

Illustrations from the Wellcome Library

An Epidemiologist at Work: The Personal Papers of Sir Richard Doll

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Introduction

The personal papers of Professor Sir Richard Doll, CH, OBE, distinguished epidemiologist, are now catalogued and available for consultation at the Wellcome Library for the History and Understanding of Medicine.¹ Illustrating a life-long commitment to epidemiological research, they evince a strong sense of historical continuity and public responsibility, and demonstrate very well the social and ethical nexus in which epidemiology is rooted. Its focus on the balance of health benefits to be gained by a given community as a whole has, therefore, a utilitarian philosophical cast in its careful and disinterested weighing of risk and benefit. Ample evidence of epidemiology's statistical core—from computer-generated data to graphs and tables—is contained in the papers, as are the reasoning processes that lead to a balanced and supported set of conclusions. In addition to illustrating the epidemiologist at work, the papers allow us to hear something of the voices of those individuals and constituent groups of society who—through vested interest, uncertainty or vulnerability—have kept a close watch on many of the conclusions drawn, conclusions that may have seemed to some, from a professional, corporate or community point of vantage, to be more balanced in expression than they would have liked. Certainly there is no doubting on the evidence of the papers preserved—in the multiple drafts of papers, and in the close readings of the papers of others—that Doll was meticulous in his choice of words and their import. Taken as a whole, the Doll papers provide an insight into the practice of epidemiology in the second half of the twentieth century, a period in which the randomized trial—now much elaborated and often great in scale—has flourished.

As far as the practice of epidemiology in the period following the Second World War is concerned—when Doll began to work on clinical trials under Francis Avery

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¹ PP/DOL comprises 460 files stored in 60 boxes, spanning the years 1943–98. The collection is organized as follows: A. Regius Professor of Medicine, University of Oxford; B. Research; C. Consultancy; D. Lectures and Papers; E. Audio-visual resources.

Jones at Central Middlesex Hospital and under Austin Bradford Hill at the Statistical Research Unit of the Medical Research Council—he is in no doubt about the significance of Bradford Hill's contribution to the direction that epidemiology was to take. Doll's obituary for Sir Austin Bradford Hill notes the impact on the field of Bradford Hill's series of introductory papers on statistical principles, first published in the *Lancet* in 1937,² in which he “laid the foundation for the burgeoning science of epidemiology and transformed the conduct of clinical trials by demonstrating the advantages of randomisation.”³ In his subsequent paper on Bradford Hill's contribution to the progress of medical science, Doll identifies “the retrospective and prospective studies designed by Bradford Hill” as “the basic tools of epidemiology throughout the world.”⁴

It was, of course, Doll's early work under Bradford Hill that established smoking—the single word most readily associated with Doll in the mind of the general public—as the overwhelming cause of the lung cancer epidemic of the twentieth century.⁵ Following Bradford Hill's retirement in 1961, Doll was appointed Director of the MRC Statistical Research Unit, and his subsequent work on smoking and lung cancer with statistician Richard Peto further substantiated the causal link. Despite, however, the centrality of smoking and lung cancer to Doll's professional career, it does not dominate the collection of papers at the Wellcome Library, although cancer research in general is its thread of continuity. Indeed, it is disappointing to find that the early research conducted with Bradford Hill is not represented, although there is a limited range of material relating to the subsequent prospective study of doctors that would later resoundingly confirm earlier conclusions. Years later, in the course of preparing the paper ‘Medical effects of smoking: problems and perspectives’,⁶ Doll checked his memory of events with Bradford Hill, wanting to, as he put it, set the historical record straight. The file (PP/DOL/D.3/24) contains a brief exchange of letters between the two in which a prevailing anecdotal suggestion—that the original idea to base a prospective study on doctors' smoking habits had come to Bradford Hill whilst he was playing golf—is dismissed as “apocryphal”, albeit, as the story has it, a stroke of genius.

² Introducing the series, the *Lancet* leader begins: “For most of us figures impinge on an educational blind spot . . .” (2 January 1937, p. 31). The series was immediately re-published as *Principles of medical statistics* (1937).

³ Doll, ‘Obituary: Sir Austin Bradford Hill’, *Lancet*, 1991, 337: 1154. More recently, Alan Yoshioka, *Br. med. J.*, 1998, 317: 1220–3, has argued that the MRC streptomycin randomized trial of 1946, devised by Bradford Hill, is “not as novel as it is usually portrayed”, citing the procedures proposed in Feldmen and Hinshaw's tuberculosis paper of 1944, which presented various strategies for patient allocation, including chance. A much earlier instance of the randomized clinical trial is discussed by A

Hróbjartsson, P C Gotzsche, C Gluud, ‘The controlled clinical trial turns 100 years: Fibiger's trial of serum treatment of diphtheria’, *Br. med. J.*, 1998, 317: 1243–5.

⁴ Doll, ‘Sir Austin Bradford Hill and the progress of medical science’, *Br. med. J.*, 1992, 305: 1521–6, p. 1523. For retrospective studies read case control studies, and for prospective studies read cohort studies.

⁵ Richard Doll and A Bradford Hill, ‘Smoking and carcinoma of the lung’, *Br. med. J.*, 1950, ii: 739–48.

⁶ The Heath Clark Lecture, delivered at the London School of Hygiene and Tropical Medicine, 15 January 1985.

