Wellcome Witnesses
to Twentieth Century Medicine

POPULATION-BASED RESEARCH IN SOUTH WALES:
THE MRC PNEUMOCONIOSIS RESEARCH UNIT AND THE MRC EPIDEMIOLOGY UNIT

The transcript of a Witness Seminar,
'The MRC Epidemiology Unit (South Wales)',
held at the Wellcome Institute for the History of Medicine,
London, on 23 March 1999,
with extracts from additional interviews
conducted by Andy Ness and from a
Witness Seminar, 'Pneumoconiosis in Coal Workers',
9 November 1994.

Volume 13 – November 2002

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PREFACE

The extensive published record of modern medicine and medical science raises particular problems for historians: it is often presented in a piecemeal but formal fashion, sometimes seemingly designed to conceal rather than reveal the processes by which scientific medicine is conducted. Study of unpublished archives may provide helpful insights but there are difficulties. Official archives may be limited in range and depth and in the UK public records are subject to a restriction that keeps papers hidden for at least 30 years. The survival of personal papers can be patchy. Many are lost during the lifetime of an individual, as space constraints or relocation demand the jettisoning of material without proper regard for its significance. Probably even more papers are wrongly discarded as worthless and uninteresting by their owners, or by relatives acting immediately after a bereavement. Thus historians of contemporary medicine and science are increasingly turning, or returning, to the traditional technique of oral history to supplement, or extend, existing records, and to create new resources.[1]

This volume is a departure from the standard *Wellcome Witnesses to Twentieth Century Medicine* format of a single Witness Seminar transcript per volume. The complete transcript of the witness seminar in 1999 entitled 'The MRC Epidemiology Unit (South Wales)' follows (page 15). But this is preceded by a selection of relevant material from a partly unpublished Witness seminar in 1994 'Pneumoconiosis in Coal Workers'. This is included to provide details of the origins of the work of the MRC Pneumoconiosis Research Unit, from which the Epidemiological Research Unit (later Epidemiology Unit) emerged in 1960. Quotations taken from interviews conducted by Dr Andy Ness between March 2000 and August 2001 with former members of both units follow the four chronological sections. These quotations provide additional information on matters discussed at the two Witness Seminars and topics not covered at the seminars.

A small project grant from the Wellcome Trust to Dr Andy Ness, Professor George Davey Smith and Dr Tilli Tansey made these further interviews possible (listed on page 2). These interviews were undertaken to explore the rich varieties of experience of those who had been at the cutting edge of epidemiology over more than five decades. It also enabled us to hear from those who had been unable to attend the original meetings and to follow up in detail some of the views and opinions expressed there. This approach has also allowed us, inter alia, to preserve records of early fieldwork practice, and to record accounts of the problems associated with the subsequent analysis, and storage, of the vast quantities of data generated in the Unit over many years.

In planning the Witness Seminar (and subsequent interviews), we identified appropriate participants with the help of the meeting's chairman and external adviser, in this case Sir Richard Doll, and our co-editor, Dr Andy Ness. Invitations inevitably

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[1] For further details, see 'What is a Witness Seminar', in Tansey E M, Catterall P P, Christie D A, Willhoft S V, Reynolds L A. (1997) *Wellcome Witnesses to Twentieth Century Medicine*, vol. 1. London: Wellcome Trust, i–v.

lead to further suggestions of people to invite, and we relied heavily on such recommendations. Despite this process some individuals were overlooked, and the records of the meeting include correspondence and recollections offered to us at a late stage in the production process. No Witness Seminar claims to offer a definitive history of a subject, as, naturally, the discussion and reminiscences flow only from those who contribute on the day. Often key people are unable to attend, a constant problem when many we invite are elderly. For example, the late Professor Charles Fletcher suffered a bad and incapacitating fall just days before he was due to join Dr Philip D'Arcy Hart as one of the two principal witnesses at the 'Pneumoconiosis' meeting in 1994.

Balance and purpose

Our aim has been to trace the development of field epidemiology and epidemiological methods in South Wales from the late 1940s onwards and to assess the contribution of this work to methodological advances and to medical knowledge. We have tried to include the voices of epidemiologists, statisticians and fieldworkers who worked in South Wales during this period, including those who worked there for a long time and others who worked there for only a brief period.

In focusing on the work of the Epidemiology Unit, we have also tried to recognize and acknowledge the work of the MRC Pneumoconiosis Unit, from which it evolved. Mrs Sheila Wright and Mrs Margery McDermott have argued that the important contributions made by the Pneumoconiosis Research Unit, particularly those of non-medical scientists in physics, chemistry, petrology, and electronics, should not be neglected.[2] Their comments arrived after the text had been finalized and will be deposited in Archives and Manuscripts of the Wellcome Library for consultation by interested researchers, along with all other correspondence, tapes and other records from the seminar.

The other group that is not well represented is those who were enrolled in these epidemiological studies. As our primary intention was to study the scientific process from the perspective of those running the studies we did not attempt to contact study subjects. Though it was beyond the scope of this project, others have written about the mining communities, and their attempts to get compensation[3], the impact of the unions,[4] and the working conditions they endured.[5] We believe that more information

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[2] See note 31, 180–184. For example, see Timbrell V. (1965) Human exposure to asbestos: dust controls and standards. The inhalation of fibrous dusts. *Annals of the New York Academy of Sciences* **132**: 255–273. Wagner J C, Gilson J C, Berry G, Timbrell V. (1971) Epidemiology of asbestos cancers. *British Medical Bulletin* **27**: 71–76. Glover J R, Bevan C, Cotes J E, Elwood P C, Hodges N G, Kell R L, Lowe C R, McDermott M, Oldham P D. (1980) Effects of exposure to slate dust in north Wales. *British Journal of Industrial Medicine* **37**: 152–162. Oldham H G, Bevan M M, McDermott M. (1979) Comparison of the new miniature Wright peak flow meter with the standard Wright peak flow meter. *Thorax* **34**: 807–809. Clark R L, Bugler J, McDermott M, Hill I D, Allport D C, Chamberlain J D. (1998) An epidemiology study of lung function changes of toluene diisocyanate foam workers in the United Kingdom. *International Archives of Occupational and Environmental Health* **81**: 169–179.

[3] Bartrip P W J, Burnam S. (1983) *The Wounded Soldiers of Industry: Compensation policy, 1833 to 1897*. Oxford: Clarendeon Press. Bartrip P W J. (1983) *Workmen's Compensation in the Twentieth Century: Law, history and social policy*. Avebury: Gower Publishing Co. Ltd. Our thanks to Mark Bufton for bringing these to our attention.

on the study subjects and their communities, and the impact of the studies, would create a richer picture of the historical place of this epidemiological work in South Wales.

Have the interviews enhanced and extended our understanding?

The additional reminiscences and contributions have allowed us to expand an individual's contributions, enlarged upon subjects mentioned in passing in the seminar, and introduced new topics. The interviews have filled several gaps in our knowledge of the evolution of the subject and revealed other lacunae. For example, the interviews with Peter Sweetnam, a statistician at the unit from 1966 until its closure in 1999, revealed how important technical developments in computing had been. He described how statistical analyses that take only a few seconds on a modern computer were only feasible on small samples and would require hours (or even days) of hand calculations or calculations using an electromechanical calculator.

Voices not well represented at the witness seminar had an opportunity to be heard. Dr Philip Hugh-Jones described contributions by physiologists in the early years at the PRU. Mrs Janie Hughes told of an earlier, less regulated way of life when recruiting samples in the valleys, or 'cold calling', involved knocking on front doors that were not locked, and using Post Offices as authoritative sources of local information on those who had moved away or died.

The excerpts from interviews also illuminate several perspectives, as distinctly different views emerge on a variety of subjects. By interviewing subjects about the whole of their lives we can begin to trace the paths that led people into epidemiology. For example, the interest in (and experiences of) studying birds described by Professor Estlin Waters (collecting data on the wrens of St Kilda in the Outer Hebrides) perhaps provided an ideal grounding for a future in epidemiological research.

The selected quotes represent only a small part of the material available and reflect a range and diversity of views and experiences – memories, anecdotes, opinions – that can only be hinted at in the published text. The tapes of seminars and interviews and the corrected transcripts along with accompanying correspondence have all been placed in the Wellcome Library and are available for further historical study. We hope that these records will add to the resources available to historians of present and future generations who wish to study the development of medical research and ideas over the second half of the twentieth century.

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[4] Bloor M. (2000) The South Wales Miners Federation, Miners' Lung and the instrumental use of expertise, 1900–1950. *Social Studies of Science* **30**: 125–140.

[5] Howells G, Rees C. (1999) Pneumoconiosis: a study of its effect on miners' health in South Wales, 1900–1980. *Nursing Standard* **13**: 39-41. Coggon D, Inskip H, Winter P, Pannett B. (1995) Contrasting geographical distribution of mortality from pneumoconiosis and chronic bronchitis and emphysema in British coal miners. *Occupational and Environmental Medicine* **52**: 554–555. Carpenter R G, Cochrane A L, Clarke W G, Jonathan G, Moore F. (1993) Death rates of miners and ex-miners with and without coalworkers' pneumoconiosis in south Wales, 1955. *British Journal of Industrial Medicine* 50: 578–585. Woodward N. (2000) Why did south Wales miners have high mortality? Evidence from the mid-twentieth century. *Welsh History Review* **20**: 116–141.

Acknowledgements

'The MRC Epidemiology Unit (South Wales)' was suggested as a suitable topic for a Witness Seminar by Dr Andy Ness. Professor George Davey Smith and Dr Ness provided many of the names of individuals to be invited, and assisted us in deciding the topics to be discussed. We are particularly grateful to Sir Richard Doll for his excellent chairing of the occasion. The 'Pneumoconiosis in Coal Workers' Witness Seminar, held on 9 November 1994, was suggested as a topic by Dr Tilli Tansey and Sir Christopher Booth, and ably chaired by the latter. A series of additional interviews was conducted by Dr Ness, and we thank all who contributed to that project, which was supported by a grant from the Wellcome Trust to Dr Ness, Professor Davey Smith, and Dr Tansey.

Dr Ness was generous with his time in pursuit of illustrations, as were Dr Peter Elwood and Mrs Janie Hughes. For additional help with the photographs, we thank Dr Estlin Waters, Dr Stewart Kilpatrick, Professor John Pemberton, the *Lancet,* the Medical Research Council, the National Institute for Medical Research, Mr Brian Furner of the London School of Hygiene and Tropical Medicine, Ms Mari Ann Hilliar of the Cochrane Library at the Llandough Hospital, Mr Keith Bellamy of the Media Resources Centre of University of Wales College of Medicine, Ms Caroline Moss-Gibbons of the Royal College of Physicians of London, and the Medical Photographic Library of the Wellcome Trust. The World Wide Web has been a great help for photographs of early equipment, our thanks to Mr David Weil of the Computer Museum of America and Mr Nigel Tout of Vintage Calculators. We are particularly grateful to Professor Davey Smith for writing the Introduction, Dr Mark W Bufton, who read through earlier drafts of the transcript, and offered us helpful comments and advice, and Dr Philip D'Arcy Hart, Dr Peter Elwood, Mr Peter Sweetnam, and Miss Nicola Weston from the Library of the National Institute for Medical Research for additional help with the text.

As with all our meetings, we depend a great deal on our colleagues at the Wellcome Trust: the Audiovisual Department, the Medical Photographic Library, and Mrs Tracy Tillotson of the Wellcome Library; Ms Julie Wood, who supervised the design and production of this volume, our indexer, Mrs Liza Furnival, our readers, Ms Lucy Moore and Mr Simon Reynolds, and Mr Mark Krüger for bibliographic research. We are particularly grateful to our Information Technology colleagues, Mr Gwyn Griffiths and Ms Vera Man, at the Wellcome Trust Centre for their help with the requisite hard and software used in preparing this publication. Mrs Jaqui Carter is our transcriber, and Mrs Wendy Kutner and Dr Daphne Christie assist us in running the meetings. Finally we thank the Wellcome Trust for supporting this programme.

Andy Ness
Lois Reynolds
Tilli Tansey

WITNESS SEMINARS: MEETINGS AND PUBLICATIONS[1]

In 1990 the Wellcome Trust created a History of Twentieth Century Medicine Group, as part of the Academic Unit of the Wellcome Institute for the History of Medicine, to bring together clinicians, scientists, historians and others interested in contemporary medical history. Among a number of other initiatives the format of Witness Seminars, used by the Institute of Contemporary British History to address issues of recent political history, was adopted, to promote interaction between these different groups, to emphasize the potential of working jointly, and to encourage the creation and deposit of archival sources for present and future use. In June 1999 the Governors of the Wellcome Trust decided that it would be appropriate for the Academic Unit to enjoy a more formal academic affiliation and turned the Unit into the Wellcome Trust Centre for the History of Medicine at University College London from 1 October 2000. The Wellcome Trust continues to fund the Witness Seminar programme via its support for the Centre.

The Witness Seminar is a particularly specialized form of oral history where several people associated with a particular set of circumstances or events are invited to meet together to discuss, debate, and agree or disagree about their memories. To date, the History of Twentieth Century Medicine Group has held over 30 such meetings, most of which have been published, as listed in the table on pages xi–xiii.

Subjects for such meetings are usually proposed by, or through, members of the Programme Committee of the Group, and once an appropriate topic has been agreed, suitable participants are identified and invited. These inevitably lead to further contacts, and more suggestions of people to invite. As the organization of the meeting progresses, a flexible outline plan for the meeting is devised, usually with assistance from the meeting's chairman, and some participants are invited to 'set the ball rolling' on particular themes, by speaking for a short period of time to initiate and stimulate further discussion.

Each meeting is fully recorded, the tapes are transcribed and the unedited transcript is immediately sent to every participant. Each is asked to check their own contributions and to provide brief biographical details. The editors turn the transcript into readable text, and participants' minor corrections and comments are incorporated into that text, while biographical and bibliographical details are added as footnotes, as are more substantial comments and additional material provided by participants. The final scripts are then sent to every contributor, accompanied by forms assigning copyright to the Wellcome Trust. Copies of all additional correspondence received during the editorial process are deposited with the records of each meeting in Archives and Manuscripts, Wellcome Library, London.

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[1] The following text also appears in the 'Introduction' to recent volumes of *Wellcome Witnesses to Twentieth Century Medicin*e published by the Wellcome Trust and the Wellcome Trust Centre for the History of Medicine at University College London.

As with all our meetings, we hope that even if the precise details of some of the technical sections are not clear to the nonspecialist, the sense and significance of the events are understandable. Our aim is for the volumes that emerge from these meetings to inform those with a general interest in the history of modern medicine and medical science; to provide historians with new insights, fresh material for study, and further themes for research; and to emphasize to the participants that events of the recent past, of their own working lives, are of proper and necessary concern to historians.

HISTORY OF TWENTIETH CENTURY MEDICINE WITNESS SEMINARS, 1993–2003

1993 **Monoclonal antibodies**[1]
Organizers: Dr E M Tansey and Dr Peter Catterall

1994 **The early history of renal transplantation**
Organizer: Dr Stephen Lock

Pneumoconiosis of coal workers[2]
Organizer: Dr E M Tansey

1995 **Self and non-self: a history of autoimmunity**[1]
Organizers: Sir Christopher Booth and Dr E M Tansey

Ashes to ashes: the history of smoking and health[3]
Organizers: Dr Stephen Lock and Dr E M Tansey

Oral contraceptives
Organizers: Dr Lara Marks and Dr E M Tansey

Endogenous opiates[1]
Organizer: Dr E M Tansey

1996 **Committee on Safety of Drugs**[1]
Organizers: Dr Stephen Lock and Dr E M Tansey

Making the body more transparent: the impact of nuclear magnetic resonance and magnetic resonance imaging[4]
Organizer: Sir Christopher Booth

1997 **Research in General Practice**[4]
Organizers: Dr Ian Tait and Dr E M Tansey

Drugs in psychiatric practice[4]
Organizers: Dr David Healy and Dr E M Tansey

The MRC Common Cold Unit[4]
Organizers: Dr David Tyrrell and Dr E M Tansey

The first heart transplant in the UK[5]
Organizer: Professor Tom Treasure

1998 **Haemophilia: recent history of clinical management**[6]
Organizers: Professor Christine Lee and Dr E M Tansey

Obstetric ultrasound: historical perspectives[7]
Organizers: Dr Malcolm Nicolson, Mr John Fleming and Dr E M Tansey

Post penicillin antibiotics[8]
Organizers: Dr Robert Bud and Dr E M Tansey

Clinical research in Britain, 1950–1980[9]
Organizers: Dr David Gordon and Dr E M Tansey

1999 **Intestinal absorption**[10]
Organizers: Sir Christopher Booth and Dr E M Tansey

The MRC Epidemiology Unit (South Wales)[11]
Organizers: Dr Andy Ness and Dr E M Tansey

Neonatal intensive care[12]
Organizers: Professor Osmund Reynolds and Dr E M Tansey

British contributions to medicine in Africa after the Second World War[13]
Organizers: Dr Mary Dobson, Dr Maureen Malowany,
Dr Gordon Cook and Dr E M Tansey

2000 **Childhood asthma, and beyond**[14]
Organizers: Dr Chris O'Callaghan and Dr Daphne Christie

Peptic ulcer: rise and fall[15]
Organizers: Sir Christopher Booth, Professor Roy Pounder and Dr E M Tansey

Maternal care[16]
Organizers: Dr Irvine Loudon and Dr Daphne Christie

2001 **Leukaemia**[17]
Organizers: Professor Sir David Weatherall, Professor John Goldman,
Sir Christopher Booth and Dr Daphne Christie

The MRC Applied Psychology Unit[18]
Organizers: Dr Geoff Bunn and Dr Daphne Christie

Genetic testing[19]
Organizers: Professor Doris Zallen and Dr Daphne Christie

Foot and mouth disease[20]
Dr Abigail Woods, Dr Daphne Christie and Dr David Aickin

2002 **Environmental toxicology: The legacy of silent spring**
Organizers: Dr Robert Flanagan and Dr Daphne Christie

Cystic fibrosis
Organizers: Dr James Littlewood and Dr Daphne Christie

Innovation in pain management
Organizers: Professor David Clark and Dr Daphne Christie

2003 **Thrombolysis**
Organizers: Mr Robert Arnott and Dr Daphne Christie

Beyond the asylum: Anti-psychiatry and care in the community
Organizers: Dr Mark Jackson and Dr Daphne Christie

The Rhesus factor story
Organizers: Professor Doris Zallen and Dr Daphne Christie

[1] Tansey E M, Catterall P P, Christie D A, Willhoft S V, Reynolds L A. (eds) (1997) *Wellcome Witnesses to Twentieth Century Medicine,* vol. 1. London: The Wellcome Trust, 135pp.

[2] Hart, P D'Arcy, edited and annotated by Tansey E M. (1998) Chronic pulmonary disease in South Wales coalmines: An eye-witness account of the MRC surveys (1937–1942). *Social History of Medicine* **11**: 459–468.

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[6] Tansey E M, Christie D A. (eds) (1999) Haemophilia: Recent history of clinical management. *Wellcome Witnesses to Twentieth Century Medicine*, vol. 4. London: The Wellcome Trust, 90pp.

