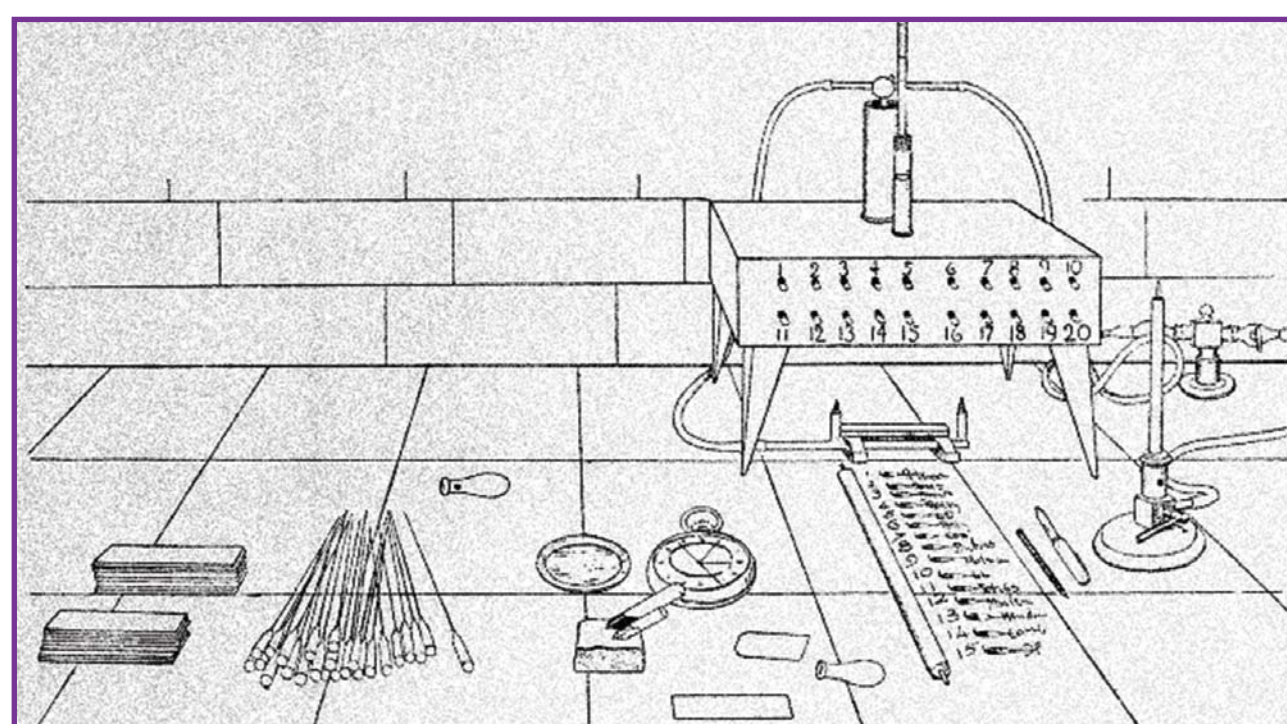
- Still convinced of the value of anti-typhoid vaccine Wright started a production unit in partnership with Parke Davies and arranged for a second study on British troops stationed in India. The promising results were ignored by the army
- 1914 on the eve of war, Wright appealed to the War Office to inoculate troops against typhoid and petitioned Lord Kitchener who agreed and ordered a mandatory inoculation programme
- Thanks to 10 million vaccine doses produced at St. Mary's Britain was the sole combatant with troops immunised against typhoid at the start of World War 1

Laboratory Instruments

During this period laboratory instruments were generally crude and home-made, so Wright - a pioneer in laboratory testing - made his own, developing and producing capillary tubes large enough to hold only a few drops of blood. With these instruments he could test blood without the necessity of drawing a great deal of it from a patient; all that was required was a finger prick. Wright also recognized the importance of uniformity in laboratory testing, so he made sure each tube was identical.