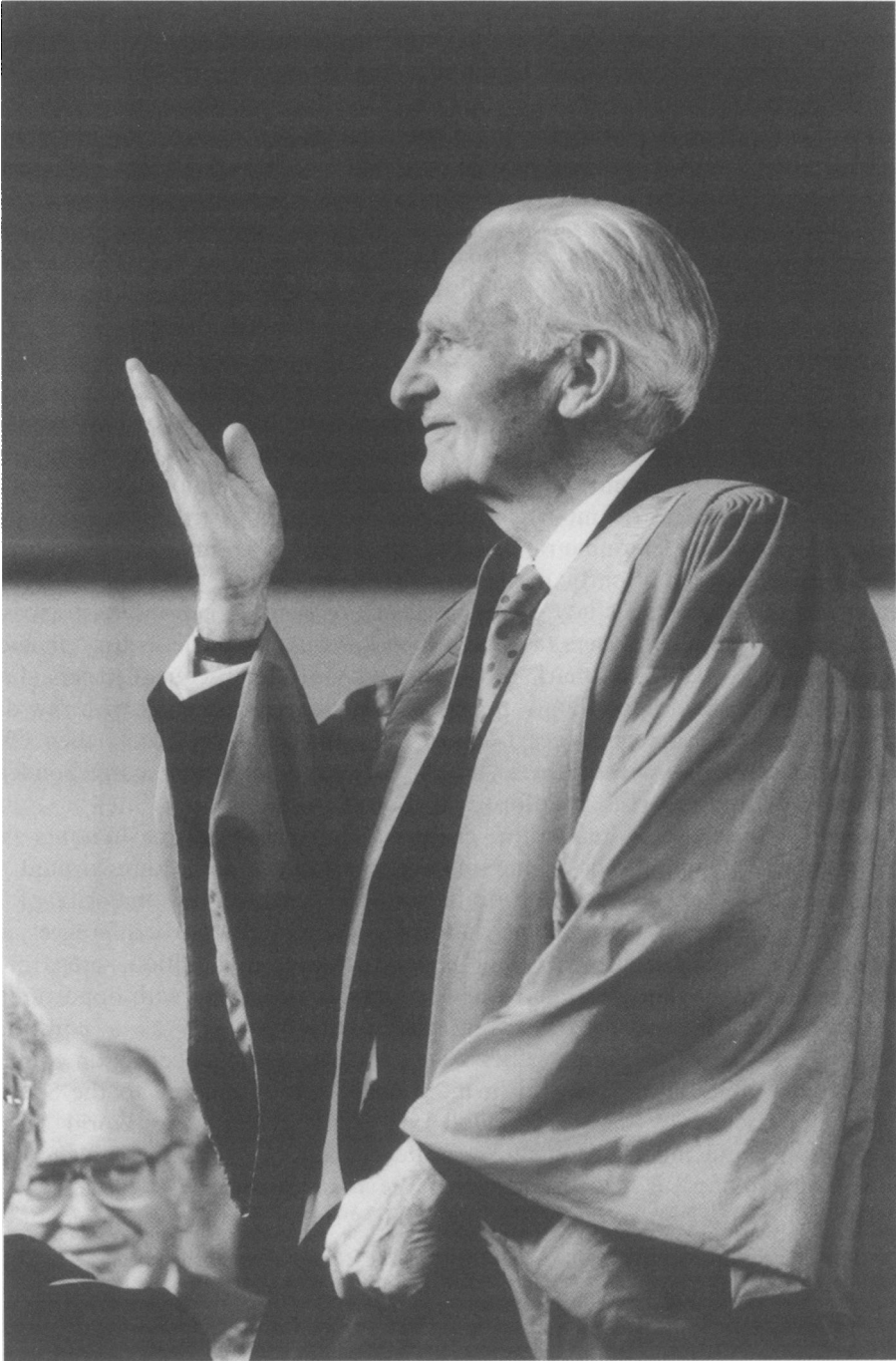


Figure 1: Sir Richard Doll at Harvard University Commencement, 9 June 1988, at which he received an Honorary Doctor of Science degree. PP/DOL/D.3/59.

The most extensive primary research materials represented in the collection are drawn from the numerous trials in the field of gastroenterology conducted at Central Middlesex Hospital (1945–69):⁷

In 1945 I was looking for a job ... when I had the good fortune to be introduced to Dr Avery Jones. He had just then had the idea that clues to the causes of gastric and duodenal ulcers might be obtained if differences could be found in the frequency with which they occurred in men and women in different occupations... His clinical responsibilities, however, prevented him from conducting a survey himself and he obtained a grant from the Medical Research Council to employ a medical assistant to conduct one under his supervision. I was offered an appointment to work on the project and secured[,] as a result, a lifelong friend and teacher with whom I collaborated actively in research for twenty-four years.⁸

The collection contains material from a range of clinical trials of treatments of gastric ulcer: from an investigation of the influence of smoking, to the role of blood group distribution and family history; from the efficacy of liquorice treatment, to the efficacy of intragastric milk drips in uncomplicated gastric ulcer; and from comparative trials to determine rates of healing, to cortisone in ulcerative colitis.

Other early material of particular interest, of which I shall have more to say in a moment, is the influential study of the incidence of lung cancer amongst asbestos workers at the Turner Brothers (as it was then known) Rochdale factory: included are several drafts of the landmark 1955 paper, as well as subsequent papers (1965, 1966 and 1968), based upon data supplied by the company, together with raw data and much related correspondence between Doll and Dr John Knox, then Chief Medical Officer at Turner Brothers Asbestos Co. Ltd, and later correspondence between Knox and I D Hill (Bradford Hill's son).

As Doll's international reputation grew, he received numerous honours (see, for example, Figures 1 and 2) and many opportunities to lecture around the world. The collection contains the drafts and final texts of the majority of the later papers (1968–91) delivered at national and international conferences and meetings. Many of the files of these papers contain, in addition, preparatory notes, background reading and germane correspondence. Along with opportunities to lecture came invitations to act, at times controversially, as a consultant epidemiologist and as an expert witness. Thus, for example, the collection contains much original material (considered in more detail below) relating to the Spanish Toxic Oil epidemic of the 1980s. Doll was appointed by the World Health Organisation as an independent and respected expert to weigh the evidence that adulterated cooking oil was the cause of the toxic syndrome, a judgement, as we shall see, not all Spanish doctors accepted. A further example offered by the

⁷ "Early randomised trials can properly be criticised on the grounds that they were often too small to have any chance of detecting moderate effects. Small trials can be successful when the effect is large but this seldom occurs. They can also be successful when the effect is moderate and the outcome is measured quantitatively, as in the

series of trials of treatment for gastric ulcer conducted by Avery Jones and me in the 1950s and '60s, which recorded the percentage reduction in the size of the ulcer over a fixed time." Doll, 'Controlled trials: the 1948 watershed', *Br. med. J.*, 1998, 317: 1217–20.

⁸ 'The controlled trial' (1984), PP/DOL/D.3/14.



Figure 2: Sir Richard Doll and the operatic soprano Jessye Norman, Honorands, Harvard University Commencement, 9 June 1988. PP/DOL/D.3/59.

collection of Doll's expert opinion is provided by a case against the petrochemical company EniChem, which had asked Doll to review evidence and prepare an expert's report. The collection contains Doll's report ('Cancer caused by vinyl chloride'), together with correspondence with Italian lawyers and background materials for a case that concerned more than 400 workers exposed to vinyl chloride between 1960 and 1993 at the EniChem production plant (the largest in Italy) at Porto Marghera, Venice.