[7] Tansey E M, Christie D A. (eds) (2000) Looking at the unborn: Historical aspects of obstetric ultrasound. *Wellcome Witnesses to Twentieth Century Medicine,* vol. 5. London: The Wellcome Trust, 80pp.

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[10] Christie D A, Tansey E M. (eds) (2000) Intestinal absorption. *Wellcome Witnesses to Twentieth Century Medicine*, vol. 8. London: The Wellcome Trust, 81pp.

[11] Ness A R, Reynolds L A, Tansey E M. (eds) (2002) Population-based Research in south Wales: The MRC Pneumoconiosis Research Unit and the MRC Epidemiology Unit. *Wellcome Witnesses to Twentieth Century Medicine*, vol. 13. London: The Wellcome Trust Centre for the History of Medicine at UCL, 150pp.

[12] Christie D A, Tansey E M. (eds) (2001) Origins of neonatal intensive care in the UK. *Wellcome Witnesses to Twentieth Century Medicine*, vol. 9. London: The Wellcome Trust Centre for the History of Medicine at UCL, 84pp.

[13] Reynolds L A, Tansey E M. (eds) (2001) British contributions to medical research and education in Africa after the second world war. *Wellcome Witnesses to Twentieth Century Medicine*, vol. 10. London: The Wellcome Trust Centre for the History of Medicine at UCL, 93pp.

[14] Reynolds L A, Tansey E M. (eds) (2001) Childhood asthma and beyond. *Wellcome Witnesses to Twentieth Century Medicine*, vol. 11. London: The Wellcome Trust Centre for the History of Medicine at UCL, 74pp.

[15] Christie D A, Tansey E M. (eds) (2002) Peptic ulcer: Rise and fall. *Wellcome Witnesses to Twentieth Century Medicine*, vol. 14. London: The Wellcome Trust Centre for the History of Medicine at UCL, 143pp.

[16] Christie D A, Tansey E M. (eds) (2001) Maternal care. *Wellcome Witnesses to Twentieth Century Medicine*, vol. 12. London: The Wellcome Trust Centre for the History of Medicine at UCL, 88pp.

[17] Christie D A, Tansey E M. (eds) (2003) Leukaemia. *Wellcome Witnesses to Twentieth Century Medicine*, vol. 15. London: The Wellcome Trust Centre for the History of Medicine at UCL, in press.

[18] Reynolds L A, Tansey E M. (eds) (2003) The MRC Applied Psychology Unit. *Wellcome Witnesses to Twentieth Century Medicine*, vol. 16. London: The Wellcome Trust Centre for the History of Medicine at UCL, in press.

[19] Christie D A, Tansey E M. (eds) (2003) Genetic testing. *Wellcome Witnesses to Twentieth Century Medicine*, vol. 17. London: The Wellcome Trust Centre for the History of Medicine at UCL, in press.

[20] Reynolds L A, Tansey E M. (eds) (2003) Foot and Mouth Disease: The 1967 outbreak and its aftermath. *Wellcome Witnesses to Twentieth Century Medicine*, vol. 18. London: The Wellcome Trust Centre for the History of Medicine at UCL, in press.

INTRODUCTION

Field epidemiology in south Wales: from tuberculosis to non-communicable disease

In 1952 a history of American epidemiology appeared, documenting the development of the discipline up until the mid-twentieth century.[1] It was almost exclusively concerned with infectious disease, although it contained hints that the chronic diseases then rapidly taking over from the declining infections as the leading cause of death would become the focus of future epidemiological work. The book is frequently used as a benchmark for considering the development of epidemiology in the second part of the twentieth century.[2] In Britain the population-based research in south Wales from 1937 onwards provides a window into the emergence of what has come to be termed 'modern epidemiology'. The armament of case-control studies,[3,4,5] prospective cohort studies[2,6] and randomized controlled trials[7] all have pre-histories stretching back over the twentieth century, and even before, but a moment of particular importance for all three was the appearance of a series of case-control studies on smoking and lung cancer,[8,9,10,11] the establishment of the Framingham heart disease study[12] and the MRC streptomycin trial for treatment of pulmonary tuberculosis.[13,14]

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[1] Winslow C-E A, Smillie W G, Doull A, Gordon J E, edited by Top F H. (1952) *The History of American Epidemiology*. St Louis: CV Mosby Co., 114–167.

[2] Susser M. (1985) Epidemiology in the United States after World War Two: the evolution of technique. *Epidemiologic Reviews* **7**: 147–177.

[3] Lane-Claypon J E. (1926) *A Further Report on Cancer of the Breast, with special reference to its associated antecedent conditions*. Reports on Public Health and Medical Subjects No 32. London: HMSO

[4] Stocks P, Karn M. (1933) A co-operative study of the habits, home life, dietary and family histories of 450 cancer patients and of an equal number of control patients. *Annals of Eugenics* **5**: 237–79.

[5] Schairer E, Schöniger E. (1943) Lungenkrebs und tabakverbrauch. *Zeitschrift fur Krebsforschung* **54**: 261–269. (Reprinted and translated as 'Lung cancer and tobacco consumption', see (2001) *International Journal of Epidemiology* **30**: 24–27).

[6] Armstrong D B. (1918–19) The medical aspects of the Framingham community health in tuberculosis demonstration. *American Review of Tuberculosis* **2**: 195–206.

[7] Chalmers I. (2001) Comparing like with like: some historical milestones in the evolution of methods to create unbiased comparison groups in therapeutic experiments. *International Journal of Epidemiology* **30**: 1156–1164.

[8] Schrek R, Baker L A, Ballad G, Dolgoff S. (1950) Tobacco smoking as an etiologic factor in disease; cancer. *Cancer Research* **10**: 49–58.

[9] Wynder E L, Graham E A. (1950) Tobacco smoking as a possible etiological factor in bronchogenic carcinoma. *Journal of the American Medical Association* **143**: 329–336.

[10] Levin M L, Goldstein H, Gerhardt B R. (1950) Cancer and tobacco smoking. ibid.: 336–338.

[11] Doll R, Hill A B. (1950) Smoking and carcinoma of the lung. *British Medical Journal* **ii**: 740–748.

[12] Dawber T R. (1980) *The Framingham Study. The epidemiology of atherosclerotic disease*. London: Harvard University Press.

[13] Medical Research Council. (1948) Streptomycin treatment of pulmonary tuberculosis: an MRC investigation. *British Medical Journal* **ii**: 769–782.

[14] Yoshioka A. (2002) Streptomycin in postwar Britain: A cultural history of a miracle drug, in Heteren G M Van, Gijswijt-Hofstra M, Tansey E M. (eds) *Biographies of Remedies: Drugs, Medicines and Contraceptives in Dutch and Anglo-American Healing Cultures*. Amsterdam: Rodopi B V, 203–227.

Tuberculosis was, as the US epidemiologist George Comstock has pointed out, a bridge to chronic disease epidemiology.[15] While tuberculosis was clearly an infectious disease, it was not one that was tractable by the standard methods of infectious disease epidemiology. It re-established the importance of host susceptibility after the apparent triumph of simple germ theories of disease and had no clear incubation period (with many cases of late adulthood clinical tuberculosis being recrudescence of infection acquired decades earlier[16]). As the pioneering US epidemiologist Wade Hampton Frost wrote in 1933 for TB,

> we cannot assume that the risk with which we are concerned is concentrated within the year or even the decade following the establishment of the known exposure. It may, perhaps, be manifested by excessive morbidity or mortality in any subsequent period of life. Hence, observation of the exposed group must extend over a sufficient number of years to define the rates of morbidity and mortality prevailing in successive periods throughout the usual in span of life. To keep a sufficiently large group of people under systematic, exact observation for such length of time is a difficult task which has, indeed, been undertaken in various places, but to the best of my knowledge has not been carried much beyond a decade. However, such simple facts as lie within the knowledge and memory of the average householder may be obtained by *retrospective* investigation, tracing familial histories backward into the past.[17]

Frost emphasised the need for careful retrospective data collection, although clearly prospective study was preferable. In fact, a prospective investigation of tuberculosis had been established in Framingham, USA, during the First World War,[6] and the existence of this study was one factor leading to the establishment of the seminal Framingham heart disease study three decades later.

Prospective epidemiological studies of chronic (believed to be non-infectious) diseases can be seen as a development of the methods applied to the study of tuberculosis. Although Frost established retrospective studies of tuberculosis and investigated the biases, which could be introduced into these[18] formal case-control studies do not seem to have been used in investigating tuberculosis. However the rise of lung cancer stimulated investigations of the possible role of old tuberculosis scars as a source of the disease, early studies generally concluded that this was not the case.[19] Investigators of this issue considered that smoking was an important cause of lung

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[15] Comstock G W. (1986) Tuberculosis – a bridge to chronic disease epidemiology. *American Journal of Epidemiology* **124**: 1–16.

[16] Davey Smith G, Kuh D. (2001) Commentary: William Ogilvy Kermack and the childhood origins of adult health disease. *International Journal of Epidemiology* **30**: 696–703.

[17] Frost W H. (1933) Risk of persons in familial contact with pulmonary tuberculosis. *American Journal of Public Health* **23**: 426–432.

[18] Comstock G W. (1985) Early studies of Tuberculosis. *National Cancer Institute Monograph* **67**: 23–27.

[19] Hoffman F L. (1929) Cancer of the lungs. *American Review of Tuberculosis* **19**: 392–406.

cancer by 1931,[20] well before the first formal case-control studies in Germany in 1939 and 1943.[21] Several of the early case-control studies of lung cancer investigated tuberculosis as a possible cause or co-factor. With respect to randomised controlled trials, while others had been carried out before the landmark streptomycin for tuberculosis trial,[22] it is the latter study, which established the methodology as central to evaluating the effectiveness of medical treatments.

The initial population-based research in south Wales was chronic pulmonary disease research. Here there is a link between the old and new epidemiology. Dr Philip D'Arcy Hart, who had worked on tuberculosis, directed surveys of south Wales coal miners in the late 1930s and early 1940s.[23] He was also involved in the MRC streptomycin trial,[13] as well as an earlier and largely forgotten randomised controlled trial of treatment of the common cold. Archie Cochrane returned from a Rockefeller fellowship in the USA to Britain in 1948 and hoped to obtain work from his friend D'Arcy Hart, who was then engaged in the streptomycin trial.[24] Cochrane intended to investigate the impact of BCG immunisation and mass X-ray surveillance on tuberculosis rates in Scottish border towns, and only when that project proved unfeasible did he take up the offer to join the MRC's recently established Pneumoconiosis Research Unit (PRU) in Cardiff. The radiographical and other similarities between tuberculosis and progressive massive fibrosis (PMF) of the lungs led to a belief that there could be an interaction between dust exposure and tuberculosis in generating the disease. A major study was set up by Cochrane and others in the PRU to examine this by reducing the level of tuberculosis infection in one of two comparable mining valleys and establishing the effect of this on the subsequent risk of PMF in the two valleys.[25] The continuing general decline in tuberculosis prevented any definitive results from the study, although the effort put into it was considerable. However, a major part of the output of the PRU until the early 1960s dealt with tuberculosis.

The subsequent development of the work of the unit built on both the methods developed for these earlier studies and on the contact established with populations that were well defined, relatively stable and willing to participate in research. In 1959 Archie Cochrane applied for and secured the David Davies Chair of Tuberculosis at the medical school at Cardiff University [then the Welsh National School of Medicine]. When he was moving to Cardiff the idea was mooted that a separate unit

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[20] *idem* (1931) Cancer and smoking habits. *Annals of Surgery* **93**: 50–67.

[21] Davey Smith G, Ströbele S A, Egger M. (1994) Smoking and health promotion in Nazi Germany. *Journal of Epidemiology and Community Health* **48**: 220–223.

[22] MRC Patulin Clinical Trials Committee. (1944) Clinical trials of patulin in the common cold. *Lancet* **ii**: 373–375.

[23] See introductory note on page 3.

[24] See page 20, note 20, 119.

[25] See page 36, note 62.

for epidemiological studies under his direction should be set up. In a memo circulated in the MRC toward the end of 1959,[26] presumably written by Dr Dick Cohen[27] at the MRC, it was suggested that the techniques which had been developed in the pneumoconiosis work – of surveying whole populations and using standardised methods – could be applied to many other fields, including rheumatoid arthritis, asthma, blood pressure, coronary heart disease, diabetes and bronchitis.

The epidemiological studies of the south Wales Unit produced a wide range of important findings with respect to specific health outcomes. These are discussed at length in this volume, but an important principle of the studies is the generalizability of the findings. Direct clinical or health policy relevance of the findings is also evident, something which is often not seen in epidemiological research. For example, the studies on iron deficiency anaemia had important implications for clinical practice (and in this sense the distinction between population and clinical epidemiology is sometimes hard to maintain, with the most robust evidence for clinical practice coming from population studies), as did the trials of nutritional influences on asthma, child growth and myocardial reinfarction.

The south Wales work is perhaps best remembered in the epidemiological community for two aspects of its work. First, the high response rates that were obtained, something that has slipped somewhat in more recent epidemiological studies, perhaps because of reduced engagement with the studied communities.[28] Second, the promotion of randomised trial evidence, most famously in Archie Cochrane's *Effectiveness and Efficiency*[29] published in 1972. While the unit did carry out trials – in particular two important early trials of aspirin following myocardial infarction – more of its resources were devoted to observational epidemiology. The Cochrane Collaboration, however, will make certain that this contribution continues to be widely recognised.[30]

Perhaps less widely appreciated by epidemiologists in the second part of the twentieth century was the importance of large sample sizes in randomised controlled trials with regard to producing robust evidence for clinical practice.[31] In observational epidemiology the situation is in some ways different, and more precise or repeated measurements on smaller sample sizes have value, particularly in the situation where

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[26] See page 40, note 68 and Figure 31.

[27] See Wilson J M G. (1998), Cohen biographical note on page 131.

[28] Hart J T with Davey Smith G. (1997) Response rates in south Wales 1950–96: changing requirements for mass participation in human research, in Maynard A, Chalmers I. (eds) (1997), page 15, note 14, 31–57.

[29] See Cochrane A L. (1972), page 15, note 14.

[30] Chalmers I, Sackett D, Silagy C. (1997) The Cochrane Collaboration, in Maynard A, Chalmers I. (eds) (1997), page 15, note 14, 231–249.

[31] Collins R, Peto R, Gray R, Parish S. (1997) Large-scale randomised evidence: trials and overviews, in Maynard A, Chalmers I. (eds) (1997), page 15, note 14, 197–230.

there is substantial confounding.[32] Several of the prospective studies from the unit, particularly the Caerphilly cohort study, are unusual in terms of having repeated data to allow the investigation of this issue.

Epidemiology in the twenty-first century is certain to be more concerned with genetic contributions to disease than was twentieth century epidemiology. Exciting advances in technology that allow for such studies should not take away from the importance of good study design and relating study findings to biological reality.[33] The developments in 'population laboratory' research pioneered in the south Wales valleys will continue to inform epidemiological practice as long as epidemiology continues to have anything to offer to health sciences and public health.

George Davey Smith
Department of Social Medicine, University of Bristol

[32] Phillips A N, Davey Smith G. (1993) The design of prospective epidemiological studies: more subjects or better measurements? *Journal of Clinical Epidemiology* **46**: 1203–1211.

[33] Terwilliger J D, Goring H H H. (2000) Gene mapping in the twentieth and twenty-first centuries: statistical methods, data analysis and experimental design. *Human Biology* **72**: 63–132.

POPULATION-BASED RESEARCH IN SOUTH WALES:
THE MRC PNEUMOCONIOSIS RESEARCH UNIT AND THE MRC EPIDEMIOLOGY UNIT

The transcript of a Witness Seminar,
'The MRC Epidemiology Unit (South Wales)', held at
the Wellcome Institute for the History of Medicine,
London, on 23 March 1999,
with extracts from additional interviews
conducted by Andy Ness and
from a Witness Seminar,
'Pneumoconiosis in Coal Workers',
9 November 1994.

Edited by A R Ness, L A Reynolds and E M Tansey

WITNESS SEMINAR PARTICIPANTS

Sir Christopher Booth
Dr Michael Burr
Professor Sir Richard Doll (Chair)
Dr Peter Elwood
Dr Joan Faulkner (Lady Doll)*
Dr Julian Tudor Hart
Mr Nick Henderson
Dr Sheila Howarth (Lady McMichael)†
Mrs Janie Hughes
Professor Stewart Kilpatrick
Dr Shaun Murphy
Dr Andy Ness
Professor John Pemberton
Dr Stephen Stansfeld
Professor David Strachan
Professor George Davey Smith
Dr Hugh Thomas
Dr David Tyrrell
Professor Owen Wade
Professor Estlin Waters
Dr Jean Weddell

Others attending the meeting: Dr Derek Bangham, Dr Yoav Ben-Shlomo, Professor Michael Bloor, Dr Tim Boon, Dr Gordon Cook, Dr Rosemary Elliot, Professor Stephen Frankel, Ms Ceri Hughes, Dr Diana Kuh, Professor Peter Pharoah, Dr Geoffrey Tweedale, Ms Elizabeth Willis

Apologies: Sir Donald Acheson, Dr Michael Ashley-Miller, Dr David Bainton,‡ Dr Ian Baker, Professor Hubert Campbell, Professor Sir Iain Chalmers, Professor Gareth Crompton, Dr Peter Graham, Dr David Gunnell, Dr Philip Hugh-Jones, Dr Peter McCarron, Professor Jim McEwen, Dr William Miall, Mr Fred Moore, Dr S G Owen, Dr Selwyn St Leger, Mr Peter Sweetnam, Dr J C Wagner,§ Dr Martin Wright,¶ Dr John Yarnell, Dr Carsten Timmermann

ADDITIONAL INTERVIEWS BY DR ANDY NESS

		Date interviewed
Dr David Bainton‡	ERU 1971–74	11 July 2000
Dr Peter Elwood	ERU 1963–95	14 April 2000, 28 February 2001
Dr Julian Tudor Hart	ERU 1960	14 June 2000
Dr Philip Hugh-Jones	PRU 1949–58	5 July 2000
Mrs Janie Hughes	ERU 1964–97	28 March 2000; with M Jones, 10 May 2000
Ms Marion Jones	ERU 1967–97	10 May 2000
Professor Stewart Kilpatrick	PRU, ERU 1958–68	23 May 2000
Dr Bill Miall	PRU 1950–60	13 August 2001
Dr Selwyn St Leger	ERU 1974–80	27 July 2000
Mr Peter Sweetnam	ERU 1966–99	31 May 2000
Ms Mary Thomas *(Mrs Hart)*	MRC 1960–62	14 June 2000
Professor Estlin Waters	ERU, 1965–70	14 July 2000
Dr Martin Wright¶	PRU 1950–60	26 July 2000
Mrs Sheila Wright	MRC 1950–52; 1970–80	26 July 2000
Dr John Yarnell	ERU 1975–93	18 April 2000

ERU, later EU Epidemiological Research Unit
MRC Medical Research Council
PRU Pneumoconiosis Research Unit

*Deceased 22 October 2001
†Deceased 31 July 2000
‡Deceased 23 January 2002
§Deceased 25 March 2000
¶Deceased 4 March 2001

See page 130 for bibliographical details.

