Tuberculous Scrofula: Belfast Experience

John Hedley-Whyte, Debra R. Milamed

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SUMMARY

The Belfast blitzes of 1941 are blamed in our family for the scrofula of my younger brother and sister and myself. Guinea pigs and rabbits at Musgrave Park proved that each of us had bovine derived TB infection by failure to pasteurize milk when tuberculin-tested milk was not available. The clinical head of Harvard Medical School's anti-tuberculosis effort contacted his boss, Professor Maxwell Finland, who ascertained from Selman A. Waksman that his antibiotic streptothricin was bacteriostatic against TB but too toxic for humans. Finland, born 1902, knew Waksman (born 1888) well, each having emigrated from the Czarist-ruled Ukraine. Waksman, in 1942, had hopes for an analog to streptothricin: an antibiotic from Actinomycetes griseus which had been culture-isolated in 1916 for his M.Sc. thesis. Streptomycin was still 6-9 months away ascertained from Selman A. Waksman that his antibiotic could be a year or more. The fact that we three children were diagnosed simultaneously suggested to Badger a strong infecting dose.

Badger asked me if anyone had coughed over me. He then asked if a cow had coughed over me. I laughed and said “No”. He next asked if any of the three of us had kissed a local cow. “No.” Did we like milk? “Yes.” Had we been given boiled milk? “Only at the time of the blitzes.” Our cook, Kitty Lee, and our nurse were then examined. They were, and had been, in perfect health. Badger then asked them if the milk had always been brought to a boil before being given to us. An awkward silence ensued. Kitty Lee said that once during the blitzes, when the regular tuberculin-tested milk, or guaranteed pasteurized milk could not be delivered, the milk for the nursery had been taken before her wood-fire had really warmed the local substitute. At very least, our milk should have been heated to 62º C for 30 minutes or 72ºC for 15 minutes. These were the rules of the Belfast Cooperative Society promulgated in 1913, said my father.

MANAGEMENT

What to do? Badger suggested that he preferred to use American equipment, methods and personnel. My father was in a delicate situation. The British were threatening him with court martial for purchasing illegal Éire and border-produced food for his command, the now-Allied Military Hospital at Musgrave Park. The Whiteabbey TB Hospital scandal was being exploited by the left-wing politician Harry Midgley.

In 1908 TB was made a notifiable disease in Northern Ireland. The United States authorities were convinced, not without reason, that United Kingdom TB incidence was a disgrace. In 1932, a Cattle Disease Committee was established, which reported in 1934 that approximately thirty percent of U.K. cows were tuberculous. In Ulster, control of bovine TB was, during the period 1935-40 better than in Scotland, but not as successful as in England and Wales. The Registrar-General's Annual Report for 1941 cites death rates from tuberculosis as 1.04 per 1.000 in Northern Ireland, 0.73 for England and Wales, 0.85 for Scotland and 1.24 for Éire. According to Lionel Whitby, in the U.K. 5 years

John Hedley-Whyte, Debra R. Milamed

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David S. Sheridan Professorship in Anaesthesia and Respiratory Therapy
Harvard University, 1400 VFW Parkway, Boston, MA 02132-4927 USA
Correspondence to Prof. Hedley-Whyte
john_hedley-whyte@hms.harvard.edu
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necessary diagnostic equipment and the U.S. tuberculin for
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British needles were blunt14. As to the tuberculin purity,
did my father not know of the Lübeck “massacre of the
innocents”—72 babies killed by contaminated tuberculin?15