Further clinical trial material from the later period of Doll's career is available in papers from the MRC trial (single blind) of mild hyper-tension (1978–85), for which Doll acted as Chair of the ethical committee. The papers offer an instructive window onto the functional role of ethical considerations in clinical trials, here actively asserted in confidential discussion of an appropriate trial dose for bendrofluazide, and in tracing the source of an information leak. Another later strand to the collection is the correspondence and papers from Doll's period (1969–79) as Regius Professor of Medicine in the University of Oxford. During his professorship, most of the planning and development of the John Radcliffe Hospital complex was undertaken, and many of the papers relate to this project (and include several architect's plans). Although removed from the world of immediate medical research, Doll's papers of university administration not only illustrate an unsurprising assiduous attention to detail—in this instance, administrative detail—but also reveal Doll as a skilful manager of people, demonstrating a sure-footedness in human relations that seems to have accompanied

him throughout his professional career, not least in achieving the donations that enabled the establishment of Green College, Oxford, where he served as first Warden in his last professional post.⁹

For the remainder of this introductory paper, I should like to highlight aspects of the context of epidemiological practice as it is reflected in the collection. I began by noting that epidemiology is firmly rooted in a social and ethical nexus. Two areas of study—namely, lung cancer in association with asbestos and the Spanish episode of toxicity generally referred to as Spanish Toxic Oil Syndrome—demonstrate very well something of the social, economic and political pressures that commonly surround epidemiological research, and provide illustrative instances of those voices of community and vested interest that refuse to remain silent.

*Quid pro Quo*¹⁰

Controversy and litigation continue without abatement in the grim history of asbestos and asbestos-related death and disease. It is a cruel irony that a material supremely useful, resistant to both fire and decay, and once proudly and loudly vaunted as the best protection that money could buy, should have turned out to be so deadly. A recent study produced by Julian Peto estimates that deaths in western Europe from mesothelioma will increase from 5,000 per annum (1998) to 9,000 per annum (2018), and are not expected to peak before 2020.¹¹ Sadly, it is a story that continues to unfold its unfortunate chapters. Following the eventual rejection of asbestos by European and North American construction and engineering industries, global demand for the deadly material has been maintained by sales to the Far East, which, by 1991, was purchasing 90 per cent of South Africa's chrysotile. The long-term global toll of suffering has thus transferred from developed to developing countries. The medical legacy of continued mining and use of asbestos is set to continue well into the twenty-first century: mesothelioma can take from 20 to 60 years to be detected. The history of the industry, and the role played by T&N plc (formerly Turner and Newall, formerly Turner Brothers Asbestos Co. Ltd) that emerges from documents disclosed during "discovery" in the course of American

⁹ Green College was founded in 1979 as the result of a benefaction by Dr Cecil Green, whose company, Geophysical Services Ltd, later became Texas Instruments. The eighteenth-century Radcliffe Observatory is the architectural centrepiece of the site. Purchased in 1934 by Lord Nuffield, it was presented to the hospital authorities in 1936 and the Nuffield Institute for Medical Research was established there. In 1979, the Institute moved to new premises in the grounds of the John Radcliffe Hospital, freeing

the Observatory site for its new role within Green College. There is a residential building at the western corner of the College, completed in 1981, known as the Doll Building.

¹⁰ Papers discussed in this section are drawn from PP/DOL/B.3, unless otherwise identified.

¹¹ Julian Peto, 'The European mesothelioma epidemic', *Br. J. Cancer*, 1999, 79: 666–72. See also, J Peto, J T Hodgson, F E Matthews, J R Jones, 'Continuing increase in mesothelioma', *Lancet*, 1995, 345: 535–9.

litigation¹² sets the suffering of asbestos workers in a corporate context of secretive strategic obstruction, duplicity, attempted suppression, delay and denial.¹³ Doll's study (1955) of 'Mortality from lung cancer among asbestos workers' and related papers are key documents in this secret history that is now coming to light.

The Doll collection includes not only the 1955 paper (in four texts, holograph and typescript), but also a considerable range of germane correspondence, chiefly between Doll and Dr John Knox, Doll's collaborator and source of factory data. The correspondence available in the Wellcome papers begins in 1948, however, with Doll's first line of enquiry to Dr Stephen Gloyne (23 January 1948). Gloyne was a pathologist who had published, in 1934, with W Burton Wood,¹⁴ an early paper associating lung cancer with asbestos. As well as contacting and meeting with Gloyne, Doll wrote to Dr Edward Merewether, then Senior Medical Officer for the Ministry of Labour and previously a Medical Inspector of Factories. Merewether had been co-author of a report¹⁵ that had led to the introduction of the Asbestos Industry Regulations (1931) and to the Silicosis and Asbestos (Medical Arrangements) Scheme (1931).¹⁶ Referring to concurrent research with Bradford Hill on smoking and lung cancer, Doll wrote to Merewether (21 May 1948) that he did not consider the evidence linking asbestos and lung cancer very convincing but would "like to look into it a bit further". Merewether and Gloyne evidently pointed Doll in the direction of Dr Hubert Wyers, then Works Medical Officer for Cape Asbestos, chief competitor of Turner Brothers. Wyers had written a thesis on the association of lung cancer with asbestosis, and Doll was keen for the association "to be logically proved" (Doll to Wyers, 29 June 1948). He went on:

¹² In 1995, Chase Manhattan Bank lost its US\$185m action against T&N for the removal of asbestos from Chase Plaza, its Manhattan building, constructed in 1959. Under "discovery" procedure, Chase was granted access to T&N records at their place of storage in Manchester, where a vast amount of material was microfilmed (copies of which, it is hoped, will be deposited at the Wellcome Library later this year). The material is deployed in Barry L Castleman, *Asbestos: medical and legal aspects*, 4th ed., Englewood Cliffs, NJ, Aspen Law & Business, 1996, and Geoffrey Tweedale, *Magic mineral to killer dust: Turner and Newall and the asbestos hazard*, Oxford University Press, 2000.

¹³ Tweedale, *op. cit.*, note 12 above, provides a thoroughly researched and comprehensive account. See also, Geoffrey Tweedale and Philip Hansen, 'Protecting the workers: the Medical Board and the asbestos industry, 1930s–1960s', *Med. Hist.*, 1998, 42: 439–57. For the position that gave rise to the Asbestos Industry Regulations (1931), see Morris Greenberg, 'Knowledge of the health hazard of asbestos prior to the Merewether and Price report of 1930', *Soc. Hist. Med.*, 1994, 7: 493–516, and Nick Wikeley, 'The Asbestos Regulations 1931: a

licence to kill', *J Law Soc.*, 1992, 19: 365–78. For a counter-argument (that "studies of the early history of asbestos and occupational health have been dominated by that most beguiling, though misleading, of distractions, hindsight"), see Peter Bartrip, 'Too little, too late? The Home Office and the Asbestos Industry Regulations, 1931', *Med. Hist.*, 1998, 42: 421–38.