MRC PNEUMOCONIOSIS RESEARCH,* 1937–60

Dr Philip D'Arcy Hart:[1] First of all, pneumoconiosis, in case anybody doesn't know, is really only dust disease of the lungs, that's all, and could cover asbestosis. But here we are confined to coal dust. I am going to try to rescue from threatened oblivion the initiative of the MRC some 50 years ago. This was the investigation on coal miners' pneumoconiosis in south Wales and it took place in what I think I can call two medical phases. The first was phase 1, with which I am concerned, from 1937 to 1940. That is, just before the War and just after it started, when things were rather tense out in Wales. The second part was after Charles Fletcher's unit started in 1945.

For a long time, and before X-rays of the chest existed, it was reported by many people that inhalation of coal dust produced chronic disabling disease. You have probably heard of the term 'miners' phthisis' which was one of the terms. And in Great Britain it was particularly rife in south Wales, and in south Wales it was particularly prevalent in the west, where the anthracite pits were. There was no opportunity for systematic study of coal miners' diseases, but it was generally believed they existed. It wasn't until 1929 that there was any compensation for these people and then it was for the minority of coal miners who worked in hard rock, for example tunnelling, who would develop a classical silicosis which is due to quartz inhalation. In 1934, four or five years later, the compensation scheme was extended to all underground workers. But they had to conform to the definition of classical silicosis. The great majority of workers had not worked in hard rock.

The Medical Research Council (MRC) was asked by the Home Office and the Mines Department in 1936 to investigate chronic pulmonary disease among coalminers, particularly the conditions in the south Wales coalfield. The MRC referred the problem to its Committee on Industrial Pulmonary Disease, chaired by C G Douglas. Dr P D'Arcy Hart was appointed to undertake the medical work, along with Dr E A Aslett, who was seconded from the Welsh National Memorial Association. Dr T H Belt did the pathological work, assisted by Dr A A Ferris.[2]

Figure 1: Dr Philip D'Arcy Hart in the 1950s.

* The following text is a contribution by Dr Philip D'Arcy Hart to the Witness Seminar, 'Pneumoconiosis in Coal Workers' held on 9 November 1994 at the Wellcome Institute for the History of Medicine (WIHM), London, and has been partly included in P D'Arcy Hart, edited and annotated by E M Tansey. (1998) Chronic pulmonary disease in South Wales coalmines: An eye-witness account of the MRC surveys (1937–1942). *Social History of Medicine* **11**: 459–468. The transcript of the 'MRC Epidemiology Unit (South Wales)', held at WIHM on 23 March 1999, follows on page 15.

[1] See biographical notes starting on page 130.

[2] Privy Council, Medical Research Council. (1942) *Chronic Pulmonary Disease in South Wales Coalminers.* I. Medical Studies. Special Report Series 243. London: HMSO, iii–xiii.

The Workmen's Compensation Act of 1943 took account of the Committee's findings that the key factor was prolonged exposure to airborne dust, particularly quartz mixed with coal and other materials.

A 'no fault scheme' for compensation was introduced by the British Coal Board in 1974. In 1993 the Board was privatized as British Coal. The Government assumed British Coal's liabilities on privatization and miners could claim industrial injury benefit for bronchitis and emphysema within strict limits. Chronic emphysema and bronchitis were prescribed as dangerous diseases in 1993 following American and Belgian studies that demonstated that they were an endemic risk to mining workers. The High Court ruled in 1998 that the failures of British Coal and its predecessors to control the levels of coal dust in mines from 1949 to 1970 and to a lesser extent thereafter, was the cause of emphysema, bronchitis and other respiratory illnesses in former miners. A year later vibration white finger was added to the list. It was estimated in 1999 that up to 105 500 former miners in England, Wales and Scotland would be eligible to receive £2.1 billion in compensation.[3]

The local doctors and the men themselves complained that there were conditions in coalface workers, who had never worked in hard rock, which produced disability, but because their X-rays and post mortems did not look like ordinary silicosis, they did not get compensation. So while the compensation cases granted went up rapidly during the next few years after the scheme came in, so also did the refusals, and there was great discontent.

This was the position in the mid-1930s, when the Government, through the Home Office and the Mines Department, asked the MRC to sort things out, make recommendations and to do it urgently.[4] Now looking back, I ask myself why did the Government, which doesn't usually act urgently in this sort of thing, why did they act urgently in this case? I can think of three reasons. One is that the compensation costs were going up rapidly. Secondly, there was a war round the corner and they certainly did not want a dissatisfied coal-producing force. And, thirdly, I like to believe that there was some concern for the health and welfare of the miners.

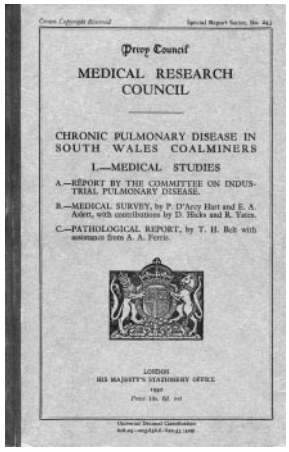
The MRC, through the Industrial Pulmonary Diseases Committee, recruited a large contingent of people from inside Wales and outside to work on the project: medical staff, Edward Aslett, a chest physician from Wales, and myself, MRC scientific staff. And then there were environmentalists, dust experts, mineralogists, geologists, inspectors of mines, and pathologists. We obtained the cooperation of the South Wales Miners Federation, that's the miners' trade union and the local miners' Lodges and the cooperation of the coal owners. There were individual coal owners then, before nationalization, privatization 'Mark 1'. You are going to have 'Mark 2' now.

Why did I join the MRC? Well it's rather confessional, but I wanted to get out of consultant medicine, because I found that I wanted to do research, with a small 'r',

[3] See discussion in House of Lords. (1998) *Hansard*, Columns 1102–1113 (16 November 1998).

[4] Meeting of MRC, 14 February 1936, Minute 28. 'Industrial Pulmonary Disease'; MRC Minute Book 3, 1927–36, MRC Archives, Public Record Office FD1/5256. Meeting of MRC, 27 November 1936, Minute 181 (a), 'Alumina Dust'; Minute 191 'Pulmonary Disease Among Coalminers', Minute Book 4, 1936–39, MRC Archives, Public Record Office FD1/5257. Meeting of MRC, 22 October 1937, Minute 119 'Pulmonary Disease Among Coalminers'; MRC Archives, Public Record Office FD1/5257.

and I found I couldn't do it, because I had to earn my living. And therefore I was looking for ways of getting out. Out of the blue, Sir Thomas Lewis on the Council, heard about this demand from the Home Office or the Government to do something about pneumoconiosis, and they were looking for somebody to do it. And he knew me (he was at University College Hospital and I was first assistant to T R Elliot's unit there, the medical unit, and I used to see Thomas Lewis and he must have gauged that I wasn't happy) and so he suggested me and they asked me.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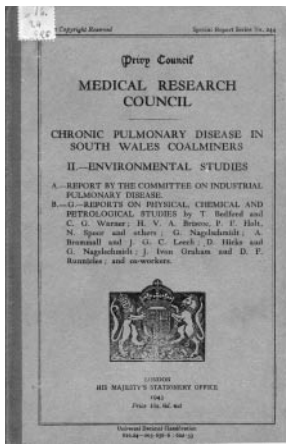
MEDICAL RESEARCH COUNCIL
CHRONIC PULMONARY DISEASE IN SOUTH WALES COALMINERS
I.—MEDICAL STUDIES
A.—REPORT BY THE COMMITTEE ON INDUSTRIAL PULMONARY DISEASE.
B.—MEDICAL SURVEY, by P. D'Arcy Hart and E. A. Adelt, with contributions by D. Hicks and R. Yates.
C.—PATHOLOGICAL REPORT, by T. H. Belt with assistance from A. A. Ferris.
LONDON
HIS MAJESTY'S STATIONERY OFFICE

Figure 2: Report 243, 1942.

I might say that at first I was offered a three-year job and that got to the ears of Thomas Lewis, who was very influential, and he apparently told the MRC (somehow or other I saw the letter), 'You can't ask this man to give up a career of consultant medicine for three years. You have got to speculate and give him a life's appointment.' And so that is how I got in those days a permanent appointment from the beginning. That's how I joined.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CHRONIC PULMONARY DISEASE IN SOUTH WALES COALMINERS
II.—ENVIRONMENTAL STUDIES
A.—REPORT BY THE COMMITTEE ON INDUSTRIAL PULMONARY DISEASE.
LONDON
HIS MAJESTY'S STATIONERY OFFICE

Figure 3: Report 244, 1943.

The medical phase, which I am calling phase 1, started work in 1937 and finished in 1940, and produced three Green reports.[5] I might say to some of you who are very keen historians, as a core of people here are, earlier history of pneumoconiosis right back, there's a lot more of that in the medical report. We started on the three stages of this phase. The first stage in 1937 was six months at one particular anthracite colliery in Ammanford, not far from Swansea. The second stage was 15 representative mines distributed throughout Wales, to be representative. The third stage was the examination of the people who load ships with coal, called coal trimmers,[6] at four south Wales docks. Meantime, a lot of work was going on with our dust experts and any autopsies were examined at Hammersmith Hospital by Dr Thomas Belt.

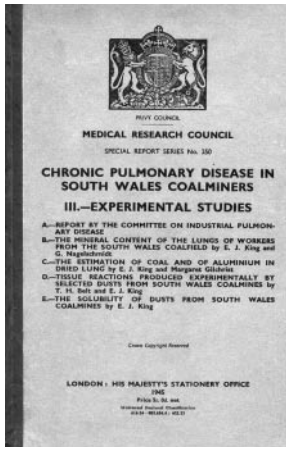

MEDICAL RESEARCH COUNCIL
SPECIAL REPORT SERIES No. 250
CHRONIC PULMONARY DISEASE IN SOUTH WALES COALMINERS
III.—EXPERIMENTAL STUDIES
A.—REPORT BY THE COMMITTEE ON INDUSTRIAL PULMONARY DISEASE
B.—THE MINERAL CONTENT OF THE LUNGS OF WORKERS FROM THE SOUTH WALES COALFIELD by E. J. King and G. Nagelschmidt
C.—THE ESTIMATION OF COAL AND OF ALUMINIUM IN DRIED LUNG by E. J. King and Margaret Gilchrist
D.—TISSUE REACTIONS PRODUCED EXPERIMENTALLY BY SELECTED DUSTS FROM SOUTH WALES COALMINES by T. H. Belt and E. J. King
E.—THE SOLUBILITY OF DUSTS FROM SOUTH WALES COALMINES by E. J. King
LONDON: HIS MAJESTY'S STATIONERY OFFICE

Figure 4: Report 250, 1945.

The work at Ammanford was very intensive – we worked from a schoolroom which was lent to us and

[5] MRC Special Reports Series 243, 244 and 250, were published between 1942 and 1945, as *Chronic Pulmonary Disease in South Wales Coalminers*. I–III, illustrated above in Figures 2–4. See also note 2.

[6] A coal trimmer was a skilled worker in the hold of a coal ship, who balanced the coal by hand. As the coal poured from the rail wagons on the staiths above the ship, the trimmers levelled the coal with specialized shovels. Colliers at the coalface, trimmers and surface workers on the screens were exposed to coal dust. Trimmers were not eligible for compensation. See MRC Special Report 243, note 2, 40–41 and Gough (1940), note 173.

Philip D'Arcy Hart

1. Compensation. Our MRC surveys (1936–42) as described above promoted, in the early 1950s, a widening of compensation to include coalface workers under a general heading of 'pneumoconiosis of coalworkers'. But even in this change of the regulations, bronchitis and emphysema were not considered integral; they were only considered to confer additional disability to that caused by the pneumoconiosis, simple or complicated, which was present also, and the worker had to have been 20 years underground. In 1992 the regulations were widened to regard bronchitis as causable by coal mine dust, but, for compensation purposes, at least simple pneumoconiosis must also be present. In 1998 the causative effect of coal mine dust to produce bronchitis was emphatically reaffirmed, and the necessity for accompanying pneumoconiosis was dropped; although underground service for 20 years was still required. A late, but radical, advance.

2. Dust control was improved following the first MRC reports in the early 1950s but later, and in the 1960s, faded as coal production and accidents became priorities. Only since about 1970 did dust control again become of serious importance, and dust is now considered to have been causative of bronchitis as well as pneumoconiosis. The improvement was especially evident in south Wales.

Addenda, July 1998[7]

did clinical examination of the miners, X-rays, some sort of respiratory disability tests, rather crude ones I have to say in retrospect, was all we could do, and history taking. There was no X-ray set-up there and we used a mobile van, Portable X-rays Limited, which trundled round the valleys, and it is amazing what beautiful X-rays they took for the period. Our history taking was important, due to the remarkable memories of the miners. We wanted to know how long they worked in certain seams, when they moved, and they were quite remarkable. And also it was due to the equally remarkable facility and ability of my clerical assistant, J I T Jones, whom I have failed to trace, who spoke Welsh and got the confidence of the miners, who started by being, as you can imagine in private ownership, extremely suspicious of any 'oddbod' that came in from outside. The second stage was much less intensive and limited to prevalences in these 15 other pits, 16 pits in all. We had no base in Wales. It was an expeditionary force, people descended and came from all over the place to work.

I lodged in Swansea and went up every day by car. I might say that the car I had was presented by Lord Nuffield, the manufacturer. Cars of that vintage had a windscreen with a hinge so you could open it. If there was an enormous amount of fog, snow and rain, you just had to push it open in order to see and put on your goggles and peer out in front. Later on I had as my base a desk at the London School of Hygiene and Tropical Medicine.

I am going to mention several achievements. The first and most important was that we confirmed by X-rays and by post mortems that coalface workers who had not worked in hard rock did have serious, disabling lesions. And they did not look like classical silicosis. So this confirmed the suspicions that had been around. Secondly, we were also able to trace the progression of these lesions according to the length of exposure to their work in the coal-seams. We were able to do that, not by following people along, of course, but by taking people who had been for different periods at Ammanford colliery, and matching them against the

[7]Additional comment by Dr Philip D'Arcy Hart in the published version, see note on page 3.

lesions they showed in their X-rays. And we were able to describe the character of the lesions, as it appeared on X-ray, starting with a reticular appearance, then a nodular appearance, and then big masses, with increasing disability. In contrast to silicosis we didn't find tuberculosis to be a leading feature of pneumoconiosis of colliers.

Our nomenclature and results were not always treated with acclamation. But, what I have just said was very much the subject, of course, of Charles Fletcher's unit which came afterwards, and they had to look into all this and we were criticized for making our descriptions and classifications only by X-ray. Afterwards he would probably have said that his unit modified the categories, improved them and linked them with the pathology more than we had, and produced a more basic classification, rather on the same lines, but suitable and accepted by international classification. Thus, the classification started with ours, but became different as regards names. I think the essentials of our findings still hold up, and the term 'pneumoconiosis of coal workers' stands today.

There was also an argument about disability. And that was quite acute. We thought there was some disability, very early changes, which we called reticulation, when people were beyond middle age. That was disputed later on by a number of people who said that it was not pneumoconiosis. Whatever it was, maybe it was due to smoking or something like that. And I think that the whole thing now has recently been cleared up and I will come back to it when I talk about compensation. So I think that what we said stands as the beginning anyway.

The third achievement needs the map. [See Figures 5 and 6] We introduced a hypothesis, we called it 'the rank of coal hypothesis'. We had noticed that the prevalence of pneumoconiosis was highest in the west and lowest in the east and intermediate in the middle. But we found a closer correlation if we compared the prevalences of pneumoconiosis in different collieries, with the rank of coal mined. Now the rank of coal, put simply, is the carbonaceous content, and that's highest in anthracite, lowest in bituminous, (which is what house coal is), and intermediate in steam coal (which is

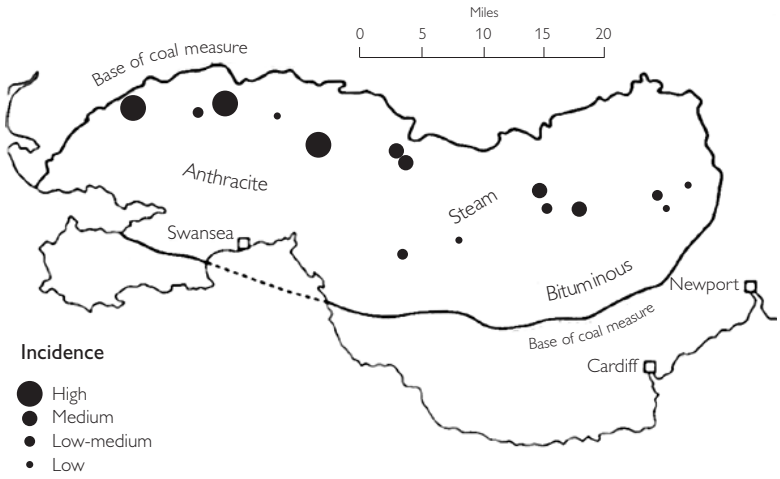


Figure 5: Map of the south Wales coalfield, showing the relative incidence of X-ray abnormalities at each of the 16 collieries.

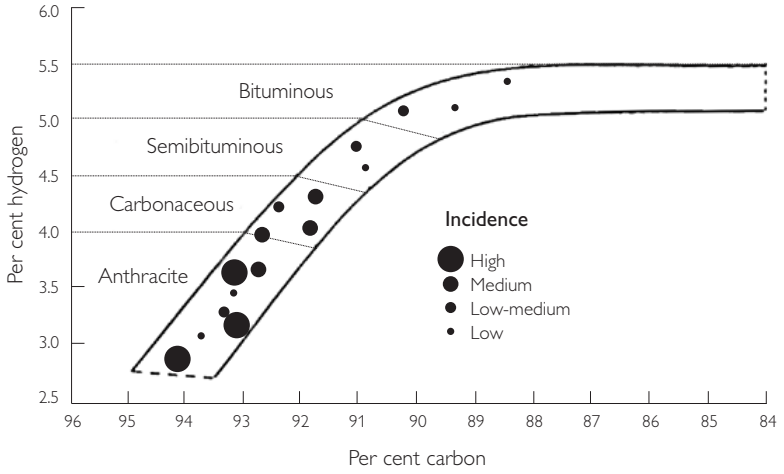


Figure 6: Relationship between the rank of coal and relative incidence of X-ray abnormalities at the 16 collieries.

what factories tended to use). The question is: is the rank of coal hypothesis any use? Well, it was found, by environmentalists,[8] that the rank and the amount of dust go in parallel and the highest amount of dust was in the anthracite and the lowest in the bituminous. It was hoped that there might be salient things in the quality of the coal too, but that has not been actually proved.

The fourth achievement was by our environmental colleagues who did an enormous amount of work and they pinpointed the areas in which they thought that coal dust could be reduced, and they introduced new techniques for measuring it. It seems, however, that their techniques were not fully adopted until later.

[8] The environmental studies were conduced by T Bedford and C G Warner, members of the scientific staff of the Industrial Health Research Board, along with Major J G C Leech, Professor H V A Briscoe, J Ivon Graham, D F Runnicles, D Hicks, G Nagelschmidt, J Thewlis and Major R Yates. See Figure 3, MRC Special Report 244, note 5.

