J R Coll Physicians Edinb 2008; **38**:89–91

Lucy Wills (1888–1964): The life and research of an adventurous independent woman

H Bastian
Head of Health Information Department, German Institute of Quality and Efficiency in Health Care, Cologne, Germany

ABSTRACT Lucy Wills was one of a pioneering generation of women in medicine and medical research in England. After a double first honours degree in botany and geology from Cambridge in 1911, she travelled to South Africa, where she worked as a nurse during the First World War. Wills then gained a medical degree in London in 1920. By the late 1920s she had developed an interest in haematology and began travelling to India to investigate pernicious anaemia in pregnancy. There she identified a substance often called 'the Wills' factor', which was later recognised as folic acid. Wills undertook a placebo trial of routine iron supplementation in pregnant women during the Second World War, hampered, but not stopped, by bombing. In retirement, she continued to study nutritional effects on health in South Africa and Fiji.

KEYWORDS Biography, folic acid, haematology, Lucy Wills, pregnancy anaemia

DECLARATION OF INTERESTS No conflict of interests declared.

Published online ***2007***

Correspondence to ***H Bastian, Health Information, German Institute for Quality and Efficiency in Health Care (IQWiG), Dillenburger Strasse 27, 51105 Köln, Germany***

tel. ***+49 (0)221 3568 5401***

fax. ***+49 (0)221 3568 5881***

e-mail ***hilda.bastian@iqwig.de***

> '(A)n experiment was started at the end of 1943 planned to show the effect on the haemoglobin level and on the general health of the pregnant woman, not only of the improved rations but also of the routine administration of iron… Unfortunately, a flying bomb incident interrupted the work, but, though the actual number of observations were not as large as expected, they were large enough for statistical analysis… Alternate patients were given, from the first attendance, either Blaud's capsules… or similar capsules containing a placebo… The laboratory workers were not told which patients were receiving iron, but after a few visits it did not require a Sherlock Holmes to ascertain the nature of the capsules being taken.'[1]

The continuation of research despite a bombing 'incident' and the wry statement about Sherlock Holmes give some insight into the personality of a pioneer in haematology who led a most eventful life. Lucy Wills' claim to international fame had come in 1931, with a paper in which she identified through research in India a substance that was later recognised as folic acid.[2] It is still sometimes called 'the Wills' factor'. She retired from London's Royal Free Hospital in 1947, around the time the article quoted above was published,[3] but continued to work on nutritional effects on health in South Africa and Fiji.[4]

The portrait of Lucy Wills in the James Lind Library (Figure 1) apparently shows her in the botanical garden to which she devoted the last quarter of her life, along with

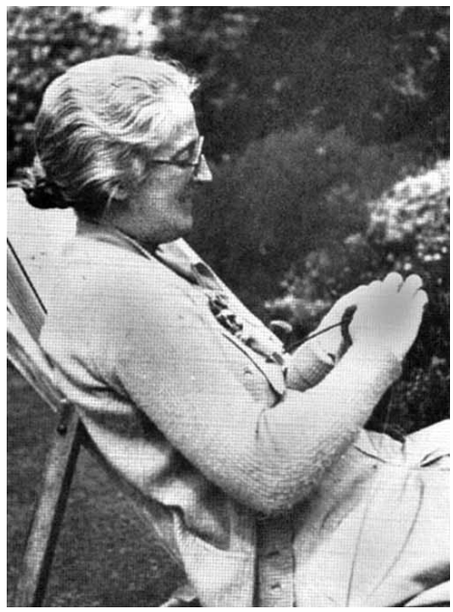

FIGURE 1 Lucy Wills.

a spell of ten years as a Labour councillor in Chelsea.[4] The photo shows a private aspect of a woman who

> 'is remembered as aristocratic, independent and radical in outlook, critical of established conservative medical and scientific committees. She rode to work on a bicycle rather than in a large car as did many of her colleagues.'[5]

Financial and intellectual independence shaped Wills' life opportunities and work. She was the third child in her family, born in England on 10 May 1888. She went to a small private school, and then to the Cheltenham College for Young Ladies.[3] Cheltenham College was in the vanguard of new boarding schools providing a high standard of academic education in formerly male-only subjects such as mathematics. Cheltenham also sought to encourage a public-spirited and achievement-oriented life for women in Victorian England. It was Gothic in architecture, but reformist in character.[6] From 1858 on, the school was steered by the strong-minded and high-achieving Dorothea Beale for more than 40 years. Beale would have been in her last years at the helm of the college when Wills attended. It was a privileged environment, intellectually as well as socially. Beale did not allow students whose parents were 'in trade' to enter Cheltenham.[6]

Beale was an early and long-time supporter of educational reform and suffrage for women, being one of the signatories on John Stuart Mills' 1867 petition to Parliament to give women the vote. She was also the founder of St Hilda's College in Oxford, although she did not live long enough to see women students accepted at Oxford University. An excellent picture gallery online at the BBC shows the environment around the time Wills was a student at Cheltenham – including the laboratory that must have helped shape her interest in science.[7]

Boarding schools such as Cheltenham were a particularly Victorian phenomenon, radical and progressive in the later quarter of the nineteenth century, but already seen as old-fashioned and oppressive by the end of the First World War.[6] Their historical progress provides some measure of the change in women's educational opportunities. The baseline for education for females had been low: consider the shocking fictional depiction of 'Lowood' by Charlotte Bronte in her novel *Jane Eyre*. Beale had briefly taught at the actual school on which Bronte had based Lowood.[8] Within decades, though, the reformist educational movement in which Beale was one of the leaders enabled the group of women in Wills' generation to gain entrance into professional and academic life.