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Mantoux and that he “should put me on M and B 693 (Table
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State Scholarship, he entered Rutgers University16-17. In 1916, his
seminal paper on Streptomycin18,19 won him his M.Sc. degree from
Rutgers. He became a U.S. citizen and was appointed a Research
Fellow at the University of California, Berkeley. The University
of California granted his Ph.D. in Biochemistry in 1918. The
remainder of Selman Waksman’s career was spent at Rutgers. He
was elected to the U.S. National Academy of Sciences in 1942.
Selman Waksman visited Ireland once, in 1946. He was confined
with his wife Deborah to “a boarding house in Adare” in County
Limerick’s Golden Vale for three full days. “We were herded like
cattle and told to wait. The facilities, especially the food, were
very poor”15. After release, the Waksmans met their physician
son, Byron, in Frankfort-am-Main, where he was stationed in the
U.S. Service after his having received his M.D. degree in 1943
from the University of Pennsylvania17. In 1952, Selman Waksman
received the Nobel Prize in Physiology or Medicine. The Nobel
Committee cited his work on “the microbiological population of
the soil, sulphur oxidation by bacteria, microorganisms and soil
fertility; decomposition of plant and animal residues, nature and
formation of humus; occurrence of bacteria in the sea and their
role in marine processes; production and nature of antibiotic
substances; and taxonomy, physiology and biochemistry of the
actinomycetes”20. After Stockholm he was decorated by the
Japanese Government with the Second Order of Merit with the
Grand Gordon of the Rising Sun and received in audience by the
Emperor. He and his wife were invited to dinner at the home of
H.I.H. Prince Takahito Mikasa, where plans for establishment
of the Japan Waksman Foundation were formulated21. Selman
Waksman died on August 16, 1973. Deborah, his devoted wife
of 57 years, and a most talented musician, died a year later.
They are buried at Wood’s Hole, Cape Cod, Massachusetts. Byron,
their son, an only child, joined the staff of the Massachusetts
General Hospital before accepting chairs at Yale and in New
York. He has returned to Harvard as a Visiting Doyen of the
Center for Neurologic Diseases, where he is now the Dean of
Neuroimmunology and Mentor Extraordinaire16,17.

Max Finland also told Ted Badger that Waksman had hopes
for his newest antibiotic, streptomycin17,22 and that Waksman
was now concentrating on Actinomyces griseus which he had
culture-isolated 26 years before for his Rutgers M.Sc.19. This,
Waksman proposed to rename streptomycin and have tested,
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3) but not my brother and sister--she could take halibut-liver
oil pills”. My TB had spread, but theirs appeared localized.
With fresh air and cod or halibut-liver oil my younger brother
and sister would cure themselves: in our adulthood there
would be a 5 percent chance of recrudescence5

Professor Waksman’s son Byron, a medical student at the
University of Pennsylvania, was now telling his father,
replayed Max Finland, to quit treating tuberculous guinea pigs
and rabbits and start on humans.

We awaited the U.S. equipment to needle biopsy our cervical
glands and my right Achilles tendon62-64 and appropriate swabs
for our tonsils. The Musgrave Park guinea pigs and rabbits
were thereafter inoculated and later autopsied. Bovine TB
Rycroft, on a visit to Windy Edge, told us we had the King’s Evil, which could be cured by a Royal laying-on of hands. My father said he had asked Arnold Stott (Figure 2), physician to the Royal Household, to take over our management. “Second best to His Majesty,” rejoined Rycroft.

After inoculation with the aspirate from my neck, the guinea pig and rabbit were unharmed, but became symptomatic when inoculated with aspirate from the lupus over my right Achilles tendon. My supratendinous aspirate was of bovine tuberculous origin. I was asked by Badger if I had ever been bitten on the right ankle by my brother or sister. “They had neck pathology, not facial,” said Rycroft. My ankle healed after a fortnight of the sulphonamide treatment, which was then terminated.

Remembering my reading lessons of the spring, I asked General Arnold Stott in September 1942 whether he had discovered Arnold’s nerves in the hiding place of earwigs. “No, it was a German, Friedrich Arnold (1803-90). He died when I was your age,” my Doctor Arnold retorted.

Arnold Stott took over our surveillance until 1952. Stott was a Governor of Wycombe Abbey, my sister’s boarding school. Our upbringing was in no way constrained. Our schools were told by Sir Arnold Stott, from 1946 KBE, that we were in no way infectious. My sister’s scrofulous neck glands were excised by a Newcastle-upon-Tyne surgeon, Ronald Watts, FRCS, Edin.—inelegantly but successfully, said my father. Stott agreed and my sister refused plastic surgery. My brother Michael’s tonsils were removed. He awoke from the chloroform shouting “John’s done this to me!” Not true, but

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Table 2:

| 1. SULPHAPYRIDINE (M and B 693) | C_{11}H_{11}N_3O_2S |
| 2. STREPTOTHRICIN | C_{16}H_{33}N_0 |
| 3. STREPTOMYCIN | C_{21}H_{39}N_7O_{12} |
| 4. PAS (PARA-AMINO SALICYLATE SODIUM) | C_{7}H_{6}NaO_{12}.2H_{2}O |
| 5. ISONIAZID | C_{6}H_7N_3O |

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Badger had concluded that maybe it was the Belfast blitzes’ infected milk, so we blamed the Germans.