And the fifth achievement was compensation. The compensation rules were, that people had to have 'silicosis'. So, many with pneumoconiosis were refused compensation. We considered this was too restrictive and we recommended that the word silicosis should be dropped and instead the scheme should be called 'pneumoconiosis of coal workers', so it would include coal miners at the face, rock workers and the coal trimmers at the docks. And we also widened the categories that were covered. New regulations embodied our recommendations. The terms of the compensation scheme since have remained practically unaltered down to 1983. But there's been one important change, that in 1992 emphysema and chronic bronchitis were included provided that the X-rays showed some evidence of pneumoconiosis.

What therefore, in summary, did we think we achieved? I think that we uncovered the natural history of this rather bastard sort of disease in phase 1, which was not really silicosis, and not really understood much before. We paved the way for things to happen and we also drew the attention of the informed public to this being a very important and widespread condition, and out of this came quite a large number of organized efforts.

Then there was Charles Fletcher's unit of course, which I can't really talk about.[9] Then there was the National Coal Board, which started doing studies by X-raying the miners periodically[10] and in 1963 they covered all of the miners of Great Britain and there was a very, very good turnout, and they could see what the prevalence of disease was. Then there was the Institute of

Sir Christopher Booth

The MRC appointed Charles Fletcher as head of this unit and Charles was, in my view, I am sure you would agree, a most unlikely choice. I mean an Old Etonian, Trinity College, rowed in the boat race in 1933, won against Oxford. One of the last social occasions his father attended was seeing that boat rowing to victory from Duke's Meadows in April 1933. You'd think that that was really a man with quite extraordinarily wrong qualifications to go to talk to coal miners in south Wales. Nothing could have been farther from the truth, because there was nobody who really managed to get people eating out of his hand in south Wales better than Charles Fletcher. He was incredibly successful in his relationships with all the people there and he deserves very great credit for that.[11]

[9] See page 15. See also C M Fletcher in a Royal College of Physicians video interview, RCP-OP/VTR3/1985. A collection of his papers, PP/CMF, are held by Archives and Manuscripts, Wellcome Library. Booth C. (1995) Obituary of Professor Charles Fletcher. *Independent* (23 December 1995).

[10] The National Joint Pneumoconiosis Committee of the Ministry of Power appointed a field research subcommittee in 1951. The following year it recommended that the National Coal Board should undertake research to establish how much and what kinds of dust caused pneumoconiosis and the environmental conditions that could reduce disablement in mine workers breathing dust at work. A Steering Committee was established with representatives from the Ministries of Power, Pensions and National Insurance, the MRC and others. Fieldwork started in 1953. See Hicks D, Fay J W J, Ashford J R, Rae S. (1961) *The Relation between Pneumoconiosis and Environmental Conditions: An analysis of the results of the first series of X-ray surveys in the National Coal Board's pneumoconiosis field research*. London: National Coal Board.

[11] Sir Christopher Booth, speaking at the Witness Seminar, 'Pneumoconiosis in Coal Workers', 9 November 1994, unpublished.

Occupational Medicine in Edinburgh which took a great interest, and they did a lot of work on the cytotoxicity of dusts, the analysis of mine dusts. They, particularly Professor Anthony Seaton, pushed for emphysema to be included, because he and his colleagues found that emphysema could occur in the fairly early stages of pneumoconiosis.[12]

Another thing I want to say is, looking back now, can we say that we know what the actual cause of the pneumoconiosis was? We know that quartz and silica are causes, but at first we thought that there might be some other silicate, some specific substance in the coal dust that does it. There has been no evidence that that really is so. And what one can say is that there is no doubt whatever that the prime suspect is the quantity of mine dust. Whether the quartz – there's always some quartz mixed in with the dust, however small – whether that plays a part is still not known, but I think there is a great suspicion that it does and that that's what makes it so peculiar. But it has not been absolutely proved, because it never seems to come out quite right quantitatively. However, I think one can say that a little quartz doesn't do you any good.

Figure 7: Swiss miner, 1930s, using a power drill.

There has been a dramatic fall in the prevalence of pneumoconiosis. In 1963, the Coal Board instituted periodic X-raying and that has gone on, eventually under British Coal, right up to 1993 and the last lot of figures were in the British Coal Report (1993–94). And it shows that there was one-thirtieth in 1993 of the level in 1963. Why did this happen? It's thought primarily because after 1975 the dust concentration was radically reduced. The other minor thing may have been shorter hours. People who have been detected with lesions have been switched perhaps to less risky parts of the mine, and also, one has to say, redundancy and retirement have played their parts.

[12] Morgan W K, Lapp L, Seaton A. (1972) Respiratory impairment in simple coal workers' pneumoconiosis. *Journal of Occupational Medicine* **14**: 839–844. See also Mossman B T, Bignon J, Corn M, Seaton A, Gee J B. (1990) Asbestos: scientific developments and implications for public policy. *Science* **247**: 294–301. Seaton A. (1990) Coalmining, emphysema, and compensation. *British Journal of Industrial Medicine* **47**: 433–435.

I am now going to ask you all to go from underground up into the fresh air and to the light. I want to deal with the lighter aspect of social history, and to give you the flavour of what it was like just before, and at the beginning of the Second World War, doing work in the coal mines. Surprising as it may seem nowadays, we were really well funded by the MRC. I give you two examples. First, there is the story of the half-crowns (2s.6d., 12½p). Some of you may have heard this before, it was published in a Welsh local paper, but as it was in Welsh maybe I can say it again, it is so highly topical. As part of our work we wanted to see whether tuberculosis was a factor in the progression of this pneumoconiosis. There was a lot of tuberculosis around there then, much more than now. So as part of our approach we decided to do tuberculin tests on a sample of men in order to see whether we could show any relationship between the lesions that they had and the tuberculin sensitivity. They were stratified according to their lesions. We selected a lot of miners and, after a lot of consultations, they agreed to have the skin test, which meant an injection of tuberculin into the skin itself. All went off well and each one collected half-a-crown reward and we were very pleased at that. Now this test, if people were negative, they required a second test exactly two days after and we assumed that that would be OK. But it wasn't, because the men grumbled and said, 'We've had one jab, we really don't know why some of us should have another one'. And there was a crisis and into the breach stepped Sir John McMichael, who happened to be down there studying some physiological aspect of respiration in miners. He made the most remarkable speech and won them all over. He told them that the job was only half done and if they gave up we should have no results at all (which was absolutely true). And so they decided to do it and we were very pleased. But then came the second crisis, 'Half-a-crown again, please'. Well, we had no half-crowns. Time was ticking over, and the second day was approaching. I rushed to the telephone in Ammanford, telephoned Westminster and told the MRC of our predicament, and I am glad to say that when I met the local train that same evening, the guard handed me a sack of half-crowns marked 'Medical Research

Julian Tudor Hart

What was said at that meeting [Witness Seminar, 23 March 1999] about the half-a-crown for participating miners, was actually true. I didn't know it was true then, but I have looked it all up since then, but the inference he drew from it was not true. The argument of the miners' union was that if any men were paid to participate, then all men should be paid to participate, because that was always the attitude of the union, and in fact this half crown was something to do with defrayment of expenses and so on. But the principle that for participants in research, it should be a voluntary act and should be unpaid, is very, very important. I think the moment people start doing something for a living, whether it is giving blood, or taking part in research or whatever, you introduce yet another source of corruption of data, it is unpredictable and destructive. I don't have documentation on it, but apparently in America it is now very difficult to get research subjects without paying them. It has certainly become very difficult to get students to participate in research without paying them.

Julian Tudor Hart

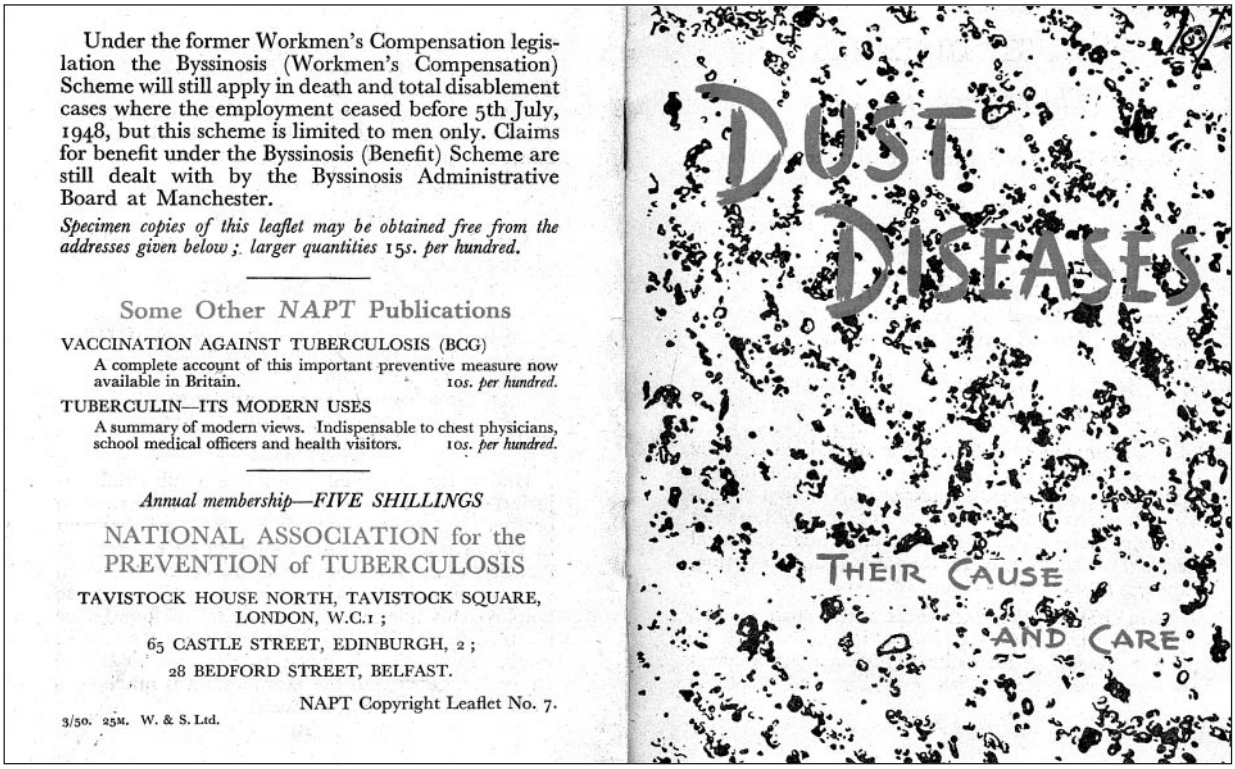
I went down to south Wales and spent a year there. Archie gave me a project where I had got to look at tuberculin sensitivity in relation to progression of progressive massive fibrosis, as a final validation or invalidation of Gough's hypothesis that the cause of progression from simple pneumoconiosis to progressive massive fibrosis (PMF, also known as complicated pneumoconiosis) was tuberculosis. It is an interesting thing historically, but we now know beyond question that tuberculosis has nothing to do with it. But it was an extremely attractive hypothesis, a hypothesis that seems so self-evidently true that you can hardly believe that you need evidence to prove it. I have seen so many people crash through having a religious belief in their hypothesis and bend data to confirm what they feel is already proven, believing that it's only for the doltish multitude that you have to produce more evidence, because otherwise they won't understand it.

Council', so we were able to carry out the tests and they did not show any relationship between the tuberculin sensitivity and the type of lesion, and that work was confirmed later on by Professor Archie Cochrane and his colleagues.[13] That's the first story.

The second one is more personal. This work was my first job with the MRC and in my briefing they said, 'Oh, by the way, you'll be travelling by train, I'm sure, in Wales. Travel first class'. So I said, 'That's very nice, why?' So they said, 'Well, we don't want you to have too many conversations with the miners'. We didn't carry out that rule, we saved a bit of money and we had some quite interesting conversations. But in any case, travelling by train wasn't very easy, because you never knew where you were. The stations were all wrong. They were all mixed up. You thought you were at one place and you were at another. That was because they thought this would confuse the Germans if they invaded. I travelled mostly by the Morris Nuffield car and one day I was in the middle of the country and it inactivated itself, so I decided that I must walk to the nearest railway station and I hoped to thumb a lift. Well, there were very few cars on the road and eventually I got a lift in a car with two big men and I asked if they would take me to the nearest railway station. As we went along they started asking me an enormous number of questions, and I couldn't make out why and I said, 'What station are you dropping me at and why are you asking me all these questions?' They said, 'We are taking you to the police station, we think you are a German parachutist.' So I said, 'Oh no, you are making a great mistake, I work for the British Government' and so we had a long conversation and eventually I convinced them and they took me to the railway station and on saying goodbye they gave me a bar of chocolate, which was a very rare treat, I can tell you.

[13] Hart J T, Cochrane A L, Higgins T T. (1963) Tuberculin sensitivity in coal workers' pneumoconiosis. *Tubercle* **44**: 141–152. For a more detailed historical view, see Meiklejohn A. (1951) History of lung diseases of coal miners in Great Britain. I. 1800–1875. *British Journal of Industrial Medicine* **8**: 127–137. *idem* (1952) ibid. II. 1875–1920. ibid **9**: 93–98. *idem* ibid. III. 1920–1952. ibid.: 209–222.

Now back to the serious matter. It's a real anticlimax. Who would have dreamt in those days and even until recently that people who knew no science, no medicine, would solve the problem of pneumoconiosis in Great Britain, by removing a large body of highly skilled craftsmen both from their work and from their risk of pneumoconiosis. But so it is. But of course this problem is still present in countries that supply us with coal – Colombia, China, Poland, and so on.



Under the former Workmen's Compensation legislation the Byssinosis (Workmen's Compensation) Scheme will still apply in death and total disablement cases where the employment ceased before 5th July, 1948, but this scheme is limited to men only. Claims for benefit under the Byssinosis (Benefit) Scheme are still dealt with by the Byssinosis Administrative Board at Manchester.

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DUST DISEASES

THEIR CAUSE AND CARE

Figure 8: Dust Diseases: Their cause and care. This pamphlet was published by the National Association for the Prevention of Tuberculosis, 1950.

THE MRC PNEUMOCONIOSIS RESEARCH UNIT, 1948–60

Sir Richard Doll: I am particularly glad that we are having the meeting today to discuss the work of this unit, because Archie Cochrane expressed his concern to me before he died that he was becoming better known because of his work on controlled clinical trials and his book, *Effectiveness and Efficiency*,[14] which of course reached almost religious qualities throughout the world after he died, and it wouldn't be much of an exaggeration to many people that one should be referring to Saint Cochrane. But he thought his epidemiological work was the major part of his scientific work, not his work in controlled trials. I must say that he and I agreed on that and it is particularly nice that it is therefore being recognized today.

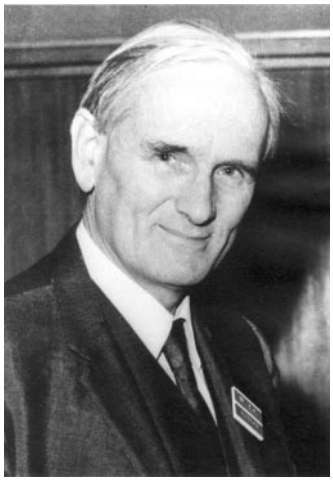

Figure 9: Professor Charles Fletcher (1911–95), 1971. © Keystone Press.

I am going to claim a lot of credit for the very early work that he did in Cardiff, for the simple reason that Charles Fletcher asked me to apply for the job of epidemiologist to work with him in 1947 and for various personal reasons I refused to do so, with the result that Archie Cochrane was appointed and really excellent work was done, which I would never have had the imagination or the energy to carry out. So I claim responsibility for the origin of his work. Now we have people here, I think, who were members of the unit in those early days, late 1940s and early 1950s, and I wonder if any of them would like to start by telling us a bit about the work that was going on then.

Professor Owen Wade: I was a junior member of the Pneumoconiosis Research Unit (PRU). I joined in April 1948 and left in April 1951. The unit was set up in 1946. At that time there were 800 000 coal miners working in the UK, of whom 120 000 were employed in south Wales. There were 20 000 men certified as suffering from pneumoconiosis, most of them from the south Wales coalfield.

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[14] Cochrane A L. (1972) *Effectiveness and Efficiency: Random reflections on health services.* The Rock Carling Fellowship 1971. London: Nuffield Provincial Hospitals Trust. See also Maynard A, Chalmers I. (eds) (1997) *Non-random Reflections on Health Services Research: On the 25th anniversary of Archie Cochrane's 'Effectiveness and Efficiency'.* London: British Medical Journal Publishing Group.

The study made by Philip D'Arcy Hart and Dr Aslett[15] between 1937 and 1941 suggested that the incidence of pneumoconiosis was related to the rank of coal, anthracite being more dangerous than steam coal, which was more dangerous than bituminous coal in the east of the coalfield. [See Figure 5 and 6, page 8] Soon after Archie Cochrane started the PRU's more extensive surveys, it became clear that the incidence was more closely related to the coal workers' exposure to dust, than to the rank of coal that they were mining. The miners' exposure to dust had been greatly increased when compressed air drills and coal cutting machinery were introduced in the late 1920s in the deep and difficult mines in the anthracite areas in the west of the coalfield and only later in the steam coal mines of the Rhondda and the bituminous mines further east. Before air drills, men had worked with pickaxes and shovels in traditional 'stall and heading' work.[16] When a power drill hits the coalface there's dust. I have been underground when there were chaps working at the stall with the pickaxe. As soon as you put in a mechanized coal cutter, it's very difficult to see them due to the dust. So I think the first thing that became clear was that the prevalence and incidence of pneumoconiosis was related to the amount of dust and that the differences were really related more to the introduction of the power drilling than to the grade of coal.

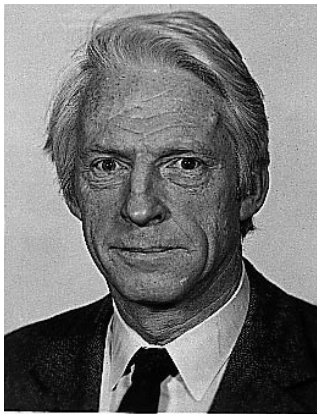


Figure 10: Dr Philip Hugh-Jones, *c.* 1980.

The second thing that was very important to me was the relationship between the severity of the X-ray changes of dust disease and the degree of disability in the patients we were seeing. I was engaged with Philip Hugh-Jones and [John] Gilson on the physiology side of things. When I first arrived in 1948 you could have two men, both of them with very severe-looking pulmonary changes in their X-rays, and one would be

[15] Hart P D, Aslett E A. (1942) *Chronic Pulmonary Disease in South Wales Coalminers.* A. Report by the Committee on Industrial Pulmonary Disease. B. Medical survey by P D'Arcy Hart and E A Aslett; C. Pathological report by T H Belt with assistance from A A Ferris. Medical Research Council Special Report 243. London: HMSO. See also note 5 and Figures 2 to 4 on page 5. Mining practices are explained in the Medical Survey, 2–31.

