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Marc Daniels (1907–1953): a pioneer in establishing standards for doing and reporting clinical trials

John Crofton[†]

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Introduction

Marc Daniels' major contribution to medicine was his charge of administration and reports of the early and classical controlled trials of anti-tuberculosis chemotherapy. These included the first trial of streptomycin given alone,¹ followed by similar trials of para-aminosalicylic acid (PAS) and isoniazid, both alone or in combination with streptomycin and/or with each other. These trials were 'classical' because the techniques used became the model worldwide for testing the effectiveness of new treatments in any disease or establishing the relative efficacy of previous alternative treatments.^{2–4}

The early trials demonstrated the initial effectiveness of streptomycin but the frequent later emergence of drug resistance. Resistance was often associated with deterioration following initial improvement. PAS proved to be less powerful but, in combination with streptomycin, greatly reduced the incidence of resistance to both drugs, with corresponding increase of cure rates.

During the later isoniazid trial, Daniels developed symptoms of his fatal liver cancer. He barely survived to see the publication of the second report which he himself had largely drafted. Isoniazid proved to be almost a wonder drug – highly effective, cheap, with few side effects – and resistance could be largely prevented by combination with other drugs.

These trials were carried out in a number of centres in the UK. They needed meticulous planning, meticulous recording and meticulous coordination of their clinical, radiological and laboratory aspects. Strict random allocation to the different treatments had to be ensured. Radiological progress was assessed by an independent panel unaware of the treatment group of each patient assessed. It needed outstanding tact and diplomacy to coordinate the range of centres and the range of specialties involved, to minimise dropout and to ensure fully accurate data. Daniels' personality, knowledge, background experience and capacity for

hard work made an outstanding contribution to the success of these trials. He was also, with Austin Bradford Hill, responsible for the analyses and for compiling the ultimate reports.

Career

Marc Daniels was born in Cairo on 11 January 1907. In 1912, the family moved to Manchester, where his father had a textile business, and Marc was educated at Manchester Grammar School. He spent a year in Paris studying natural sciences and obtained a BSc from Manchester College of Technology. He started work in his father's firm but after two years decided on a medical career. He returned to Paris and qualified MD, with award of a Bronze Medal. He worked for some months in a French tuberculosis sanatorium and then returned to England, taking the Triple Qualification Examination to obtain British medical registration.

After junior hospital posts in general medicine and at a fever hospital, he took the Diploma in Public Health course at the London School of Hygiene and Tropical Medicine. Aiming at a public health career, he became an assistant Medical Officer of Health and Tuberculosis Officer in Lincolnshire. This proved frustrating and shocked his social conscience. He moved in 1942 to serve as the third Scholar to the Royal College of Physicians of London's Proffit Survey of Tuberculosis among young adults.⁵ The work had to be extensively reorganised to meet wartime conditions. With VS Springett, Daniels demonstrated his skills in analysing the results and preparing the final report. The report showed the importance of contact exposure and the consequent enhanced risk to nurses and hospital workers. This later led to its official recognition as an industrial disease in these groups.

He had already begun work part-time in London with the United Nations Relief and Rehabilitation Administration (UNRRA), the international body concerned with the grim health problems of refugees in war-torn countries. As soon as the Proffit Report

[†]Sir Crofton died a couple of years ago

was completed, Marc Daniels went abroad as one of UNRRA's tuberculosis consultants, working in Italy, Poland, Czechoslovakia, Austria and Geneva, utilising his fluent French and reasonable knowledge of German and Italian. He later used this experience to give the Milroy Lectures of the Royal College of Physicians of London on 'Tuberculosis in Post-War Europe'.

In 1947, Daniels was sent by the British Foreign Office with a group to investigate the incidence of tuberculosis in the British Zone of Germany.⁶ They found a high incidence in Berlin, but elsewhere in Germany, it was similar to the then rate in the UK and other countries.

Controlled trials

In 1947, Philip D'Arcy Hart, the Director of the MRC's Tuberculosis Unit, invited Daniels to take charge of the first controlled trial of streptomycin.¹ This trial was conducted under the aegis of an MRC Committee chaired by Geoffrey Marshall, which included, as statistical advisor, Austin Bradford Hill, Professor of Medical Statistics at the London School of Hygiene and Tropical Medicine, with whom Daniels was to work very closely. Daniels also became engaged in the MRC's survey of tuberculin positivity in school-children and then in the design and running of the MRC's subsequent controlled trial of BCG for school leavers, yet another classic trial.⁷

In 1948, he visited New York with other members of the Streptomycin Committee and he became a member of the Streptomycin Subgroup of the World Health Organization's (WHO) Expert Committee on Tuberculosis. For the United Nations Committee for Refugees and WHO, he inspected Displaced Persons' Camps in Trieste. The same year he contributed to a colloquium on the chemotherapy of tuberculosis held by the Medical Research Council of Ireland, a topic on which he lectured in Oslo, Bergen and Paris.

Apart from this intensive professional life, his social conscience in that difficult post-war period led him to become a Member of the Association of Scientific Workers, the Socialist Medical Association and the Medical Association for the Prevention of War.

In conclusion

I reproduce here my assessment of Marc Daniels in his *Lancet* obituary in 1953:

Much of his work was done quietly behind the scenes. Often the only acknowledgement was a

small footnote to say that he had compiled a report. Yet few people have contributed so much to the attack on tuberculosis, both by the work he did himself and by his influence on other people. Not only did he help clarify much heterogeneous epidemiological data but his practical sense enabled him to give advice which, in more than one country, materially contributed to the control of the disease. Only a remarkable personality could have coordinated with so little friction the long series of MRC trials of chemotherapy and tuberculosis. The secret of his success was probably his complete honesty of purpose, his intellectual integrity and the obvious fact that he was quite uninterested in any personal credit. The striking advances made by these trials would by themselves be a fitting memorial.

But he was not only valued by his friends for his clarity of mind and his professional knowledge. His interests ranged over music, art, politics, philosophy and much else. If to be civilised is to be able to discuss any idea without prejudice he was the most civilised of men. He had a talent for friendship. He once said that his life was made up of the friends he had known. Anyone who had known him was the better for it. He faced his last illness with astonishing courage, and up to a few days before his death he was giving valuable advice on the conduct of investigations. His main care was still that the work should be well done.⁸

Marc Daniels had two children – Helen and Judith – by his first marriage to Anne Burgess in 1940. In 1949, he married Kay Graw, an American whom he had met in the course of his UNRRA work. After he died, she became the administrator in the later classical British/Indian MRC chemotherapy trials done by Wallace Fox and colleagues based in Madras, indirectly a further memorial to Daniels.

Daniels' father later endowed a still continuing series of Marc Daniels Memorial Lectures at the Royal College of Physicians in London. I was privileged to be asked to give one of the earliest of these.⁹

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