- At the RAMC Netley he began his life's work on immunity
- Typhoid Fever had a death rate of 10-30% at that time
- 1884 Gruber, Pfeiffer, Kolle & Widal had shown that patients who recovered from typhoid had antibodies in their serum which agglutinated the typhoid bacteria in vitro. The Widal Test was born
- He tested the effect of injection with heat killed typhoid culture first on himself and co-worker Semple, then on 15 soldiers
- He produced antibodies and immunity to typhoid
- Despite bad side effects he then inoculated 2835 British soldiers going to India where typhoid was common. It appeared very few developed the disease
- 1899 the War office agreed to inoculate soldiers heading for the Boer War but limiting it to volunteers only. Of the 448,000 dispatched only 14,000 were inoculated, anecdotal evidence showed its worth where only half of the inoculated men developed the disease, however record keeping during the war was poor. Wright had a deep aversion to statistics
- This was seized upon by the leading biological mathematician of the time, Karl Pearson, who said the data showed nothing
- The War Office set up an inquiry which included David Bruce. It later sided with Pearson and judged the vaccine ineffective and the programme was suspended
- Incensed by this, Wright resigned his post at Netley. Leishman, who was appointed as his successor, continued the work, modified the production method and improved the inoculum
- 1902 Wright moved on to St Mary's Hospital Medical School as Professor of Pathology and set up a vaccine and inoculation clinic

1912 published "Technique of the Teat and Capillary Glass Tube". He demonstrated the opsonic effects of serum, the principle of antibody inoculation in bactericidal infections, the bacterial efficiency of the whole blood and phagocytes and the influence of the antitryptic power of the serum on the growth of microbes. His team consisted of Freeman, Colebrook, Mathews, Fleming and others.



The Maidstone Typhoid Outbreak of 1897

- The first coordinated approach to control. This was the largest outbreak of typhoid fever ever reported in the United Kingdom. It began September 1897 and ended in January 1898 affecting nearly 2000 people, 143 of whom died. At its peak 900 people contracted the disease in a two week period. The cause was traced to contaminated mains water and its continuing spread was linked to the poor state of the drainage system and the housing of many of the victims
- It was a turning point in public health, featuring the first recorded trial of immunisation against typhoid and also disinfection of a mains water supply, using chloride of lime
- The typhoid immunisation trial was led by Professor Almroth Wright. Staff at a large psychiatric hospital near Maidstone were asked to volunteer for the trial. None of the 84 who received the new vaccine developed the disease, compared with four cases in the 120 who were not vaccinated. This established the vaccine's potential value and led to larger trials
- The chlorination of the water supply, organised by the bacteriologist Dr Sims Woodhead, was a difficult procedure that required several attempts. Its success laid the foundations for continuous water treatment. The Maidstone outbreak may also have been the first in which telephones were used in the control of an epidemic, allowing doctors and nurses in the emergency hospitals to pass on information about cases

A Different Kind of Battlefield

- Flanders Fields were cultivated, well manured and horses were in common use around the battlefields. Soldiers living in the trenches became contaminated with mud containing faecal bacteria and bacterial spores
- Projectile wounds caused by bombs, shell fragments and high velocity bullets carried in filthy mud and fragments of soldiers clothing
- Most damage was caused by Clostridium perfringens synonym C. welchii causing gas gangrene and Chlostridium tetani causing tetanus

Treatment of War Wounds

Established thinking was based on the experience in the South African War. The land was bare and dry containing few pathogens. Projectile wounds were mainly from bullets fired from a distance often passing through limbs and often healed quickly without complication. This together with accident ward experience in civil hospitals led to the treatment of wounds with antiseptic solution. This Listerian tradition was blindly followed by military surgeons.

With Alexander Fleming he showed that these antiseptics killed the macrophages and neutrophils that were gathering at the wound, and prevented healing; furthermore, the use of antiseptic paste encouraged the growth of anaerobes, with the fatal production of tetanus or gas gangrene. Wright's (successful) approach was to clean the wound with sterile hypertonic saline and suture it secondarily.

Therapeutic Methods

Wright proposed three distinct therapeutic measures when dealing with wounds (1915 University of London Press)

- Treatment by antiseptics.
- Treatment by physiological methods such as opening and draining the wound to bring the antibacterial powers of blood to bear on the infecting microbes. Cutting out damaged and infected tissue. Applying hot fermentations (poultices) to induce active hyperaemia and increasing the outflow of lymph and lymphocytes. Leaving operation wounds un-sutured.
- Treatment by vaccine therapy.

Tetanus Antiserum

1899 Behring & Kitasako demonstrated that serum from another animal immune to a disease such as tetanus could be used to treat other animals (including humans) with the disease.

- Produces antitoxins that could be used to treat others effectively
- An antitoxin was developed for tetanus and diphtheria in 1890

What would have happened without Wright's Passion?

It took two or three years to overcome the old dogmas, by which time millions more lives had been lost. Would this have been achieved at all without Wright's passion and abrasiveness?