[16] Professor Owen Wade wrote: 'Stalls about 20 feet wide were cut into the coalface with headings about 3 feet wide between each stall to hold up the roof. With this work there would have been low concentrations of coal dust. But when power-driven drills and coal cutters were introduced the dust produced in the confined area of a mine corridor was such that it was hard to see anyone more than a few feet away.' Note on draft transcript, 2 April 2002.

very modestly disabled and the other would be very profoundly disabled. One study looked at men in three age groups: those around the age of 35, around the age of 45, and around the age of 55. Each age group had ten men with no evidence of pneumoconiosis and ten men divided among four groups of increasingly severe X-ray changes of pneumoconiosis, the worst group having progressive massive fibrosis (PMF). As age increased, the disability related to any given degree of X-ray change increased, even in normal subjects with no evidence of pneumoconiosis the lung function tests deteriorated and disability increased. Some young people with very severe X-ray changes are not as disabled as some of the older people with less severe-looking pulmonary disease.[17]

It was Archie Cochrane's conviction that the total population of any colliery be identified and when we went to visit a mine, whether it was in the Rhondda or Gwaun-cae-gurwen, or the Monmouthshire field, we should interview and X-ray every man who was there. An enormous amount of work went into preparation beforehand. All of us in the unit were made to visit the colliery and meet the miners. A series of lectures was arranged. Any ability I have as a lecturer was, I am sure, because I had to go and speak in pubs, or clubs as they call them, because the pubs were shut on Sunday.

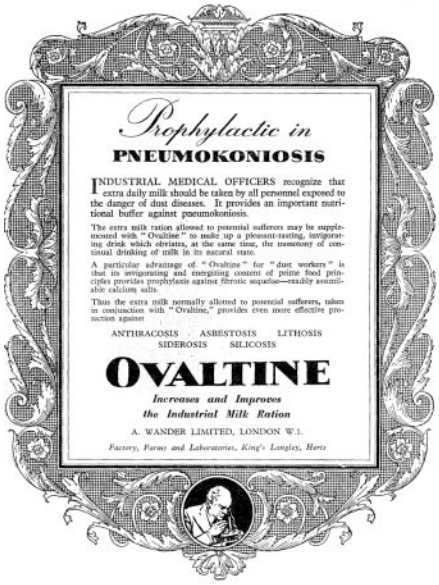
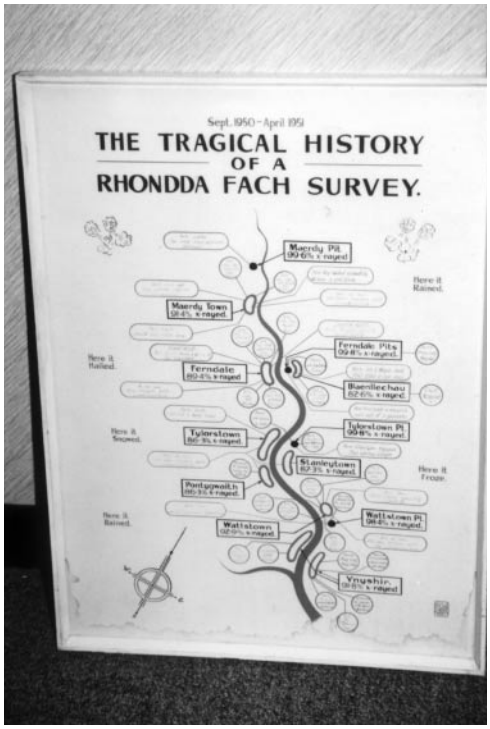


Figure 11: Advertisement in 1949 *Postgraduate Medical Journal*. Reproduced with permission of the BMJ Publishing Group.

Sir Christopher Booth: In Welsh?

Wade: Yes. Pubs shut on Sunday in Wales, therefore all miners belong to clubs, which opened on Sunday. But it didn't matter which day of the week, the procedure was always the same. The presiding chairman would introduce you, and you went up and explained to them what pneumoconiosis was, how it affected them, and why it was necessary for us to see every man in that colliery – 80 per cent wasn't good enough, 90 per cent wasn't good enough, 95 per cent wasn't good enough. We wanted to see every man. As a consequence of this,

[17] Fletcher C M, Mann K J, Davies I, Cochrane A L, Gilson J C, Hugh-Jones P. (1949) A classification of radiographic appearances in coalminers' pneumoconiosis. *Journal of the Faculty of Radiology* **1**: 40–60.



Figures 12 and 13: From a collection of PRU publicity posters, the Cochrane Archive (ALC/3/4/3i–iv).

when we did do the survey, you'd see big heavy miners carrying the youngsters out in order to get them X-rayed. They were so insistent that everybody should be X-rayed. I think it was part of Archie [Cochrane]'s genius that he saw this was very important.[18]

It was pretty arduous. You used to go out to a pub, usually there were chaps wandering up and down and beer coming in from the hatches, and I'd give my talk. As soon as I had finished, there would be men leaping up saying, 'How is it, Dr Wade, that me and my brother always worked at the same coalface, and when we went for chest X-ray, both of us went together on the same test, and he gets certified by the Silicosis Medical Board and I didn't?' You had to use language that was understood by the miners. I said, 'Well, it's like this, it isn't the amount of dust in your lung, it's the amount of scarring that's caused by that dust. You all know that if your hand is burnt badly, how the scars restricts the movement of the hand, well, it is the same with the dust scarring in the lung. It is the scarring that matters and you can't use a scarred lung as well as a normal lung, you see.' Questions like this would go on for about three-quarters of an hour, and the chairman would close the meeting, to my great relief. He would then invite the lecturer into his office and give him a pint of beer. Inevitably there were some men who wanted to consult you privately, another half-hour to three-quarters of an hour of a sort of out-patients clinic. You didn't get any more than a glass of beer, of course, but it was added interest. For me, it was a wonderful introduction to epidemiological research.

The final comment that I would like to make is the enormous contribution to the work of the unit that was made by the late Peter Oldham. At this time, in the 1940s, very few doctors and very few people outside the MRC and a few research units knew very much about statistics. Peter Oldham made a tremendous impact on

[18] See Cochrane A L, Cox J G, Jarman T F. (1952) Pulmonary tuberculosis in the Rhondda Fach: an interim report of a survey of a mining community. *British Medical Journal* **i**: 843–853. Cochrane A L, Miall W E, Clarke W G, Jarman T F, Jonathan G, Moore F. (1956) Factors influencing the radiological attack rate of progressive massive fibrosis. ibid. **ii**: 93–99. Cochrane A L. (1962) The attack rate of progressive massive fibrosis. *British Journal of Industrial Medicine* **19**: 52–64.

all members of the PRU – certainly on me. I learnt about means, standard deviations, coefficients of correlation, and analyses of variance. I wasn't the only one. There were many others working at the unit and were influenced by Peter, and this must have had a wide effect on teaching and medical students and others, in our profession and related fields – another example of the influence of the work of the Pneumoconiosis Research Unit.

Figure 14: Residents of Rhoose Farm House, 1958. L to R: Peter Oldham, Joan Kilpatrick, Martin Wright holding his son, Sheila Wright, Stewart Kilpatrick, Archie Cochrane, Mrs and Mr Barlow (housekeeper and butler), and non residents, Bill Briscoe and Mrs Briscoe. Seated: Pauline Oldham with Harriet and Rosemary Barlow.

Doll: Thank you very much for that wonderful introductory account of conditions at that time. Now who else? Have we got anyone else here who remembers that early period?

Professor Stewart Kilpatrick: I shall be brief because I am neither an epidemiologist nor a physiologist. I went first of all to the PRU in 1952 in the days of Charles Fletcher and John Gilson. It was a very stimulating environment, and I enjoyed it very much. I then realized that of all the other fields in medicine I hadn't recognized there was epidemiology with Archie Cochrane. We used to go out in the evenings as Owen [Wade] has said, up into the valleys, to talk in the pubs, to go down the mines, to do all sorts of things. It was interesting, it was exciting and for me entirely different. Archie was an incredible character. I was privileged to live in his house at Rhoose and those of you who visited him there will probably remember a very elegant house and a very beautiful garden, with servants and people who washed your car in the morning and all that sort of thing. I remember very clearly my engagement party was held in Archie's house and Bill Foreman, who was a physician superintendent at Sully [Hospital], came up to me and said, 'I really can't see why you are leaving all this to get married'.

I learnt a great deal from Archie. I think one of Archie's great strengths was, as Owen [Wade] was saying too, that he introduced the concept of defined populations that has never been surpassed. The other incredible thing about Archie I think was that he had no personal ambition. He was a scientist, he was interested in finding things out, but he hated working things out. I

was concerned at various levels with Archie over the years in the studies of dust disease, anaemia, hypertension, and all the other things that were done both in the Vale of Glamorgan and in Leigh and in Staveley.[19] It was an exciting, interesting and pleasant time. And, like Owen too, I learnt a great deal about statistics from Peter Oldham, who was an incredible chap who thoroughly enjoyed statistical work and all that sort of thing.

Figure 15: Dr Michael Burr and Dr Peter Oldham, Seminar Room at 4 Richmond Road, *c.* 1980.

Archie, as you heard, became David Davies Professor of Tuberculosis, but in 1969 he couldn't stand academic working and left. For my sins, I succeeded him in the chair. I am afraid that I enjoyed it, but then I was a clinician and a teacher, rather than an epidemiologist, but I am entirely and sincerely grateful for all the training and experience that I had at the Pneumoconiosis Research Unit (PRU) and at the Epidemiological Research Unit (ERU). They were never to be forgotten and I am very grateful.

Booth: But why Cochrane? What was his background before he went to Wales?

Kilpatrick: Who's the most recent reader of his autobiography?[20] I think the background essentially was that he was a radical person, he was a thinker, he was a double-first at Cambridge, and therefore was intellectually very bright, he had experience of tuberculosis, particularly in the prisoner of war camps where he did a great deal of very good work and even did some primitive controlled trials at that time. He then went to America for a year to study tuberculosis. I think it was the background of that and the fact that he was a very wide-ranged thinking person that attracted him to the PRU. I hope that answers your question.

Professor George Davey Smith: I was just going to say it shows the open mindedness of the [selection]

[19] Higgins I T T, Cochrane A L, Gilson J C, Wood C H. (1959) Population studies of chronic respiratory disease. A comparison of miners, foundryworkers, and others in Staveley, Derbyshire. *British Journal of Industrial Medicine* **16**: 255–268. The respiratory symptoms questionnaire appears as an appendix.

[20] Cochrane A L with Max Blythe. (1989) *One Man's Medicine: An autobiography of Professor Archie Cochrane.* London: British Medical Journal.

procedures, because the only publication on his CV at that time was a paper in the *International Journal of Psychoanalysis* in 1934 on the death instinct.[21] One wonders today what the MRC would make of someone who turned up with a 16-year-old paper on the death instinct.

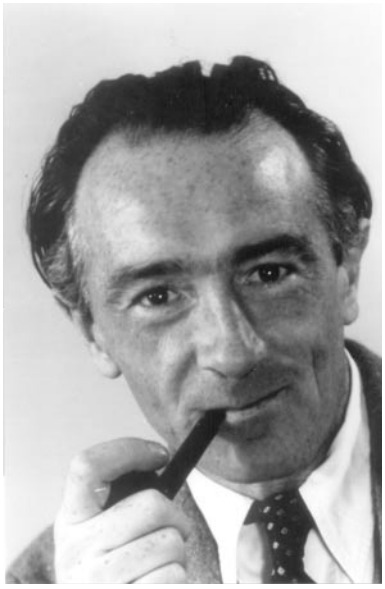


Figure 16: Professor Archie Cochrane, aged 51, 1960.

Dr Peter Elwood: Can I comment on this high response that Archie achieved? Some of it we used to call Cochrane units and a survey with a 96 per cent response rate would be one Cochrane unit and we would try to increase the number of Cochrane units. One of the ways that Archie used to stimulate and challenge us was he would come up to a survey towards the end in his Jaguar car and he would go to the reception desk and he would ask for the bundle of cards for refusals, the visiting cards for refusals. He would take the bundle and he would say, 'I'll do some of them'. He'd go out and he'd park his Jaguar car very prominently outside the house of the first, or the second, or the third, persuade one man to come. He would drive that man into the survey, see him through the procedure or whatever it was, and then say to the rest of us, 'I'll run this man home, but I have got to go, you finish off the rest.' This was one of the ways that he used to challenge us, 'No difficulty, I'll drop this man off without any difficulty'. No matter how many he had tried, he always brought in one.

Doll: Perhaps we ought to record how they did get the last 5 per cent in one mine, and that was after having discussed with the trade union representative and being told that the only way to ensure it was by payment, and I think he said it was 2s.6d. [12½p] per man, I can produce them for you. I think that was the sum and Archie had to ask the MRC for that small sum of money, and he brought in the last few per cent by paying the trade union.[22]

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[21] Cochrane A L. (1934) Elie Metschnikoff and his theory of an 'instinct de la mort'. *International Journal of Psychoanalysis* **15**: 1–14.

[22] Professor Stewart Kilpatrick wrote: 'I do not think Archie had anything to do with payment through the working men's union.' Note on draft transcript, 7 August 2000. See MRC Special Reports Series 243, 244 and 250 (note 5 above), published between 1942 and 1945 on work done before Archie Cochrane's return from the war. See also page 11.

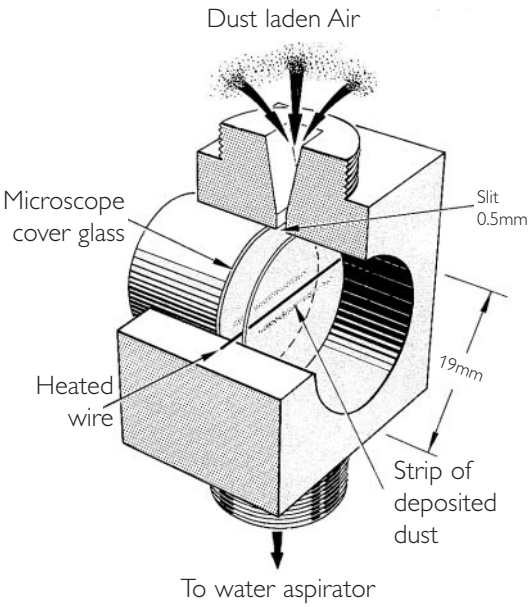

Figure 17: (above) A thermal precipitator used for sampling the concentration of airborne dust, designed by the National Coal Board, being checked by members of the PRU, 1940s, (below) Sampling head.

Wade: Archie never admitted that. I can never remember any payments of that sort in any of the collieries we visited when I was at the unit. Because of the preliminary work, which Archie insisted that we do, we had no difficulty in getting full cooperation from the miners.

One of the problems in our surveys was that we never knew the names of the men working underground. When you went to a pit to X-ray the miners when they finished work, we had the lamp number. When a miner went underground he picked up his lamp from the lamp room and the person in charge of the lamp room knew which lamps were underground.[23]

Dr Julian Tudor Hart: I do want to come in because of this question about the high response rate and the miners and the unions. It really is quite important. I am very surprised about the 2s.6d. story. Perhaps it's true, although it doesn't fit in with anything that I have ever seen or heard. I am very surprised at that story, but certainly what was much more important was not the last 3 per cent, but the first 97 per cent, and the reason we had the first 97 per cent was certainly because Archie had got round the National Union of Miners (NUM), which was a very important force in south Wales at that time, and if Dai Dan Evans had not been persuaded that this was in the interests of the miners, and that it wasn't only for the cause of humanity – which he actually cared quite a lot about – but also that it also met the immediate needs of the miners and their families, nothing ever would have happened. You would have had a 3 per cent response rate, instead of a 97 per cent response, or whatever it was. I think this is very important, because the fact that in the descendants of the original Caerphilly population originating from those days,[24] you are still getting 85 per cent response rates now in heroin-ridden valleys that are completely demoralized compared with those days and the NUM now doesn't exist. That is an extraordinary feat and I don't think will be very easily sustained or repeated.

[23] For a photograph of a lamp room, see note 20, illustration 9, following page 142.

[24] Caerphilly population, see details of cohort study on page 79.

Elwood: Can I comment on Archie and the randomized controlled trial, because I think Archie had an enormous international effect in stimulating people to do randomized controlled trials and of course he later stimulated Iain Chalmers to set up the first Cochrane Centre based on the overviews of randomized controlled trials.[25] Archie was very quick to confess that he had never done a randomized controlled trial but he stimulated everyone in the unit to think in those terms, it was almost a religion at the unit, and many, many others did randomized controlled trials. But Archie did publish a delightful paper that I am sure most people are aware of. 'My first, worst, and most successful clinical trial'[26] described his experience in the prisoner of war camp with famine oedema. His output measurement was the buckets of urine that were carried out from the different wards. I would just like to tell a little fact about that. Archie talked about it occasionally to us in the unit, but I asked him if he would address a meeting. I had arranged a conference on some topic, and I invited all the speakers and a few key people to a dinner the evening before, and when I did this I usually asked somebody to give a talk on something to entertain the guests after their dinner. I asked Archie on one occasion would he tell us about his experiences in the prisoner of war camp and about this controlled trial, and he agreed with very great reluctance. As he told the story and spoke about the horrific conditions in the prisoner of war camp he almost broke down emotionally. He had very great difficulty in finishing the story, but afterwards he came and thanked me. He said, 'You have helped me to get over that difficulty and I am glad you did it'. Very shortly after that he wrote it up and it was published in the *British Medical Journal*,[27] but that was the only controlled trial that he did and he was very quick to confess he never himself did a randomized controlled trial.

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[25] Chalmers I, Sackett D, Silagy C. (1997) The Cochrane collaboration, in Maynard A, Chalmers I. (eds) (1997) note 14, 231–249. The Cochrane Centre was opened in Oxford in 1992. For further details, see www.cochrane.org/cochrane/ccbroch.htm#CC (visited 1 October 2002).

[26] Cochrane A L. (1984) Sickness in Salonica: my first, worst, and most successful clinical trial. *British Medical Journal* **289**: 1726–1727.

[27] See note 26. See also note 20, 46–115.

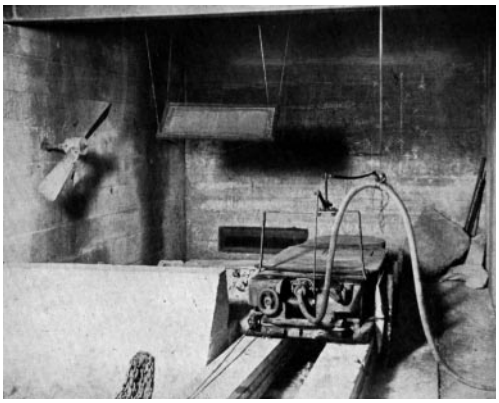

Figure 18: Mechanical coalcutter, 1930s.

Tudor Hart: Could I just add something to that? I first met Archie in 1946 – I think I had just got out of the Army. I don't know when he got back from the war, as it was very difficult, people got held up for a long time. On the whole, prisoners of war got back quicker, but I imagine he got back in 1945. This was really quite close to his coming home and I went as a student to a meeting of the Socialist Health Association, which was the Socialist Medical Association[28] in those days, somewhere in west London, and Archie was the speaker. He was telling us all about his experiences as a prisoner of war, and what was striking about this, it made a tremendous impression on me, I really remember it very well and I have forgotten most things from that time, but he described it in a quite different way than he ever did in anything that he has written, although perhaps not quite so differently from what Peter is remembering. And I had the same impression that this was a cathartic experience for him to talk about it. The biggest messages out of it were first of all the degradation that the prisoners were subjected to as soon as they were taken from Crete to Salonica, where they were systematically terrorized by the Germans, everyone had diarrhoea and so they were going all the time to the latrines to shit and the Germans would toss in hand grenades, just randomly, from time to time. They had a hospital of some sort, with a staircase with windows along the staircase, and as health personnel and patients were taken up and down these Salonica stairs, again randomly from time to time they were sniped at and shot as they went up and down these stairs. This was happening in this reception area in Salonica before the prisoners were dispersed to their destinations.[29] The big point that Archie made was how every nationality and racial group was given a place in a hierarchy, a pecking order with the Americans at the top and the British immediately after the Americans, and then all the way down to Poles and then finally Russians. This also is a perception of order and Archie was interested in the ordering of things. I

[28] See, for example, Stewart J. (1999) *The Battle for Health: A political history of the Socialist Medical Association, 1930–1951*. Aldershot: Ashgate.