¹⁴ 'Pulmonary asbestosis', *Lancet*, 1934, ii: 1383–5. Gloyne was also shortly to publish a paper that differentiated silicosis and asbestosis lung cancer: 'Pneumoconiosis: a histological survey of necropsy material in 1205 cases', *Lancet*, 1951, i: 810–14.

¹⁵ E R A Merewether and C W Price, *Report on effects of asbestos dust on the lungs and dust suppression in the asbestos industry*, London, HMSO, 1930.

¹⁶ "A number of other relatively narrow government statutes provided theoretical protection for some asbestos employees. However, the 1931 Regulations and the Medical and Asbestosis Schemes were to be the basis for asbestos workers' safety from the 1930s until 1970." Tweedale, *op. cit.*, note 12 above, p. 22.

What is wanted is a definitive population which can be observed to see what proportion die of cancer of the lung in a given period—a proportion which can be compared with expectation, based on general mortality figures. A possible way of doing this might be to define your population as being ‘certified cases of asbestosis’ and then to follow them to death. Best of all would be to limit the population to cases certified arising out of the periodic medical exam at specific factories, but I imagine that would reduce the numbers too much. I don’t know whether you’ve had anything like that number certified at the Cape Company since 1931.

A meeting at Cape Asbestos was finally arranged for 24 March 1949. By 6 May 1949, Wyers had “prepared all the figures with the exception of the series of certification dates and to my surprise I find that the Company’s records are exceedingly scrappy”. Both Wyers and Doll endeavoured to obtain the missing information (from the South Wales Pneumoconiosis Panel), but evidently were unsuccessful. There is then an unexplained hiatus in the correspondence between the two, until 15 September 1955, when Myers wrote interestedly to Doll for reprints of the published paper and there the correspondence, as we have it, concludes.¹⁷

The first communication between Knox and Doll is a letter to Doll (12 April 1953) in which Knox introduces himself, indicates a familiarity with Doll’s published papers to date and offers “some material of interest”.¹⁸ He goes on to admit that his “statistical ability is nil” but he has “approval . . . to approach a medical statistical authority to discuss this question”. Notwithstanding this opening statement, an approval to approach and an approval to publish were to prove to be two very different things in the eyes of the Turner Brothers Board. As the momentum to publication gathered pace, the Board became increasingly nervous about the paper’s principal conclusion of a lung cancer risk of ten times that of the general population for those who had been exposed to asbestos for twenty years or more. The nervousness first manifested itself in the Board’s refusal to allow Knox’s name to be associated with the paper, despite his instigative role: “I gather that my name on the paper might not be acceptable as it would naturally suggest Rochdale as the place of origin” (Knox to Doll, 4 January 1954). The title to the paper, it will be recalled, contains no reference to company or location, nor, indeed, does the text itself. There then followed a period of time in which Knox endeavoured to change the Board’s position on the omission of his name as co-author. (Simultaneously, it would seem, the Board tried to use Knox to persuade Doll against publishing at all.¹⁹) Publication

¹⁷ Tweedale, *op. cit.*, note 12 above, p. 148, refers to an approach by Doll to Cape Asbestos in 1953 which was rebuffed, although there is no reference to this in Doll’s papers.

¹⁸ This letter, and nearly all other letters from Knox to Doll in the collection, is written by hand on personal notepaper. The correspondence with Doll is conducted from Knox’s home address.

¹⁹ One strategy considered by Turner Brothers was a legal challenge to publication. “In July,

1954, the board drafted a barrister’s letter to bully Doll into withdrawing the paper. It stated that a published article ‘would be wholly premature and undesirable from all points of view.’ This was never sent and a visit from the tactful Knox was relied upon instead to extricate the company from a very difficult situation.” Tweedale, *op. cit.*, note 12 above, p. 149.

was delayed as a consequence, until it became apparent that there would be no change of position and Doll and Knox jointly decided that the paper should appear under Doll's name alone.

For my own part, I feel that any positive findings with regard to the cause of cancer must be made available to all research workers in the subject (and not limited to those few with whom we may personally be in contact). There is no knowing, but what may appear at first to have only a limited application in the industrial field may eventually prove to provide an important link in the chain of reasoning by which knowledge of the general causation of the disease may be determined. (Doll to Knox, 8 June 1954).²⁰

There was, however, a little more to the Board's determination than the removal of Knox's name from the paper. To arrive at a more complete picture of the surrounding circumstances, it is necessary to look beyond the Wellcome papers to consider material now in the public domain as a by-product of "discovery" in the Chase Manhattan Bank lawsuit. Some forty years later, Dr Richard Schilling, editor of the *British Journal of Industrial Medicine* at the time that Doll's paper was submitted, recalled under oath being paid a personal visit by a member of the Turner Brothers Board: "Well, I remember very, very clearly a man with dark hair, who was a Director of Turner & Newall's, coming to me when I was working in the physiology lab, department, of the University of Manchester, asking me to suppress the publication of this article."²¹ Schilling refused to co-operate with the request and apparently received no further requests of this kind.

The attempt at suppression recounted by Schilling furnishes further context for the period in which the paper approached its delayed publication, a period of time in which Doll re-drafted on more than one occasion the paper's concluding words. Why he did so was the subject of close scrutiny in the cross-examination of Schilling, particular attention being given to a handwritten addition to a letter Doll sent to Schilling (3 December 1954). After noting that he would prefer the paper to be held over until the April issue of 1955, "so as to give the firm an opportunity to show whether they are genuinely anxious to have further research undertaken", Doll added, in ink: "Unless I offer them quid pro quo, we may never find out" (Figure 3). Referee comments (also available in the collection) had noted that "data is [*sic*] not produced in the second half of the paper to show that the risk has now decreased." The problem Doll and Knox faced in this regard was that of a considerable latency period of at least twenty years

²⁰ Doll's letter is addressed not to the Board but to Knox, and it is accompanied by a (conspiratorial) covering note: "I enclose a formal letter which you may care to pass on. Should you think it is unfortunately worded in any way, please send it back to me and I will re-write it. Meanwhile, I am sending the paper off to the *British Journal of Industrial Medicine*, but we shall have at least 4 months to get your name re-inserted should the Board change their mind" (Doll to Knox, also 8 June 1954).