**FOLLOW UP**

During the 1940s and early 1950s, Stott would examine us and recite his ‘Ryki’ ballads about Rycroft’s war and horsemanship and the snakes and wild animals in Rycroft’s Number 35 Harley Street consulting rooms. We heard from Stott of Rycroft’s successful human corneal grafts later of his use of Waksman’s actinomycin D (NSC-3053) to treat certain eye tumors.

On July 1, 1960 my wife became Sidney Farber’s intern; we soon were told of Selman Waksman’s 1954 arrival at the Boston Children’s Hospital with 300 mg of actinomycin D (NSC-3053). The “little vial” was delivered and Waksman and Farber “started work immediately. To our great pleasure,” writes Professor Farber, “we quickly found—that this was the most powerful antitumor agent.” Within a few months, childhood Wilms’ and Ewing’s tumors were being cured. For gestational choriocarcinomas actinomycin was combined with Methotrexate, NSCF-740, glutamic acid, N-F-[[2,4-diamino-G-pteridinyl]methyl] methylaminobenzoyl]. Farber always gave credit to Gerhard Domagk’s group’s work on animal tumor treatment with actinomycin C.

From 1960, Ted Badger was my caring Boston physician. In 1969 our singles tennis match at The Country Club unmasked his need for an aortic valve replacement. The replacement at the Massachusetts General Hospital was entirely successful and led to a memoir and critique. Badger lived another ten years, but would never again play tennis against me.

**PARTIAL IMMUNITY**

Is bovine TB disease protective against subsequent infection with human TB? This question has been debated since Koch’s description of the bacterial causes of human and bovine tuberculosis. My father did not seem to mind my boyhood conversations with Eric Arthur Blair at Greystone, Stockton-on-Tees, the home of the O’Shaughnessy’s. Laurence Frederick O’Shaughnessy, with whom my father had grown up, was known as Eric O’Shock from an early age. O’Shaughnessy was the famous Eric then, not his sister Eileen’s husband, Eric A. Blair. Eric O’Shock’s death at the Dunkirk evacuation of the second BEF was mourned by both the Allies and the Axis. He had been Sauerbruch’s favourite assistant in Berlin.
In his 1954 autobiography Waksman reported the isolation of actinomycin in 1940, clavicipitacin in 1941, streptothricin in 1942 and streptomycin in 1943. Publication followed within the year.

Eric Blair in 1942 and 1943 questioned me at Greystone about horse herd behaviour. He was writing Animal Farm as George Orwell. We discussed the intelligence ranges of Clover the intelligent mare and Mollie the flighty but beautiful mare. I emphasized the leadership roles of mares and their territorial and herd behaviour. My mother told me not to get too close to this coughing Old Etonian. My father said I was protected by having had the King’s Evil. Is this protection more powerful than BCG vaccination? The World Health Organization has reported an estimated 440,000 incident cases of MDR tuberculosis worldwide in 2008. The World Health Association’s (WHO) twelve recommendations for the control of TB must be implemented.

Sixty-nine years after the scrofula diagnosis I have a calcified cervical gland, my sister’s neck scars are just visible, and my brother’s cervical adenopathy seems to have had complete resolution. They have approved this Medical History.

ACKNOWLEDGEMENTS

We thank Professor Douglas E. Eveleigh of Rutgers University for his assistance. H. Boyd Woodruff will receive the U.S. National Academy of Sciences 2011 Award for the Industrial Application of Science. Woodruff is being honored during the 148th Annual Meeting for “leading the development of multiple antibiotics, vitamin B₁₂, and the avermectins, the latter revolutionizing parasite treatment in livestock and humans.” The authors have no conflict of interest.

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