[29] Cochrane A L. (1945) The medical officer as prisoner in Germany. *Lancet* **ii**: 411. *idem* (1945) Tuberculosis among prisoners of war in Germany. *British Medical Journal* **ii**: 656.

think he eventually was glad to forget about all this or at least never to bring it up again. At that time he really did want to talk about it. I think it is difficult for people now to grasp really how different our view of the world is now than it was in the 1950s and the 1960s, and that's part of the whole bundle that we are talking about.

Figure 19: Sir Austin Bradford Hill (1897–1991).

Booth: I just have a comment and a question that relates to Archie Cochrane and his reaction to his very painful experiences during the war. There's a very interesting interview which some of you may have seen with Archie Cochrane at the Royal College of Physicians collection of videotapes of individuals.[30] There's no question he just broke down completely on that videotape and cried when he talked about these awful experiences in Macedonia, I think it was. It certainly made an enormous impression upon him.

My question was who were the people at the MRC who supported this unit? Because no unit survives within the MRC unless it's got good referees who are saying, 'This is good work' and so on and have made quinquennial reviews, obviously there are some very important people. My question really is to try to see if there was any link between Bradford Hill's position in epidemiology in the country at that time and what the unit was doing, because I know he had a very close relationship with Sir Harold Himsworth, in fact Himsworth got him elected as the first non-medical Fellow of the Royal College of Physicians [1963], so one wonders the extent to which other people in this field were in fact influencing the MRC at that time?

Dr Joan Faulkner: I am really not sure. Certainly Sir Austin Bradford Hill supported this unit and others in similar field, but going back before Himsworth, Sir Edward Mellanby was very interested in setting up the units with a social aspect and I think Sir Harold envisaged that. A lot of the units, like toxicology, pneumoconiosis, social medicine, were set up during

[30] A videotape interview with Archie Cochrane by Dr Max Blythe, held at the Royal College of Physicians of London (VTR RCP/OP 12). See also Cochrane biographical note on page 131 and the Oxford Brookes University Medical Sciences Video Archive, www.brookes.ac.uk/schools/bms/medical/history.html (visited 1 October 2001). A transcription of the interview is held by the Medical Film and Audio Collections of the Wellcome Library, London.

Figure 20: Dr Stewart Kilpatrick, late 1960s.
© Bassano and Vandyk Studios.

Mellanby's time[31] and I think Sir Harold had the same sympathetic attitude towards research that was going to be of immediate value to people as well as to themselves.

Booth: Let me just add one other point. I entirely agree with that point about the MRC and Mellanby. Mellanby tried to set up this unit following negotiations with the MRC and the government of the day, particularly the Department of Mines, I forget what it was, but it was a government department much interested in the question of what was going on in the mines. And Mellanby set up a subcommittee under the chairmanship of Richard Schilling,[32] to identify a chairman or a director of a unit in pneumoconiosis, and Richard Schilling told me that he went back to Mellanby and said, 'I am terribly sorry we cannot identify anybody'. The following week he was called to see Mellanby, who said 'I've got the very chap, Morley Fletcher's boy, he knows nothing about pneumoconiosis'.

Faulkner: I am extremely grateful for what Chris has just said, because I recall sitting in the tea place at the London School of Hygiene where the MRC was housed at that time,[33] because its building had been blitzed, it wasn't bombed, but it was blown up, and a colleague said to me, 'Mellanby is interviewing Charles Fletcher. You want to watch when he comes out, he's the most beautiful thing you have ever seen in your life'. Because he was interviewing people in those days and at that time, as I have said before, Mellanby was asking, 'Would you like to do so and so?'

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[31] For details of the establishment of MRC units, see Thomson A L. (1975) *Half a Century of Medical Research,* vol. 2. *The programme of the Medical Research Council (UK)*. London: MRC, 18–19, 352–370.

[32] Professor Richard Schilling was Secretary of the Industrial Health Research Board of the Medical Research Council from 1942 to 1946.

[33] The Medical Research Council was evacuated to the London School of Hygiene in 1939, and returned in 1946 to the building in Old Queen Street, Westminster, that had been their headquarters since 1928. They moved to Park Crescent, London, in 1961. See Thomson A L. (1973) *Half a Century of Medical Research,* vol. 1. *Origins and policy of the Medical Research Council (UK)*. London: MRC, 236.

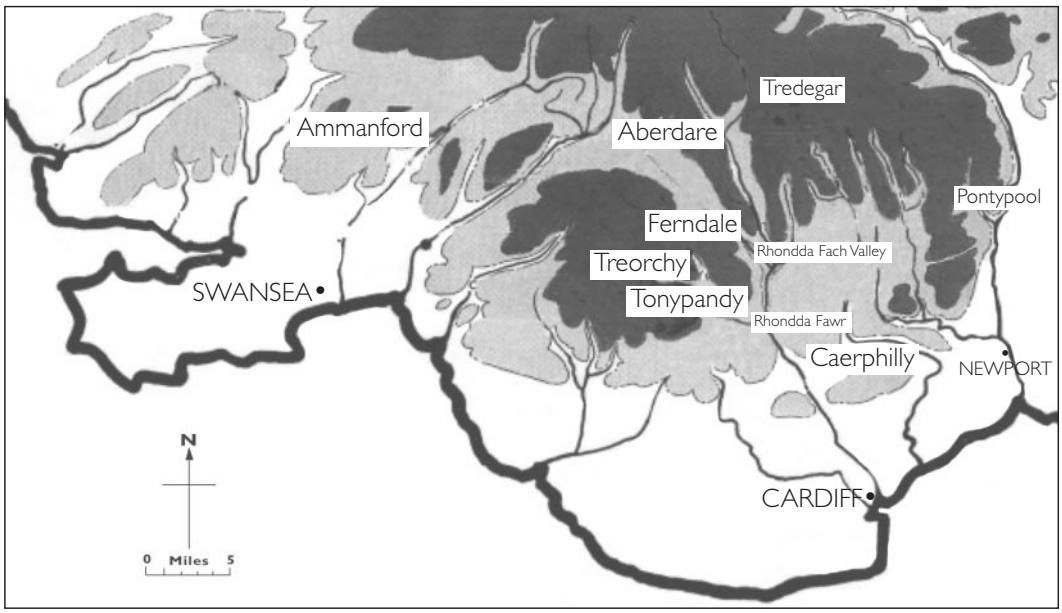

Figure 21: South Wales.

Doll: Of course, there was a social medicine unit set up at that time too, under Jerry Morris.[34]

Booth: At the Central Middlesex.[35]

Kilpatrick: Again, Charles Fletcher, when he was appointed, he felt he had been posted to some outlandish part of Wales, had never really been there, didn't really understand it, and would only accept the job provided he could have unlimited visits back to London to the various scientific societies.

Doll: Unfortunately we haven't got Bill Miall here, but I would like to read something that he has written. It's quite a long account of his work at the unit and his association with Archie.[36]

I think that brings us into the phase in which the epidemiological group had broken away and developed into a new unit.

Figure 22: Dr Bill Miall, 1958.

[34] See Thomson A L. (1975), note 31, pages 93–96, 185–188, 359. See also Paffenbarger R S Jr, Blair S N, Lee I. (2001) A history of physical activity, cardiovascular health and longevity: the scientific contributions of Jeremy N Morris, DSc DPH, FRCP. *International Journal of Epidemiology* **30**: 1184–1192. Loughlin K. (2001) Epidemiology, social medicine and public health. A celebration of the 90th birthday of Professor J N Morris. ibid.: 1198–1199.

[35] See Thomson A L. (1975) note 31, for details of Jerry Morris's unit.

[36] See extracts on page 33. See also note 55. Dr Bill Miall's letter will be deposited along with the records of this meeting in Archives and Manuscripts, Wellcome Library, London.

Booth: I think Charles Fletcher always used to make the case that it was the unit work that showed the importance of observer error[37] and that was something that was not accepted in clinical medicine. I mean the average chap would tap out the heart and that was it. I remember meeting Evan Bedford on one occasion and telling him about some famous man and he said, 'Yes, I once examined his heart, absolutely true'. But, that's all he had examined.

Wade: There is another member of the unit that no one has mentioned and that's Chris Wagner. He came from South Africa and was a big influence. He was the pathologist and certainly influenced both Peter Elmes and me, because a lot of the work on asbestos troubles with the shipyards that we did in Belfast was stimulated by Chris Wagner. I never worked with him, because I left long before he came. I don't know whether anybody else remembers him.

Figure 23: Miner working in a cramped position, 1940s.

Doll: Chris Wagner was invited to this meeting, but unfortunately couldn't come.[38] Would anyone like to comment on Chris Wagner's work? His initial work had been done outside the unit, but he did develop it to a very great extent in the unit.

Kilpatrick: I can say a little bit about Chris Wagner, because I knew him well, I did some work with him. He was instrumental really in the discovery of the relationship between asbestos and mesothelioma.[39] This work was done originally in South Africa and he continued it in the Pneumoconiosis Unit at Llandough Hospital. He did a great deal of other dust work, particularly in relation to asbestos, and he is and was a contributor. I think he probably isn't here today because he hasn't been very well recently.

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[37] Cochrane A L, Chapman P J, Oldham P D. (1951) Observers' errors in taking medical histories. *Lancet* **i**: 1007–1012.

[38] McConnochie K. (2000) Chris Wagner. *Guardian* (1 July 2000), 22. Anonymous. (2000) Christopher Wagner. *Daily Telegraph*, (12 July 2000), 27.

[39] Wagner J C, Sleggs C A, Marchand P. (1960) Diffuse pleural mesothelioma and asbestos exposure in the North Western Cape province. *British Journal of Industrial Medicine* **17**: 260–271.

Doll: He was not actually a member of the Epidemiology Unit.

Kilpatrick: No, he was a member of the Pneumoconiosis Unit, not the Epidemiology Unit.

Dr Sheila Howarth: There was another lady down in south Wales. I don't know whether she impinged on the activities of the Epidemiology Unit, namely one Alice Stewart.[40]

Elwood: We all know Alice Stewart and know her work, and have a tremendous admiration for it. The only contact I had was when she was very critical of one of my studies, but otherwise to my knowledge she never had any direct contact.

Doll: She went to Oxford very early, after the war.

Tudor Hart: She [Alice Stewart] preceded the PRU. She came down with the first sort of scouting forays in south Wales with Philip D'Arcy Hart. She worked on what happened to miners and so on.

Howarth: She was actually there when Charles Fletcher was the Director of PRU.

Dr Hugh Thomas: Yes, we have actually got a list of all the reprints of PRU from when it started in 1945, and then of publications from about 1948 onwards,[41] and she was involved in some of the early publications, partly linked to dust disease, but also to tuberculosis, which was her interest there.

Wade: There are three other members of the PRU no one else has spoken very much about. Philip Hugh-Jones played a big part in the physiological work of the unit. During the war he worked with the

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[40] See, for example, Greene G. (1999) *The Woman Who Knew Too Much: Alice Stewart and the secrets of radiation*. Ann Arbor, MI: University of Michigan Press. See also Stewart A, Davies I, Dowsett L, Morrell F H, Pierce J W. (1948) Pneumoconiosis of coalminers. A study of the disease after exposure to dust has ceased. *British Journal of Industrial Medicine* **5**: 120–134. PRU paper no. 3.

[41] The Unit was disbanded in September 1985. A complete list of publications produced by the MRC Pneumoconiosis Unit is held by the Medical Research Council and the MRC Unit, Llandough Hospital, Cardiff. See Cotes J E. (2000) Medical Research Council Pneumoconiosis Research Unit, 1945–1985: A short history and tribute. *Occupational Medicine* **50**: 440–449.

Figure 24: Dr John Gilson (1912–89).

Ministry of Defence. He almost died in a tank carrier in Lulworth Cove, where had been testing the carbon monoxide concentrations in the air in the tank-carrying vessels when all the tank engines were started, as would be the case when the vessel approach the landing beach in Normandy. In the vessel he was inspecting the big fans to carry away the tank exhaust which had been installed the wrong way round so that the carbon monoxide was routed back into the tank carrier. Philip developed methods of measuring the transfer of gas from alveoli of the lung to the blood in the pulmonary capillaries using carbon monoxide in very dilute concentration. Philip was a very enthusiastic if rather excitable man who contributed a lot to the unit.

John Gilson had worked at Farnborough for the RAF during the war on a number of physiological problems and was older than most of the rest of us. He gave enormous support to Charles Fletcher in dealing with mine owners, trades union officers and later on with the Coal Board. You will remember when Charles Fletcher left the unit to return to London, it was John Gilson who became the Director of the unit.

One other comment that is relevant to our survey work was a problem with chest X-rays. Now I forget the name of our radiographer [Mr Clarke], but two chest X-rays could be taken of the same patient and one would look hazy showing evidence of early pneumoconiosis and the other would be much clearer and normal. The reason for this was that the definition of a radiograph is related to the number of peaks of alternating voltage that occur during the very short exposure time. Our radiographer modified the X-ray machines so that the current always switched in at exactly the same phase of the alternating current, so that in identical exposure times there would be the same number of peaks of current voltage. This was important because so much of the work of the unit depended on an accurate assessment of the degree of radiological change caused by pneumoconiosis.[42]

[42] Clarke W G. (1952) Essential characteristics and suggested improvements in mass radiography technique. *Bollettino Schermografico* **5**: 1–34. *idem* (1953) A new automatic X-ray exposure control, the Iontomat (Siemens). *Radiography* **19**: 171–178.

Philip Hugh-Jones

After the war I decided, having got that far in medicine, I ought to do the Membership [of the Royal College of Physicians], the MRCP, and to go back and do some house jobs. I had only done one house job. And I went to Sir Edward Mellanby, who was the Secretary of the Medical Research Council, and I said that I would like now to stop doing this sort of research and do some other junior hospital doctors jobs and so do the Membership examination. Mellanby's reaction was extraordinary. It was as if I had said something obscene. He jumped in the air and banged the desk and said, 'Wasting your time as a good researcher doing these stupid exams, no.' And he opened a drawer and flung medals across the desk and said, 'You will get things like that if you get on and do some research, you just go down to Cardiff, we have got a big problem on there'. I think I just said, 'Yes, sir'. This was how I first met Charles Fletcher and went to the Pneumoconiosis Research Unit.

One thing Charles Fletcher did was to keep everybody keen. He was a wonderful PR man with the miners; he couldn't have been better, and he was very concerned, as a clinician, for their welfare, as his subsequent work with relationships between doctors and patients showed.[43] *He was a very warm human sort of person, very bright and very competent. I don't think Charles was a scientist as such, I don't think I ever think of him as that, but he was a very surprising person because, as you know, he had been up at Eton and was a Cambridge rowing blue at Trinity, was to have been the great consultant, and the last person one would think would ever have gone down to south Wales. He packed up all that and took on this job on Mellanby's recommendation. But he did it with superb skill and created a very, very good team. He was a delightful person and he acquired very good people working around him. Everybody had a great loyalty to Charles.*

Charles Fletcher employed John Gilson and me as combined clinicians and physiologists. John Gilson had been doing similar work to mine, but with the RAF. Similarly I think as a civilian in the RAF, but doing physiological work on the design of clothing and all sorts of odds and ends. John Gilson and I were faced with the problem of assessing the breathlessness of the south Wales coal miners. The generally accepted and only lung function test then available was essentially the 'vital capacity', which had been going since 1875, that sort of time. I have forgotten when Hutchinson published his paper,[44] *but it was in general use in medicine. We set about trying to do other things. First of all, we looked at the possibility of measuring the total volume of gas in the lungs, which at that time the Americans were doing by getting patients to breathe oxygen in and out of their lungs and measuring the rate at which the nitrogen originally in the air in the lungs was washed out. From that you could calculate what the volume in the air must have been by the serial dilution of the nitrogen. It was a cumbersome and tedious method and we decided to use a closed-circuit method instead. In this patients re-breathed round a close-circuit spirometer with their carbon dioxide being removed by a cylinder containing caustic soda. Oxygen, with a small amount of helium, was in the gas apparatus. We then measured the change in concentration of helium using a catherometer which did the measurement by the cooling ability of the helium. John Gilson made the catherometer himself, which I thought was very impressive. He coiled up a fine platinum wire and put it into a metal block so that the helium concentration was then measured by its cooling. We did publish that method separately, as a way of measuring lung capacity.*[45] *I don't know whether we were the first to do that or not, but it was an early way of doing it, and has since become one standard method.*

Having done that, we then decided that we would like to know how much miners could pant as one way of assessing their breathlessness relative to their chest X-ray. We used a rather cumbersome method, which was the only way we knew, of getting them to pant in and out of one of those big Douglas bags,[46] *but using a valve just to catch only the expired gas. Thus, we measured how much air they got out of their lungs when they were panting as hard as they could over 15 seconds (maximum voluntary ventilation). We used to say, 'Go on pant, pant'. It was*

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[43] See also Fletcher C M. (1973) *Communication in Medicine*. London: Nuffield Provincial Hospitals Trust.

[44] Hutchinson J. (1846) On the capacity of the lungs, and on the respiratory functions, with a view of establishing a precise and easy method of detecting disease by the spirometer. *Medico-chirurgical Transactions* **29**: 137–252.

[45] Gilson J C, Hugh-Jones P. (1949) The measurement of the total lung volume and breathing capacity. *Clinical Science* **7**: 185–216.