²¹ 'Deposition of Professor Richard Selwyn Francis Schilling, taken at 199 The Strand, London WC2R, England, on the 12th day of January, 1994, commencing at 10:10 a.m.' The Chase Manhattan Bank v. T&N plc (87 Civ. 4436, US District Court, Southern District of New York). A copy of the transcript was made available to Chris Beckett by Dr Maurice Greenberg, 25 January 2002. See also Castleman, *op. cit.*, note 12 above, pp. 99–100.

3rd December, 1954.

Dear Richard,

I have given some further thought to the problem of publication and I think I would like you to hold the paper over till the April issue so as to give the firm an opportunity to show whether they are genuinely anxious to have further research undertaken. If they are, it should be possible to make an estimate (within a month or two) of the survival rate of workers taken on in the last 25 years. Should the survival rate be shown to be the same as that for other inhabitants of Rochdale, we could make an addendum to the paper of a half a dozen lines pointing this out and promising more detailed results later. If, on the other hand, the survival rate is not yet normal (and I doubt if it is), the sooner the firm are made to realise it the better.

Unless I offer them quid pro quo, we may never find out -

As ever,

Richard Doll

Dr. R.S.F. Schilling,
The Muffield Department of Occupational
Health,
University of Manchester,
Clinical Sciences Building,
York Place,
Manchester 13.

Figure 3: Doll to Richard Schilling, 3 December 1954. "Unless I offer them quid pro quo, we may never find out." PP/DOL/B.32/2.

before the development of malignancy (over twenty-six years was the average period for the cases of lung cancer and asbestosis reported in the paper). With the implementation of new regulations in 1931, it was premature to draw, in 1954, firm conclusions about their positive impact on the problem, and an early draft had concluded: "Insufficient data are available to determine whether the risk has yet been eliminated by the improved conditions which now exist." However, this conclusion was to become, in the published text, one that adopted the past tense ("lung cancer was a specific industrial hazard") and a conclusion that suggested that times were beginning to change: "The risk has become progressively less as the duration of employment under the old dusty conditions has decreased" (see Figure 4). Doll had taken up a suggestion of one of the referees²² and managed to find sufficient comparative data to substantiate a conclusion that offered at the very least the prospect of improvement and, furthermore, served to keep the door open to subsequent studies that might provide conclusions of greater certainty. In fact, it was not long before the world was to change around the Rochdale factory irrevocably as the link between mesothelioma and asbestos began to emerge in incontrovertible data from South Africa, linking forty-five out of forty-seven cases of mesothelioma with exposure to crocidolite (commonly referred to as blue asbestos).²³

Doll's *quid pro quo* can be seen either as the beginning of a working relationship with T&N that would lead to him becoming, in the words of one critic, "a litigation consultant, too, by the early 1980s",²⁴ or it may be viewed, alternatively, as the experienced tactics of a pragmatic epidemiologist. Meanwhile, the paper of 1955 is presented by Sir Donald Acheson to today's generation of aspiring epidemiologists as "a classic in its own right, which would have gained [Doll] a place in the history of epidemiology had it been his only publication."²⁵

²² The transcript of Schilling's deposition (p. 100) reveals that one of the three referees for the paper was Austin Bradford Hill, although the referee comments relayed anonymously by Schilling to Doll (see letter of 9 July 1954) cannot be attributed.

²³ J C Wagner, C A Sleggs, P Marchand, 'Diffuse pleural mesothelioma and asbestos exposure in the North-Western Cape Province', *Br. J. ind. Med.*, 1960, 17: 260–71. However, as late as 1967, a *Lancet* leading article argued that "there is a danger that workers' representatives may overrate the dangers of dealing with asbestos." The leader went on to argue, in true utilitarian style: "Situations arise where the use of asbestos can save more lives than it can possibly endanger." *Lancet*, 1967, i: 1311–12.

²⁴ Castleman, *op. cit.*, note 12 above, p. 101. Tweedale, *op. cit.*, note 12 above, pp. 253–4, 283–5. It is pertinent to note that the printed proceedings of a conference on vinyl chloride (New York, 1974), in which a remark of Doll's that crocidolite should be banned was mis-

transcribed as "we ought . . . to ban the use of asbestos", provoked in him a measure of consternation: "In the current situation in England, in which the industry is coming under quite unjustifiable attack, the attribution to me of the opinion that the use of asbestos ought to be banned is, as you will appreciate, embarrassing." (Doll to Dr E Cuyler Hammond, 26 May 1977: PP/DOL/D.1/34.)

²⁵ Acheson's introduction to Doll's paper in John Ashton (ed.), *The epidemiological imagination: a reader*, Oxford University Press, 1994, p. 12. Acheson continues: "Almost as an aside Sir Richard's paper also gives one of the first and unquestionably one of the simplest descriptions of the man-years method of calculating expected numbers. Subsequently this technique rapidly became established as a standard way to measure risk in cohort studies. Previously risk was usually estimated by a 'snapshot' of the situation at the beginning of the period of exposure, thus wasting much of the available information."

One hundred and thirteen men who had worked for at least 20 years in places where they were liable to be exposed to asbestos dust were followed up and the mortality among them compared with that which would have been expected on the basis of the mortality experience of the whole male population. Thirty-nine deaths occurred in the group whereas 15.4 were expected. The excess was entirely due to excess deaths from lung cancer (11 against 0.8 expected) and from other respiratory and from cardiovascular diseases (22 against 7.6 expected). All the cases of lung cancer were confirmed histologically and all were associated with the presence of asbestosis.

From the data it can be concluded that lung cancer was a specific ~~certain~~ ^{certain} ~~average~~ ^{average} ~~among men~~ ^{among men} ~~employed for 20 or more years~~ industrial hazard of asbestos workers and that ~~the risk~~ ^{the risk} ~~may have been of~~ ^{has} the order of 10 times that experienced by the general population. ~~Insufficient~~ data are available to determine whether the risk has yet been eliminated by the improved conditions which now exist. ~~The risk has become progressively less as the duration of employment~~ ^{before 1933} ~~has decreased. During the regulations for the control of dust were made under the old dusty conditions has decreased. It is likely that the risk is now much smaller but insufficient data are available to determine whether it has yet been completely eliminated. It would certainly not now be expected to reappear but it~~
~~The risk has become progressively less as the duration of employment under the old dusty conditions has decreased. It is unlikely that the risk is now large but insufficient data are available to determine whether it has yet been completely eliminated.~~

Figure 4: The much-revised concluding paragraph to 'Mortality from lung cancer among asbestos workers' (1955). PP/DOL/B.3/2.