From the strong grounding that she received at Cheltenham, Wills went on to Newnham College at Cambridge, one of the first colleges that was open to women in England.[6] Wills' primary interest at that time was still science, not medicine,[3] and she received a double first honours degree in botany and geology in 1911.[3]

After Cambridge, Wills travelled to South Africa with Margaret Hume, a fellow student at Cambridge who remained a lifelong friend.[3] Hume was a lecturer in botany in Cape Town at that time, and she also had an interest in the work of Sigmund Freud. This became of such interest to Wills that she considered studying psychiatry. However, a stint working as a nurse in South Africa during the First World War led her to decide on a career in medicine, which had only recently been an option for women in England. She returned to London and entered the London School of Medicine for Women, England's first medical school for women,[9] and gained her medical degree through London University in 1920.[3]

After graduating, Wills began working with another friend from Cambridge in the Department of Chemical Pathology at the Royal Free Hospital, which was not a very busy department at that time.[10] At the same time as her interest in and knowledge of medical biology was growing, the area of haematology was beginning to make advances. In 1926 Minot and Murphy published their groundbreaking work in Boston on diet to treat pernicious anaemia.[11] In India, Margaret Balfour, working at the Haffkine Institute in Bombay,[12] became aware of a high prevalence of a particularly severe and often fatal form of anaemia in pregnancy.[13]

It is not clear why Balfour made contact with Wills, but it may have been because the London School of Medicine for Women had a history of student and teaching involvement with India,[9] although such links also existed throughout the Victorian feminist movement.[14] By the late 1920s, Wills had begun a series of trips to India, where she undertook studies to try to isolate whether dietary factors played a part in the so-called pernicious anaemia of pregnancy.[15]

Wills has been criticised for taking a narrow biomedical approach, which did not pay sufficient attention to the social conditions limiting women's lives.[16] However, she undertook an extensive programme of observation, which included possible infective causes and living conditions as well as diet:[13]

> 'I spent many hours plating stools and doing Widal tests in an attempt to determine the nature of the diarrhea and the cause of the high temperature that affected so many of my patients with nutritional macrocytic anemia, only to find negative Widals and non-pathogenic organisms in the majority of patients.'[3]

Ultimately, though, Wills' studies suggested that some kind of vitamin deficiency was involved.

Wills worked closely with Sakuntala Talpade, Robert McCarrison and Manek Mehta in attempts to find a supplement that might overcome the deficiency they were observing. They tried many substances on rats. Wills was concerned, however, that an infection common in the rats might be playing a role in their anaemia,[13] so she decided to test some dietary interventions in monkeys. One particular monkey did especially poorly, and for reasons which are not recorded – perhaps in

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desperation – she tried the cheap yeast extract Marmite. It had a dramatic effect. Thus, after all the intensive examination of diets and exhaustive testing on rats, it was a chance intervention with a single animal that led to the breakthrough.[13] Wills had taken the first step to the discovery of folic acid.

Extensive testing of a variety of active and deactivated substances in women was the next step, and Marmite proved to be the substance that could help.[2,17] Wills' conclusion was that:

> 'These findings provide further evidence in support of the opinion, expressed in the previous paper, that the extrinsic factor… is not vitamin B2 but some other factor, as yet undetermined, which is present in both animal protein and Marmite.'[18]

Folic acid was named in 1941, when it was isolated from spinach.[5]

Lucy Wills returned to London at the outbreak of the Second World War,[4] where she continued her work on anaemia and on the effect of diet on health and illness. In her 1933 paper in *The Lancet* she had described her systematic experiments as 'clinical trials'.[17] However, the placebo-controlled test of iron supplementation in pregnancy, carried out with her colleagues at the Royal Free Hospital, appears to be the only report of a formal test of a treatment comparing two groups of people.[1] Wills and an all-woman cast[19] of researchers started their experiment in 1943, to address the question:

> 'Can it be shown that the pregnant woman whose haemoglobin has been raised by the routine administration of iron is in any way better off than her "untreated" sister?'[1]

And that question, they said, could only be answered by comparing results in comparable women, 'some receiving and some not receiving routine iron treatment from the very beginning of pregnancy'. We do not know what path led them to conclude that a trial using alternation either to a haematinic preparation or to a placebo was what they needed to do.

Despite the restrictions imposed by flying bombs, Wills and the rest of the team at the Royal Free Hospital, together with close to 500 pregnant women, were among the first to address a question that has remained important for generations of other women.[20]

Acknowledgements I am grateful to Professor Sally Davies for casting her haematologist's eye over this text before publication.

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19 Woodgate-Jones NP. Obituary: Gladys Hill. *BMJ* 1998; **316:**1172. (This obituary notice in the *BMJ* tells us a little about Wills' second coauthor, Gladys Hill (1894–1998). She qualified in medicine in 1923, went to Paris to study radium with Marie Curie, and became a consultant obstetrician and gynaecologist at the Royal Free Hospital in 1935. It was Hill who managed to keep clinical care operating throughout the war, including during the bomb 'incident' – not surprising, perhaps, for a woman who had worked for MI5 during the First World War. At an age when many people are beginning to retire (56), Hill set off to the US to learn cervical cytology, and later started one of the earliest 'well woman' clinics. Eventually she retired to Somerset where she 'took an interest in many local activities', living to several years past 100. According to her obituary in the *BMJ*: 'Miss Hill had a flair for teaching, having a horror of slovenly thought and shoddy work, and was examiner to London University and the Royal Colleges of Surgeons and Obstetricians and Gynaecologists.' I could find no further information on their other coauthors and would welcome learning more about any of them from readers.)
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