[46] Douglas C G. (1911) A method for determining the total respiratory exchange in man. *Journal of Physiology* **42**: xvii–xviii. See Figure 25.

almost as tiring for us as for the miners. We suddenly realized that one breath was very like another and if we measured one breath and multiplied it by a rate factor, we ought to be able to get the right answer for their maximum possible ventilation more easily, but it never correlated well with the Douglas bag results. It was left to a very bright Frenchman called Robert Tiffeneau,[47] *who realized that the actual stroke volume of the breath is not the vital capacity, it's much less than that, and is a fixed proportion of about 70 per cent of the vital capacity in normal subjects (he called his test the Tiffeneau index, I think). We subsequently renamed it the forced expired volume.*[48] *It is most extraordinary that this has become such a universal test, though it was Tiffeneau's bright idea and not ours. It was rather like when I worked in the army, I went to a textbook, thinking I could find out how much a man could push on a pedal, for example at maximum effort, and finding no information, but had to set about finding out.*[49]

But, we did not think of a good way of measuring gas transfer into the lungs until Professor F J W Roughton, the grand old man of physiology, came to visit us, and said, 'Oh, you want to use carbon monoxide'. That was a very bright idea, because Marie Krogh had done it for measuring the diffusion capacity or diffusion constant of the lungs.[50] *In fact, various people came to see us and thought it a wonderful idea so published it before us, which was rather irritating. That too has become a standard method of measuring the gas transfer in the lungs.*

Stemming from the applied work we did, three essential parameters of lung function were developed in the PRU at that time and have all been in use subsequently – the measurement of the total lung volume and its subdivisions, maximum breathing capacity, and carbon monoxide transfer. The Medical Research Council published the results of our research over about five years in a Green book,[51] *so called because official HMSO reports had green covers at that time. We realized during the preparation of that report that if you measure vital capacity you were measuring partly what was measured as maximum breathing capacity now derived from the FEV [forced expiratory volume]. None of these tests were pure tests, but they interacted with the others. We couldn't think how to sort out this difficulty, but Peter Oldham, who was the unit statistician then, produced a model of a factor analysis which appears in the Green book. This analysis showed the extent these different tests of lung function measured*

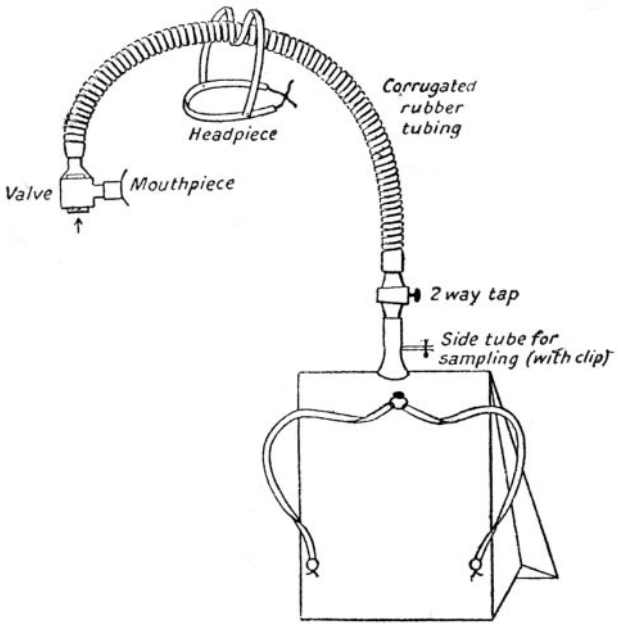

Figure 25: Douglas bag, *c.* 1930.

[47] Yernault J C. (1997) The birth and development of the forced expiratory manoeuvre: a tribute to Robert Tiffeneau (1910–61). *European Respiratory Journal* **10**: 2704–2710.

[48] Gandevia B, Hugh-Jones P. (1957) Terminology for measurements of ventilation capacity: a report to the Thoracic Society. *Thorax* **12**: 290–293.

[49] See, for example, Hugh-Jones P. (1946–47) The effect of limb position in seated subjects on their ability to utilize the maximum contractile force on the limb muscles. *Journal of Physiology* **105**: 332–334.

[50] Krogh M. (1915) The diffusion of gases through the lungs of man. *Journal of Physiology* **49**: 271–300. See also Schmidt-Nielsen B. (1995) *August and Marie Krogh: Lives in science.* New York and Oxford: American Physiological Society, 106–108.

[51] Gilson J C, Hugh-Jones P, in collaboration with P D Oldham and F Meade. (1955) *Lung Function in Coalworkers' Pneumoconiosis.* Medical Research Council Special Report 290. London: HMSO.

the same thing, and to what extent each was unique. Computers weren't around at that time and I remember sitting for hours in front of a Friedman electric calculator, doing multiple correlation coefficients, between all the tests on all the subjects. It took me days on end, not just hours. At the end of the war I wrote to the Medical Research Council asking for a Friedman calculator because of the research work I was going to do. I had to put in a special grant for it before it was approved. Now I could go to Woolworths and buy an equivalent calculator for about £3. It's staggering what has changed in electronics.

Charles Fletcher and I, and John Gilson, also had charge of the ward for the miners, and although I didn't have my Membership [of the Royal College of Physicians] at that time, I was promoted to somebody of clinical competence, but then went to Oxford and by incredible good fortune got the Membership from a junior registrar job.

Stewart Kilpatrick

John Gilson, a very able director who succeeded Charles Fletcher, was more mechanically interested at that time, I suppose, in as much as he constructed and made a dishwasher machine for his invalid wife from first principles, a very able person. His wife had been ill, but she got better and is still surviving, living in Devon. He was interested in research, particularly in respiratory function, and published a number of papers on that. He was a very stimulating person with whom to work, and the combination of Charles Fletcher, John Gilson, Archie Cochrane and Peter Oldham, was an environment in which I was involved for some three or four years and I learned a great deal. I hope I contributed to a certain extent as well, but I learnt a lot.

I first met Peter Oldham, funnily enough, with Kingsley Amis, the author, in a pub in Cowbridge. And then I went to stay with Archie Cochrane and Peter Oldham was a resident there at that time. He was an extremely able statistician, a very pleasant person, and a very interesting one, tried to help people to do research and did, but was quite prepared to put people off if he didn't think it was a reasonable thing to do. A very pleasant companion, he died about ten years ago now. These trials were instigated by Bradford Hill, who was one of Peter Oldham's mentors.

Jeffrey Chapman

I joined the Pneumoconiosis Unit in the early days of the field surveys, and the first field survey we did up at Haig Colliery, Whitehaven, Cumberland, in 1949. My introduction to pneumoconiosis was late on a spring evening when it was hissing down with rain and I'd waited at the station at Whitehaven for a very long time to contact two people whom I didn't know but had heard about. One was John Gilson and the other was Archie Cochrane and after waiting there for hours the most decrepid prewar Vauxhall came along and in it there were two immense figures. John Gilson you may recall was an absolutely huge man. They were both drenched in the prewar car, the hood had broken down and the rain was hissing in. We then drove at what I can only describe as a rate of knots out to St Bees, near the Sellafield Nuclear Station, where they were staying. I had just come back from Australia and then we started the work up at Whitehaven where, I think, that wonderful thing, observer error, tended to be born. And out of that came a paper by Archie Cochrane which showed that if you were a smoker, as many of us were in those days, then of the people that you were interviewing to take histories from, you saw more smokers if you were a smoker, whereas if you weren't a smoker, you didn't see as many smokers. I think that was the sort of beginnings of observer error.[52] *I think the first British demonstration of it was somebody who asked a series of distinguished cardiologists in London to percuss with their fingers the left-hand border of the heart, which is something that all good cardiologists count as one of their great skills. I think ten were selected and it was marked on the chest and there were ten different left borders of the heart.*[53]

Bill Miall

So in 1951, ten years after meeting Archie Cochrane in Salonica [in the prison hospital],[54] *I became his assistant in the early days of epidemiology in south Wales. The Pneumoconiosis Research Unit (PRU) was a very impressive place in terms of its staff. Charles Fletcher was its first Director*

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[52] See note 37.

[53] Dr Jeffrey Chapman (1923–2000), formerly a senior administrator at the headquarters of the Medical Research Council, speaking at the Witness Seminar, 'Pneumoconiosis in Coal Workers', 9 November 1994, unpublished. See biographical note on page 130.

[54] See note 20, 61–62.

[from 1945 to 1952] and had collected together a team of people covering a wide spectrum of interests – physicians, physiologists, pathologists, physicists, bioengineers, and statisticians. John Gilson was Deputy Director. John had been at Cambridge with Charles and during the war had been investigating respiratory problems of flying at Farnborough. When Charles resigned the Directorship and went on to be Reader and later Professor of Clinical Epidemiology at the Postgraduate Medical School (later Royal Postgraduate Medical School, Hammersmith Hospital, London) John Gilson took over the unit [until 1976] and was an excellent choice for a post, which required someone with a wide range of interests and expertise. Archie Cochrane came third in the hierarchy at that time. He had also been at Cambridge and may have overlapped with Charles there. Two others playing leading roles were Peter Oldham, an excellent statistician, and Martin Wright, an equally bright pathologist, who was always more interested in bioengineering than in pathology.[55]

Figure 26: Dr Martin Wright (1912–2001).

Stewart Kilpatrick

Archie was a very interesting person. He was an atheist. He was a heavy consumer of cigarettes, he enjoyed a drink, though not in any way excessively, he was very fond of foreign travel, he had a sister, (Helen Stalker, d. 2002), in Galashiels in Scotland. She developed porphyria and Archie Cochrane went up when he heard his sister was ill, and when they made the diagnosis of porphyria he decided he would like to know a bit more about it, so he bought all the books he could on the subject, looked up all the articles on it, and then did a study of his family tree in relation to porphyria,[56] *which took him all over the world, and he got specimens from all over the world. He was a great reader, he was a great thinker, he was a very good and meticulous research worker – he enjoyed doing research, but didn't like writing up the research work that he did, he couldn't really be bothered about that. He was fortunate in being of independent financial means. I think that he suddenly realized when his grandfather's will was read out that he never need again fill in the stub of any cheque that he ever issued. Independent financial means, not extravagant, except perhaps in cars: he used to drive a large Jaguar car which he enjoyed very much, and I always remember the second Jaguar he got, he was in Llandough hospital and a girl said, 'I have come to deliver your Jaguar, here are the keys'. He said, 'Thank you very much'. She said, 'Well, aren't you going to go and look at it?' And he said, 'I will see it when I go home'. Completely off-hand in relation to that sort of thing. His house in Rhoose was very pleasant and had a very lovely garden. He didn't know very much about gardening, but was prepared to take advice, some of which he got from my wife. He had a servant and his wife, who looked after them, and looked after the house and garden and the swimming pool, where we used to go and see him.* [See Figure 14] *On occasions he was a slightly selfish man, very critical and could be rude and abrasive if necessary. It didn't worry him. But in some ways he was, I won't say undependable, but slightly problematical. I got on with him very well, because I think we were on the same sort of wavelength, possibly because we were both Scots.*

Figure 27: Archie Cochrane, 1940s.

Sheila Wright

I was terribly disillusioned when I actually met Archie Cochrane. I had heard about this beautiful boy, this very handsome man who went off to the Spanish Civil War, when I worked for Dick Cohen, who had known him as a young man at Cambridge, along with C P Snow, there was a whole lot of them there at the same time. I

[55] Letter from Dr Bill Miall to Dr Tilli Tansey, 15 March 1999.

[56] Rees H A, Goldberg A. Cochrane A L, Williams M J, Donald K W. (1967) Renal haemodialysis in porphyria. *Lancet* **i**: 919–921. Cochrane A L, Goldberg A. (1968) A study of faecal porphyrian levels in a large family. *Annals of Human Genetics* **32**: 195–208.

had this image, then when I met him, his face had fallen in and he'd lost all his teeth as a prisoner of war, though of course they had been replaced. He was terribly haggard, and he looked about 50, though of course he wasn't. Of course, he was tremendously lively.

Philip Hugh-Jones

Just after the 1955 report[57] *on lung function, Dr Martin Wright was appointed to the unit. He almost eclipsed John Gilson in his engineering ability and ideas. He decided that even the measurement of FEV could be improved if one could measure the actual peak gas flow during exhalation instead of a volume related to time. With this idea in mind he designed the peak flow meter.*[58] *That test too has become of almost universal clinical use and later developed into the breathalyser.*[59]

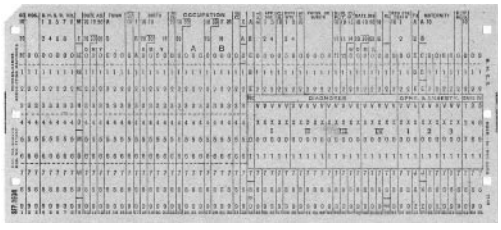
Figure 28: Using a spirometer to measure lung function in the 1950s.

Stewart Kilpatrick

Archie Cochrane's relationship with the miners was particularly good. He was very particular. He worked fairly closely with the National Union of Mineworkers, who were initially a little suspicious of it all, but eventually Archie persuaded about 99 per cent of the people to get X-rayed, history taken, and all the rest of it. And the relationship with Charles Fletcher and the miners was very good. My only regret at that time and subsequently was that the PRU wasn't more closely associated with the Cardiff Medical School, University of Wales College of Medicine. Why this was so, I don't know. I think partly, a lot of the PRU people lived on the west side of Cardiff, whereas the medical school was in the centre of Cardiff, and they didn't particularly want to go into Cardiff, and they had a loyalty to Llandough Hospital, which was perfectly understandable. The other problem that Archie and Charles Fletcher had was that the relationship with Professor Gough was not necessarily very good. He was the Professor of Pathology, an opinionated, very able man, but not an easy man, and he and Archie Cochrane and Charles Fletcher didn't get on very well together, which was a pity. This relationship with Cardiff and local researchers got a little closer when Archie Cochrane and Harold Scarborough, who was Professor of Medicine then, and myself as a research fellow, did some work on anaemia and hypertension and coronary artery disease. So there was a closer relationship at that time.[60]

Bill Miall

I came in when the Little Rhondda [Rhondda Fach, the smaller of the two valleys] had been X-rayed for the first time and the X-raying of the miners and ex-miners in Aberdare valley was still to be done. Archie had recruited a team to help with the survey work. Some, like Gwilym Jonathan, Hugh Bates,



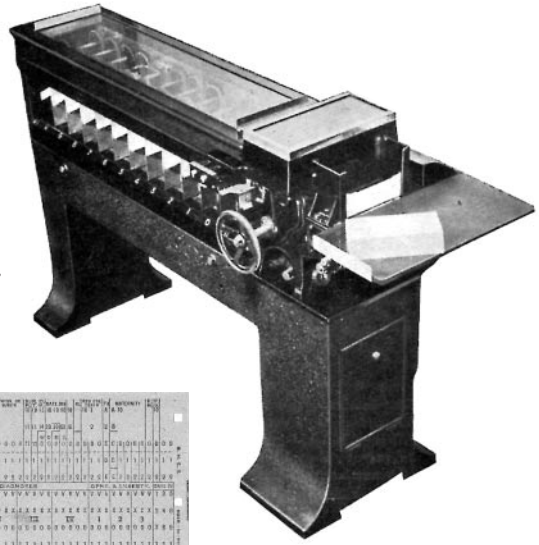


Figure 29: Hollerith card (left) and sorting machine (right), 1940s.

[57] See note 51.

[58] Wright B M, McKerrow C B. (1959) Maximum forced expiratory flow rate as a measure of ventilatory capacity with a description of a new portable instrument for measuring it. *British Medical Journal* **ii**: 1041–1047.

[59] Hugh-Jones P. (2000) Reflections of work of the Medical Research Council Pneumoconiosis Research Unit, 1945–55, manuscript prepared for the interview with Dr Andy Ness, 5 July 2000. Quote from pages 8–9.

[60] Branch R A, Clark G W, Cochrane A L, Jones J H, Scarborough H. (1971) Incidence of uraemia and requirements for maintenance haemodialysis. *British Medical Journal* **i**: 249–254.

and Tom Benjamin,[61] *were ex-miners living in and well known in the valleys; their role was particularly to persuade folk to collaborate, usually by visiting them at home. Response rates of less than 90 per cent were not acceptable. Others were chosen for different skills. Fred Moore, for example, was a male nurse who was obsessionally accurate and meticulous about keeping orderly records. At that time Archie and I were the only medics.*

From the early 1950s we recognized the potential of the Rhondda Fach as a field for epidemiology research into other conditions which could be accurately defined and reproducibly measured. Having the Rhondda Fach population defined by private census and on Hollerith cards – the nearest approach to computerization in those days – we were in a position to obtain representative samples of the general population and become involved with research into other conditions. This was in the very earliest days of chronic disease epidemiology as it is currently known.

Philip Hugh-Jones

Dr Archie Cochrane joined the team shortly after Alice Stewart had left. Cochrane had a very penetrating mind and was meticulous in his work and, as an epidemiologist, he pointed out that it was important to study not only those who came up to hospital complaining of breathlessness and had an X-ray taken (when it was assumed that their breathlessness was related to the spots on the X-ray, if present), but also those still working in the mines, as some of them might well have the same spots on their X-rays, but had no breathlessness. This was found to be the case.[62]

Bill Miall

It was very non-medical work in a way. I was busy learning how to read pneumoconiosis in chest X-rays, interviewing miners, Welsh miners, and my job largely was, apart from the X-ray reading, going round the houses, interviewing those who had abnormal X-rays, or who ought to be recommended to go for compensation. I was doing that sort of thing for a year or two and then we were increasingly realizing that the facility of having a general population all censused [counted and their data recorded] on what were then Hollerith cards, or punch cards. It was an opportunity to look at other diseases apart from miners' chest diseases.

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[61] According to Archie Cochrane, Tom Benjamin was a watch repairer. See note 20, 165–166.

[62] See note 17. The two valleys scheme (later Rhondda Fach scheme) was a long-term study of the relationship between tuberculous infectivity in the community and the development of complicated pneumoconiosis (progressive massive fibrosis) in coal miners. Starting in 1949 the entire population of one valley, the Rhondda Fach, was X-rayed, and those with TB were treated. The number of new cases of complicated pneumoconiosis after 1949 could be compared with those in a neighbouring valley where no control measure had been taken. See Cochrane A L, Fletcher C B, Gilson J C, Hugh-Jones P. (1951) The role of periodic examination in the prevention of coalworkers pneumoconiosis. *British Journal of Industrial Medicine* **8**: 53–61. See also Cochrane A L, Cox J G, Jarman T F. (1952), note 18.

1954–58 Blood pressure and respiratory surveys[63]

Bill Miall

I was keen to start studies of the factors influencing blood pressure, and we consulted with George Pickering and Fraser Roberts about them. It was about this time that a heated debate was starting between Robert Platt and George Pickering about the nature of essential hypertension.[64] *Platt took the view that essential hypertension was a discrete entity transmitted by a single gene and therefore due to one specific biochemical disorder which you either had or you didn't have. Pickering believed it represented no more than the upper end of a continuous distribution of blood pressure and was influenced by many factors, of which one was polygenic inheritance. One of the difficulties faced by both Platt and Pickering was that they had to start their studies with hospital populations and chose to study patients selected as having blood pressures above some arbitrarily selected threshold. We, with access to more representative populations, were in a position to study people, and their families, who were not selected in that sort of way. This is not the place to describe the findings in details, but in general this and later studies strongly supported Pickering rather than Platt.*[65]

Julian Tudor Hart

I think for archive there was also an element that was political and social, also to do with the 1945 election and postwar expectations in Britain, which were very different from America. In America the Cold War was already going on. Very early on, the Cold War stopped the liberal social programme in America, which never since has managed to get round to providing a health service for the whole of the American people. It all got tied up with hostility to social ways of doing things, collective ways of doing things. Already collectivism was equated with communism, and they were looking for individual solutions for everything. We weren't like that. So I think that had an effect early on. It is of course true that if you focus on pneumoconiosis as a topic, then you are going to go to an industrial working class area with a militant political tradition. For me, I saw in Pickering's work an opportunity to apply my political ideas to clinical medicine as a medical student; my politics was more important than medicine, and it still is. Politics, in the sense of changing the world, is an overall context within which medicine operates, so in that sense it is more important. I had wanted a way to be a useful person, politically changing the world while actually doing something useful with my hands. I always wanted to be a GP. I assumed I could never get to be a consultant anyway, because I assumed that you would get shut out from that area of work if you were political. Quite correctly too, people like me who did try to become consultants, for example Ian Gilliland and Michael Tempest, had a terrible time getting jobs. I had very primitive ideas about being a kind of tribune of the people.