The Spanish Toxic Oil Syndrome²⁶

During the month of May, 1981, clinics in northern Spain were suddenly overrun with people complaining of nausea, rashes, fever, and breathing difficulties. Many would eventually die, and those who survived the epidemic developed wasted muscles, damaged nerves, hair loss and weakened bones. First recognized in May 1981 (some early cases appearing in April), the peak of the epidemic occurred in the following June, and would eventually affect some 30,000 people, including more than 1000 deaths. Geographically, the epidemic was almost confined to fourteen provinces in central and north-west Spain (although Madrid itself was little affected), and spread progressively north-west, from the area around Madrid to Leon.²⁷ The Spanish authorities rapidly determined the cause as adulterated rapeseed oil, sold as inexpensive olive oil. At the time, Spain did not permit rapeseed oil to be imported for human consumption and sought to protect its olive oil industry by ensuring—through the compulsory addition of aniline²⁸—that any rapeseed oil that was imported was used only industrially. Through numerous street market vendors, however, supplies of the oil were made available for human consumption. It seems that such illegal sales were not a new phenomenon and had previously led to no known ill-health consequences. Had the process of aniline-removal changed in some way, or been imperfectly executed, such that the illicit oil then sold became lethally toxic? Was there a rogue batch, and could it be traced? Not everyone was convinced, however, by the cooking oil theory, and from the very beginning there was a competing theory, that those affected had been poisoned not by adulterated oil but by the over-zealous use by some Spanish farmers of organo-phosphate fertiliser. Tomato crops in particular were suspected. Nevertheless, in 1983, at a specially-convened WHO conference in Madrid, the toxic oil theory was formally accepted by the international health community and the epidemic received the name by which it is now known: Spanish Toxic Oil Syndrome.²⁹

Despite the confidence of the assertion, there remained a number of unresolved epidemiological and toxicological issues, not least that the toxin responsible for causing the outbreak had not been identified (and remains unidentified to this day). On 29 August 1984, Dr Roy Goulding, Chair of a WHO steering committee that

²⁶ Papers discussed in this section are drawn from PP/DOL/C.2/1, unless otherwise identified.

²⁷ Doll, 'The aetiology of the Spanish Toxic Syndrome: interpretation of the epidemiological evidence'. Report prepared for WHO, October 1985. Doll's report refers to 20,000 cases. My figure of 30,000 cases is taken from Woffinden (see note 30 below).

²⁸ A colourless, oily, organic compound, aniline is of great importance in the dye industry, being used as the starting substance in the

manufacture of many dyes. Aniline is also important in petroleum refining and in the manufacture of rubber-processing chemicals and antioxidants. It is highly toxic and a suspected carcinogen.

²⁹ For the original study on which the oil theory is founded, see Juan Manuel Tabuenca, 'Toxic-allergic syndrome caused by ingestion of rapeseed oil denatured with aniline', *Lancet*, 1981, ii: 567–8.

was endeavouring to resolve these outstanding matters, wrote to Doll, then Warden of Green College, to ask if he would consider reviewing the epidemiological evidence:

Not much progress, I fear, has so far been achieved. However, most of us, I think, are convinced . . . that there is strong association statistically between the occurrence of the disease and the consumption of what is termed the 'illicit oil.' Nevertheless there are certain, vociferous movements and individuals in Spain who argue otherwise. With a view to resolving this dispute the WHO people and I are agreed that it might be helpful to refer the epidemiological data now assembled to, as it were, arbitration.

It was not long before Doll reported that he was "getting deeper into T.O.S—and into the mire" (Doll to Goulding, 22 May 1985). In particular, he was concerned to discover that the Spanish government had provided incentives to case-reporting in the form of promised compensation and free medical care, and that the available epidemiological data, much of which seemed to have been gathered in haste, may not have been free from bias. An interim report, presented by Doll at the steering committee meeting of 1 July 1985, outlined the key questions as he saw them. Whilst case-control studies strongly suggested an association of the disease with the adulterated oil, was the association real or an artefact of the method of inquiry? And, if it was a real association, did it reflect cause and effect or was it due to the confounding of the consumption of the oil with something else that was the direct cause? Doll refused to express a conclusive opinion until he had met the Spanish scientists who supported the alternative theory of organo-phosphate poisoning.

Doll met with Dr Clavera Ortiz and Dr Martínez Ruiz in Madrid on 21 September to discuss their views. However, in the absence of hard evidence (Doll to Goulding, 6 December 1985), he did not find "the alternative suggestion . . . at all impressive." He was, however, impressed by their complaint that "the early review committees in Spain consisted almost entirely of people who had been responsible for the positive epidemiological studies", and noted with interest that:

. . . so-called 'industrial oil' had been more or less routinely imported into Spain for human consumption and that there was likely to have been bias in Spain in the late summer of 1981 in the classification of illnesses which could or could not regularly be associated with the consumption of oil bought in the affected region.

Struck by their sincerity, it was apparent to Doll—and here we glimpse, in his remark, something of his disposition to professional practice—that "they were now emotionally concerned with disproving the oil hypothesis." Following the WHO Madrid conference of 1983, at which the adulterated oil theory did not receive unanimous support, the Spanish authorities had decided to make a renewed enquiry into the evidence so far amassed. Along with a number of other specialists, Clavera Ortiz and Martínez Ruiz formed an official team of investigation which, after reviewing the distribution of the oil and the distribution of the epidemic, quickly came to the inconvenient conclusion, as some have seen it,

that there was little correlation between the two. Before long, it seems they were dismissed from their investigative roles and the commission was disbanded.³⁰ Doll had delayed in producing his report until he had met them. Although his report of October 1985 did not, unsurprisingly, favour an alternative theory, it did not support the adulterated oil theory with anything like the confidence that its supporters had hoped. "Laboratory studies have . . . failed to demonstrate toxicity in any of the samples that were recovered, no specific chemical that might have caused the disease has been identified, and the conclusion that the oil was responsible rests primarily on the epidemiological evidence." As for the epidemiological evidence, there were "too many gaps in [it] to allow the conclusion that oil was definitely the cause." Doll wanted a more exact correlation between the supply of oil and the epidemic's temporal and geographic distribution. Furthermore, there was the issue of linking the numerous sporadic cases to demonstrable exposure to the adulterated oil. Doll's position left the door ajar, however, and pointed ways towards achieving greater certainty. In particular, the problem of sporadic cases turned upon a fundamental principle of epidemiological inquiry, one that calls to mind the widow of Hampstead and her niece who played significant roles in John Snow's investigation of the London cholera outbreak of 1854. It will be recalled that the widow in question was partial to water from a particular pump in Broad Street, Soho, near to where her husband had owned a factory, and therefore insisted upon a daily supply of her favourite water being brought to her. When cholera swept through Soho in the summer of 1854, her taste for water from the Broad Street pump was to cost her dearly, as the only inhabitant of Hampstead to contract cholera and die. She drank the water on Thursday 31 August and died two days later. Her niece, who had chosen an unfortunate time to pay a visit to her aunt, also drank the infected water, then returned to her home in Islington and died the following day.³¹ Meanwhile, Doll looked forward to obtaining "a list of sporadic cases" of the Spanish toxic syndrome "with a note of the extent to which they were known to be exposed."³²

Following the (limited) circulation of Doll's report, concerns were expressed privately between other WHO experts working on the epidemic that its conclusions "might well lead to pressure within Spain to do a great deal of investigation of highly improbable alternative hypotheses" (Dr E M Kilbourne to Dr S Tarkowski, 25 November 1985). Kilbourne continued:

³⁰ Bob Woffinden, 'Cover-up', *Guardian*, 25 August 2001, provides a recent (partisan) overview, available at: <http://www.guardian.co.uk/Archive/Article/0,4273,4244093,00.html>.

³¹ John Snow, 'Instances of the communication of cholera through the medium of polluted water at Hampton West End (the water being carried from Broad Street)', *On the mode of communication of cholera*, 2nd ed., London, J

Churchill, 1855. The text is also available at: <http://www.ph.ucla.edu/epi/snow/snowbook2.html>. Snow's work on cholera was referred to by Doll during his testimony in Madrid at the trial of thirty-eight Spanish oil merchants charged with fraud and public health offences (see cutting from *The Times*, 7 July 1987, in PP/DOL/C.2/1/20).

³² Doll, WHO Report, 1985, op. cit., note 27 above, p. 27.

To avoid such an eventuality, I wonder if Sir Richard might consider making a more specific conclusion regarding his opinion on the likelihood of the oil hypothesis? To those of us working on the 'front lines' it would be most helpful if he were to underline among his conclusions a point to which the rest of the report seems to lead: that the oil hypothesis, while not unequivocally [*sic*] established, is sufficiently probable that studies designed to confirm or disprove its role in the etiology of TOS are the ones most appropriately pursued at the present time. Of course, he could only make such a statement if I am correct in my inference, that this is his own view on the subject.

Four days later, Kilbourne forwarded a copy of his letter directly to Doll, together with, to add weight, a signed statement from members of the discontinued Spanish clinical investigation commission.³³ Doll's response was to send Kilbourne a copy of a letter to Tarkowski (11 December 1985) in which he had reiterated his position, that he did not consider the case for adulterated oil to be proven, and that "it might come to be regarded as proved if it were possible to undertake further research along the lines suggested in the last paragraph of [his] report." Further research continued, such that, by June 1987, Doll had added an Addendum to the report in which he made the unequivocal statement that—notwithstanding an opening caveat that the new evidence was "of variable quality"—many interested parties had been waiting for, and other parties had hoped not to read: "With the addition of this new evidence, I conclude that adulterated oil was the cause of the toxic syndrome."³⁴ It was a shift in position on which Doll was to be closely examined at the trial of the oil suppliers in Milan (Doll testified 6–7 July 1987). Privately, however, Doll wrote to Goulding (1 April 1987) in a manner that suggested some niggling doubts remained about unresolved details and the manner in which much of the epidemiology had been conducted:

The evidence produced is of course strong evidence in support of the association. What is worrying is the omission of any reference to the third convent where the association is far from clear. The selective publication of positive evidence ignoring the little contrary evidence justifies the accusation that only positive evidence is published and makes one wonder whether there may be some justification for the belief that the whole picture has been distorted. I do not believe that this is likely but it strengthens the need for an independent review of the laboratory results in Sevilla, which I recommended, to check that the diagnosis of TOS in the few individuals in the town had not been conditioned by knowledge of their exposure to the oil. I remain most disturbed that Kilbourne should have allowed himself to be used in this way.

Nevertheless, Doll stuck steadfastly to his revised conclusion at the Milan trial, a testimony that was to last for thirteen hours over two days, from which he emerged

³³ 'Comments of Drs. Tabuenca, Abaitua, Castro, Díaz de Rojas, and Posada (Members of the former Subcommission for Clinical Investigation, National Program for the Toxic Syndrome) regarding the preliminary report of Sir Richard Doll.' The document is dated 27

November 1985, and signed by the individual doctors.

³⁴ 'The aetiology of the Spanish Toxic Syndrome: interpretation of the epidemiological evidence: Addendum 8.6.87', p. 7.

into the light of day—gentleman guarantor of justice and compensation³⁵—to the cheers of victims of the epidemic and their families.

It is striking how significant a role is played by the choice of words in the presentation of epidemiological findings over and above non-verbal data more readily associated with scientific communication. The 1955 paper on lung cancer and asbestos exposure received, as we have seen, considerable re-drafting to strike an appropriate note. Whilst we can safely assume that an appropriate note is one that presents to its readership research findings with both fidelity and clarity, the additional shaping pressure of audience is another influential factor, particularly when the interested readership comprises more than the professional attention of peers. In the case of the Spanish “arbitration” exercise that Doll undertook, there were also language and cultural barriers to surmount. When Kilbourne expressed doubts about the wording of Doll’s conclusion to his report, fearing “misinterpretation”, he was noting the likely influence of culturally-determined differences in reception between an English and a Spanish audience. “I fear this based on the way I have seen criticism given and taken here” (Kilbourne to Doll, 29 November 1985). Kilbourne wanted a more explicit statement, that further research in support of the adulterated oil theory was the likeliest avenue of pursuit to provide the conclusive evidence desired by all. Even the vagaries of (a WHO) translation played a not insignificant role in the presentation of Doll’s argument, when Kilbourne advised Doll that *decena* can be translated as either *ten* precisely or, less precisely, *ten or so* or *about ten* (Kilbourne to Doll, 9 September 1985). Here, the difference in translation was not a point of style but was material to the epidemiological evidence, in so far as it determined whether or not the nuns of the convent at Casarrubios del Monte had purchased supplies of adulterated oil (it having been firmly established that adulterated oil was not available for sale before 11 February 1981).³⁶

Concluding Remarks

As we have seen from the two examples discussed above, many sections of society are likely to have a stake in the outcome of any given exercise of epidemiological research. Its public health orientation, encompassing occupational health, guarantees that many voices will conspire to ensure that the wise epidemiologist is one who chooses his or her words with care, fully cognizant of the scrutiny they will receive from many pairs of eyes. Misrepresentation by the press, however, is one prospect that cannot be easily guarded against, and, within the mass of material in the Doll papers, there is a remarkable file of letters to Doll from a section of the general public perhaps least expected to give vent to invective. I shall conclude with some brief comments on these letters.

In June 1973, on the eve of health service reorganization and shortly before delivering his Nuffield Lecture, ‘Monitoring the Health Service’ (PP/DOL/D.1/27),

³⁵ “As 200 people, many of them related to victims of the episode, waited to see him, one woman shouted: ‘That’s what I call a real gentleman, not like what we have here.’”

The Times, 8 July 1987 (newspaper cutting from PP/DOL/C.2/1/20).

³⁶ Doll, WHO Report, 1985, op. cit., note 27 above, pp. 19–21.

Doll addressed the Medical Journalists' Association to provide them with a summary of his key points. Doll's remarks proved to be the stuff of which newspaper headlines are made. The sentiment that stirred a quiet senior citizen "cohort" to loud and angry epistolary action was the notion that they should not "cling to life" but should, instead, as socially responsible citizens, "live dangerously". The *Daily Telegraph*, to cite a less sensational example, wrote:

Old people over 65 should be prepared to accept death and should not be thinking of how to preserve their life a few more months, a 60 year-old professor of medicine said yesterday. It was their social responsibility to 'live dangerously' and not expect the Health Service to spend time and money on research into prolonging their lives.³⁷

More than seventy senior citizens wrote to Doll to complain about his views, many struck by how close in age Doll was himself to the threshold that he was advocating.³⁸ Some letters were supportive, but most were, by turns, abusive and racist, and still others were the indignant reactions of the active old. Doll's paper addressed the theme of scarce Health Service resources, a theme that has resounded through the years. "I'm afraid my views when divested of their newspaper presentation are not very exciting", Doll wrote to one colleague. "So far as the National Health Service is concerned," he continued, "I have suggested that it was more important for it to seek out and attempt to relieve disability than to undertake research on methods of increasing the present biological lifespan."³⁹ I draw the researcher's attention to these letters from the general public not because they are representative in any way that an epidemiologist or a statistician might find useful. Rather, they represent the sort of buffeting response, from which authors of epidemiology papers are usually sheltered, that will always potentially lie in wait for social commentators, and many of Doll's later papers tend towards pondering health and social policy. Now preserved amongst the papers of a distinguished epidemiologist, these letters sit as fearful and awkwardly individual human voices, for the most part unpleasantly so, caught—like paradoxical flies in amber—in the archival record of a medical science oriented not towards the individual cry but towards population groups and the statistical patterns they make. The letters appear bigger than life-size, as if viewed from the wrong end of the epidemiologist's telescope. They reveal a human rawness, absent elsewhere in the papers, displaying indignation, prejudice

³⁷ Clare Dover, 'Over-65s should "live dangerously and expect to die"', *Daily Telegraph*, 28 June 1973, p. 19 (PP/DOL/D.1/28).

³⁸ Doll was born on 28 October 1912.

³⁹ Doll to Dr W H Lloyd, 9 July 1973 (PP/DOL/D.1/28). One of Doll's correspondents (Dr H M White) recalled the words of Sir Keith Joseph, reported in newspapers only two weeks prior to Doll's headlines, that Britain was a fine country in which to be injured or acutely ill "but do not be old or frail or mentally ill here, at least not for a few years". In 'The route back to Methusaleh' (PP/DOL/D.2/17), the Hunterian Society Lecture for 1980, Doll concludes:

"Bernard Shaw's concept of creative evolution . . . postulates a stable old age not subject to progressive deterioration, in which life is terminated by an inevitable accident . . . What is more plausible is Aldous Huxley's concept in his *Brave New World*, the inhabitants of which lived at a peak of fitness for 65 years until their life was terminated by sudden physical and mental deterioration over a few weeks. Something like this may be possible, though the period of deterioration is likely to last years rather than weeks and, as a sexuagenarian, I am glad to note that the model span should be at least 20 years longer."

and a survival-determination that instinctively springs from fear and threat. Doll took the trouble to reply to each correspondent (in the file, there is a clutch of letters marked *No address*, reminiscent of material from a Central Middlesex Hospital trial) outlining his misrepresentation, and some wrote back to retract hasty words, some astonished that a Knight of the Realm should contact them directly.

Doll's strong sense of historical tradition would have alerted him to a certain irony in his position. Indeed, there are several ironies that can be teased out. For Doll was not the only knighted Regius Professor of Medicine to be associated in newspaper headlines with the suggestion of natural limitations to the human span, and to human abilities as the years advance. In 1905, on retiring from John Hopkins University as Professor of Medicine, shortly to take up his appointment as Regius Professor of Medicine in Oxford, William Osler's valedictory address to his American colleagues asserted "the comparative uselessness of men above forty years of age" and, losing the "comparative" qualification, "the uselessness of men above sixty years of age."⁴⁰ The title of Osler's address, 'The fixed period', was taken from a novel by Anthony Trollope by the same name.⁴¹ Set in the late twentieth century—approximately, that is, co-terminous with Doll's briefing to the Medical Journalists' Association, to cite another irony—on a fictitious island off New Zealand in which "men retired for a year of contemplation before a peaceful departure by chloroform",⁴² Trollope's dystopia unfolds the social dynamic of ageism. On the imaginary island of Britannula, the young inhabitants, in the guise of relieving suffering and benefiting society, devise a system that discriminates against the elderly. However, as they grow old themselves, we are not surprised to read that they begin to see things differently and rebel against the system they had devised.

Osler claimed that his valedictory words were intended "to relieve a situation of singular sadness", although he did not change his view that "after the sixtieth year it would be best for the world and best for themselves if men rested from their labours."⁴³ Notwithstanding, Osler was to continue working at Oxford for another ten productive years, and Sir Richard Doll, born in 1912, who will be enjoying his ninetieth birthday this year, did not publish his earliest work of note before vigorously peering across Osler's first threshold of uselessness.

⁴⁰ Sir William Osler, *Aequanimitas*, 2nd ed., London, H K Lewis, 1922, pp. 397–8.

⁴¹ To add to the ironies at play, Trollope's *The fixed period* was published in 1882, his sixty-seventh year and the year in which he died.

⁴² Osler, *op. cit.*, note 40 above, p. 399.

⁴³ 'Preface to the Second Edition', *ibid.*, p. viii.