Stewart Kilpatrick

I think again one of Archie's strengths was that he had carefully defined populations which he used. These have not been quite so strictly viewed recently, but by and large people in Wales have got to know about studies and surveys, and I think that on the whole are prepared to take part in them. At one time somebody said look can you extrapolate from the studies in Wales to the rest of England, the rest of the country, and I think the answer is yes. We did studies in hypertension, anaemia, and other things in the Rhondda, in the Vale of Glamorgan, in Wensleydale, in Annan, in the south of Scotland, and in parts of the Midlands, Staveley, and on the whole these were reasonably comparable, so I think the studies should continue in Wales, and I would like to think that they would.

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[63] For example, see Cochrane A L, Miall W E. (1956) The epidemiology of chronic disease in South Wales. *Proceedings of the Royal Society of Medicine* **49**: 261–262. Cochrane A L, Miall W E, Clarke W G. (1956) Results of a chest X-ray survey in the Vale of Glamorgan: a study of an agricultural community. *Tubercle* **37**: 417–425.

[64] Swales J D. (ed.) (1985) *Platt versus Pickering: An episode in recent medical history.* London: Keynes Press for the British Medical Association.

[65] See note 20. See also Oldham P D, Pickering G, Fraser Roberts J A, Sowry G S C. (1960) The nature of essential hypertension. *Lancet* **i**: 1085–1093.

Chart 1: Studies done by the MRC Epidemiology Unit (South Wales), 1954–1990

1954–58	Respiratory surveys – Rhondda; Leigh, Lancashire; Annandale, Vale of Glamorgan, Staveley, including the first ECG surveys
1954–56	Blood pressure surveys – Rhondda and Vale of Glamorgan
1963–65	Glaucoma surveys
1964	Industrial workers' studies – flax, asbestos, steel and slate workers
1964–69	Iron deficiency anaemia studies – observational and intervention studies
1965–70	Headache and migraine studies
1965–70	Renal disease
1966	Respiratory survey: Staveley follow-up
1969–79	Aspirin trials
1972–79	Barry–Caerphilly child growth study
1973	Asthma studies
1976–78	School milk supplementation study
1976–82	Environmental lead studies
1979–ongoing	Caerphilly cohort study
1983–89	Diet and reinfarction trial (DART)

Table circulated at the Witness Seminar, 23 March 1999

THE MRC EPIDEMIOLOGICAL RESEARCH UNIT (SOUTH WALES), 1960–74

Doll: I think it's about time we moved on to the second phase of epidemiological work there and this was when Archie broke away and had his own epidemiological research unit.

Dr Jean Weddell: I joined, well I didn't join, but I started working at the unit in 1964. It was when I was [a patient] in the Orthopaedic Hospital, Cardiff. I was asked to help to code the Vale of Glamorgan blood pressure study. I then joined the unit, working as a junior research assistant on cervical cytology, the whole city survey, which at that time was really making history.[66] I then got involved in the randomized controlled trial of treatment for moderately raised blood pressure. Then David Bainton and I did pilot surveys of medical care given to stroke patients, and I did some work on varicose veins.[67] The unit was great fun. By then its reputation was established. We had a lot of visitors from all over the world, it was really exciting, very stimulating and great fun.

Booth: One can understand why they wanted to recruit you [Jean Weddell], because you had a pretty good reputation by then.

Doll: There was quite a lot of discussion with the MRC as to whether or not he should have a epidemiological unit. I think Dr Faulkner will remember a good deal about how this happened if I might ask her to contribute?

Figure 30: Number 4 Richmond Road, Cardiff, the home of the Epidemiology Unit from 1962 until it returned to Llandough Hospital, Penarth, Cardiff, in 1990. Archie Cochrane's epidemiology course run for the Welsh National School of Medicine had vacated the house in favour of more appropriate space at Sully Hospital.

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[66] The city of Cardiff had a population of 350 000 and was considered by Hubert Campbell, Archie's statistician and later Professor of Medical Statistics at the Welsh National School of Medicine, to be a suitable sample for the cervical cytology survey, funded by the MRC and the Department of Health, and headed by Dr Joyce Landsman in 1965. See note 20, 202–204. Dr Jean Weddell wrote: 'I worked on the cervical cytology study, then on anaemia in Wales, followed by a randomized controlled trial of two treatments for varicose veins, surgery and injection compression treatment. This included comparative costing of the two methods by David Piachaud. I also carried out a pilot study of care given to stroke patients. I worked first in Cardiff and then at St Thomas' Hospital, London, on the two-centre study of control of moderately raised blood pressure.' Letter to Mrs Lois Reynolds, 15 March 2000.

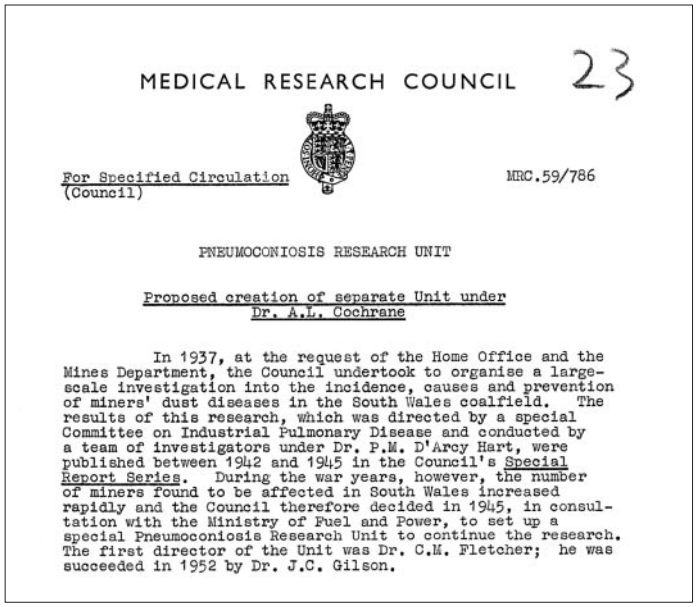
[67] See page 51 for details of moderately raised blood pressure. See also, for example, Piachaud D, Weddell J M. (1972) The economics of treating varicose veins. *International Journal of Epidemiology* **1**: 287–294. Chant A D H, Jones H O, Weddell J M. (1972) Varicose veins: a comparison of surgery and injection/compression sclerotherapy. *Lancet* **ii**: 1188–1191. Piachaud D, Weddell J M. (1972) Cost of treating varicose veins. ibid: 1191–1192.

The Council of the MRC agreed in April 1960 that the epidemiological work of the Pneumoconiosis Research Unit (PRU) should be developed in a separate unit under the direction of Professor A L Cochrane.

The PRU remained at Llandough Hospital, Penarth, Cardiff, and the Epidemiological Research Unit (ERU, later EU) was expected to move to a new £25 000 building at the Sully Chest Hospital, Penarth, but remained temporarily at Llandough until 1962 when it moved to 4 Richmond Road, Cardiff. On the scientific staff were Archie Cochrane, Ian Higgins and Bill Miall, with a seven-member survey team and clerical staff. Additional staff included an epidemiologist, a sociologist, a statistician, a chemist, a photographer, and two clerical staff, sharing the Administrative Officer, the radiographic and mobile equipment and staff with the PRU.[68]

Faulkner: I remember going down [to south Wales] after Archie had got the chair and this was a good enough reason for separating off a unit to cover the epidemiological aspects of what was going on in the PRU then. There was also a certain amount of friction between Archie and John Gilson. They were very, very different people – equivocal mercurial Archie, and a rather staid John Gilson. I loved them both dearly, but the move took a certain amount of organizing, because of Archie's nature and the demands he made when the Council agreed to do it. First of all, he wanted a huge building put up and I forget how many staff, 33 or 40 or something like that, and it was eventually whittled down. He thought Dick Cohen and I were particularly mean administrators. But I think that's really all I have to say about that time when the change was taking place.[69]

Wade: Can I just ask how many staff did he finish up with?



MEDICAL RESEARCH COUNCIL 23

For Specified Circulation (Council)

MRC.59/786

PNEUMOCONIOSIS RESEARCH UNIT

Proposed creation of separate Unit under Dr. A.L. Cochrane

In 1937, at the request of the Home Office and the Mines Department, the Council undertook to organise a large-scale investigation into the incidence, causes and prevention of miners' dust diseases in the South Wales coalfield. The results of this research, which was directed by a special Committee on Industrial Pulmonary Disease and conducted by a team of investigators under Dr. P.M. D'Arcy Hart, were published between 1942 and 1945 in the Council's Special Report Series. During the war years, however, the number of miners found to be affected in South Wales increased rapidly and the Council therefore decided in 1945, in consultation with the Ministry of Fuel and Power, to set up a special Pneumoconiosis Research Unit to continue the research. The first director of the Unit was Dr. C.M. Fletcher; he was succeeded in 1952 by Dr. J.C. Gilson.

Figure 31: MRC 59, 16 October 1959. PRO FD7/1046.

[68] Separate unit proposed in MRC 59/786 above, confirmed by the Council on 22 April 1960, having considered 'Proposed Epidemiological Research Unit', MRC 60/541, 13 April 1960. See also Minute from Dr J Faulkner to Sir Harold Himsworth, 18 November 1959, PRO FD7/1046. The unit's proposed staffing was for two scientific and technical staff, five administrators, including one health visitor. See note 20, 176–178; 187–189. See also Jones H. (1989) Industrial health research under the MRC, in Austoker J, Bryder L. (eds) *Historical Perspectives on the Role of the MRC: Essays in the history of the Medical Research Council of the United Kingdom and its predecessor, the Medical Research Committee, 1913–1953*. Oxford: Oxford University Press, 137–161.

[69] See extracts, notes 107 and 108, on page 66.

Faulkner: I think it was about 15, I am not sure, but it is in one of the MRC annual reports. Ian Higgins, Archie himself, and Bill Miall were the three medically-qualified people,[70] and then there were a whole group of interviewers and secretarial staff. There was a lot of discussion about a pathologist, because there were things like blood lipids to be done and Archie wanted a first-class research biochemist and when we asked him why he wanted this – because it wasn't really a job for such a person; what kind of stimulus was this chap going to get? – he replied, 'Well, it will be much nicer for me to have someone like that to talk to'.

Doll: Good enough reason. It actually did need in those days a pretty good biochemist to get reliable results which were repeatable on a separate occasion. Well, I think, Julian Tudor Hart, you were in a pretty early part of that period, I wonder whether you would like to give us some more reminiscences?

Tudor Hart: Well I got there just before they moved to Richmond Road and they were still at the PRU. I wasn't aware of these frictions, they all seemed absolutely weird people to me. That was 1961. Rationing ended as far as I remember in 1951 something like that,[71] but they still weren't having any butter on their bread or jam for tea. You just had this dry choice of white or brown stale bread and some red stuff that you could put on it. All the rest of the staff, this terrific team that Archie gathered round (who ought to be better represented here today I think) all those people ate proper human food, post-rationing food in another room, or another part of the library. But all these mean doctors, because that's what it was, it was just meanness, sat there eating their bread and 'jam', they wouldn't even have marge, and I asked John Gilson, because he seemed the most approachable and normal person, why this was so and he said, 'I don't know. Ian,

[70] Bill Miall and Ian Higgins were Honorary Assistant Directors to Archie Cochrane, before Miall went to direct the Epidemiological Research Unit (Jamaica). See Committee of Privy Council for Medical Research. (1962) *Report of the Medical Research Council for the Year 1960–1961*. Cmnd 1783. London: HMSO, 12. By 1965, the Annual Report listed eight scientific staff and one part-time administrator as senior staff, with A L Cochrane as Honorary Director and W E Miall as Honorary Assistant Director. The Epidemiological Research Unit (Jamaica) had six scientific staff, one of which was honorary part-time and the other a visiting worker. *idem* (1965) *Report of the Medical Research Council, October 1963 – March 1965*. Cmnd 2787. London: HMSO, 159–160.

[71] Food rationing ended in Britain in 1954.

why don't we have butter?' and Ian Higgins said, 'Oh, I don't know. Archie, why don't we have butter?' So they all muttered like this, 'Why didn't they have butter?' None of them could actually bring themselves to say that it was because they had to pay for it. They had to pay for it themselves, it wasn't provided by the National Health Service. I can't remember what the upshot of it was. I suppose eventually somebody must have bought butter. So it was that kind of odd place and an awful lot of time was wasted, a lot of it by me, but because of Archie's demands to be talked to and to have entertaining people around. He did do an awful lot of that and I must admit I felt that there was an atmosphere, there was a certain amount of aristocratic dilettantism about research altogether in those days.

Figure 32: Receptionist during an anaemia survey, *c.* 1968.

In fact, how I got the job seemed to be rather like that. There weren't any interviews or anything like that, so I remained rather an onlooker and a bystander, not being terribly good at the job anyway and finding it a great disappointment, until I could work on my own hypotheses later on. It was a very good school, I think, for people entering epidemiology because it was at that time such early days of the discipline and nearly all the people associated with it there ended up being very important people and very interesting people. But I didn't actually find the work enormously stimulating if you still had a big interest in clinical medicine. I think it's much more interesting nowadays. There are much better chances now for people genuinely to have both interests, really to be clinical epidemiologists, than at that time. There was within the unit quite a lot of reciprocated hostility to clinicians, I think that was part of the problem between John Gilson and Archie. I don't think it was just personalities, I think it was that the PRU people were becoming more clinical and actually had people on the wards and so on. Archie could be very scathing about clinicians. Sometimes I think excessively so. That was one of the reasons I left. They were a good gang of people that Archie recruited, but they weren't all

miners. Tom Benjamin had never been a miner, I am not sure whether Gwilym [Jonathan][72] had ever been a miner, and certainly Fred Moore had never been a miner, but they were all very plebian folk, they were very streetwise. Doctors in general were extremely ignorant of the real reasons that prompt people to do things or not do things in those days, much more so than now. And Archie was very cunning in employing people who were right at the centre of gossip machines and had a really streetwise approach to getting cooperation. He wasn't a terribly good team leader because he was often rather divisive in his approach to managing a team, but he was very, very good at perceiving talent in people without qualifications or education. Other people who ought to be here are Bill Clarke, whom Owen [Wade] was trying to remember in the X-ray department, and Sheila Wright. Archie got a lot of very high-quality supporting staff of all kinds. He did infect everybody with obsessional attitudes to high-quality data. You couldn't live with yourself if you didn't do things very, very well for Archie. Some of that was

Figure 33: Gwilym Jonathan in full voice in the Rhondda in the late 1960s.

Figure 34: Fieldwork team for a survey of anaemia, migraine and urinary tract infections led by Peter Elwood and Estlin Waters (both standing, back row, far right), *c.* 1968.

[72] See note 20, 165–166.

1963–1965
Glaucoma surveys[73]

Estlin Waters

Peter Graham was the consulant ophthalmologist. I was very much a field worker. The survey involved measuring intraocular pressures and the detection of glaucoma. I wasn't really very involved in that study and I wasn't involved in the writing up. This survey was one of the many Archie Cochrane was involved with to establish whether screening for various diseases was scientifically justified.

Fred Moore too. A terrible old woman, but exactly what you needed in an epidemiology unit.

Doll: Well, I think Peter Elwood came in about then. Would you like to say something?

Elwood: I joined Archie Cochrane in 1963. I would like to pay tribute to John Pemberton. I learnt much of my epidemiology from John Pemberton and I gained a tremendous enthusiasm for epidemiology from him. I had been in general practice, I did a diploma in public health and was exposed to epidemiology during that, and a name that came up very frequently was Archie Cochrane. I joined a research team with John Pemberton and worked on flax byssinosis[74] and we did what I think was a very fine survey and then we followed it up 20 years later. But John Pemberton suggested I should go over and see Archie Cochrane, and see if there was a chance of working with him.

I had also done, as a separate study from the main task, a survey of anaemia in women in Belfast.[75] I picked a random sample from the electoral roll and I achieved 97 per cent in that survey and I know that that was one of the things that endeared me to Archie Cochrane. We differed on many things, particularly on religious beliefs. We had a delightful two or three days. He took me round everywhere. I stayed in his home and I had a delightful time and I know it was because of the work that I'd done with John Pemberton and this high response rate that we had had, both in the flax survey, which was an industrial population, but perhaps more particularly in the random sample, a representative

[73] See, for example, Graham P A. (1966) Screening for chronic glaucoma. *Proceedings of the Royal Society of Medicine* **59**: 1215–1220. *idem* (1969) The definition of pre-glaucoma. A prospective study. *Transactions of the Ophthalmological Society UK* **88**: 153–165. *idem* (1972) Epidemiology of simple glaucoma and ocular hypertension. *British Journal of Ophthalmology* **56**: 223–229.

[74] Elwood P C, Pemberton J, Merrett J D, Carey G C R, McAulay I R. (1965) Byssinosis and other respiratory symptoms in flax workers in Northern Ireland. *British Journal of Industrial Medicine* **22**: 27–37. McAulay I R, Carey G C, Merrett J D, McClarin R H, Elwood P C, Pemberton J. (1965) A survey of dust concentrations in flax mills in Northern Ireland. ibid. **22**: 305–310. See also note 111, and Elwood P C, McAuley I R, McLarin R H, Pemberton J, Carey G C R, Merrett J D. (1966) Prevalence of byssinosis and dust levels in flax preparers in Northern Ireland. ibid. **23**: 188–193.

[75] Elwood P C. (1964) Distribution of haemoglobin level, packed cell volume, and mean corpuscular haemoglobin concentration in women in the community. *British Journal of Preventive and Social Medicine* **18**: 81–87.

Figure 35: Fieldwork team for a large survey of more than 5000 women in the Rhondda Fach conducted by Peter Elwood (far right), Ferndale Clinic, *c.* 1965, with Fred Moore (second row, far left), Estlin Waters (back row, middle), and Janie Hughes (front row, third from right). See note 75.

sample, of the women in Belfast. So I came over to Archie Cochrane shortly after that three-day interview and one of the tasks I was asked to pursue was looking at iron deficiency anaemia. I arrived at the unit when the glaucoma survey was at its height [1963–65] and I think we should talk about that a little, because Archie was immensely proud of the way he was able to stimulate the ophthalmic people in Cardiff to do a survey. He did a magnificent survey, the Ferndale glaucoma survey,[76] which is still talked about, still quoted by ophthalmologists. I think that Archie was tremendously proud of it and rightly so, because it was one of the first very big excursions out of the ivory tower into clinical practice and they looked at a number of conditions, but chiefly glaucoma and they then went on with a randomized controlled trial. This got into various difficulties, but was a very fine effort and Archie was immensely proud of it. One of the things that I valued Archie for was he allowed us to do our thing and get on with it and he never seemed to have much team work within the unit, he was very happy with me doing work on anaemia and later on other things and with the glaucoma team upstairs in the attic. We rarely met, even when on survey in the Rhondda, I was seeing women in connection with anaemia, and the other team was

[76] Hollows F C, Graham P A. (1966) The Ferndale glaucoma survey. In Hunt L B. (ed.) *Glaucoma: Epidemiology, early diagnosis and some aspects of treatment.* Proceedings of a symposium held at the Royal College of Surgeons of England, London, June 1965. Edinburgh: Livingstone, 24–44. *idem* A critical review of methods of detecting glaucoma. ibid. 103–115. See also Graham P A, Hollows F C. (1964) Sources of variation in tonometry. *Transactions of the Ophthalmological Society of the UK* **84**: 597–613.

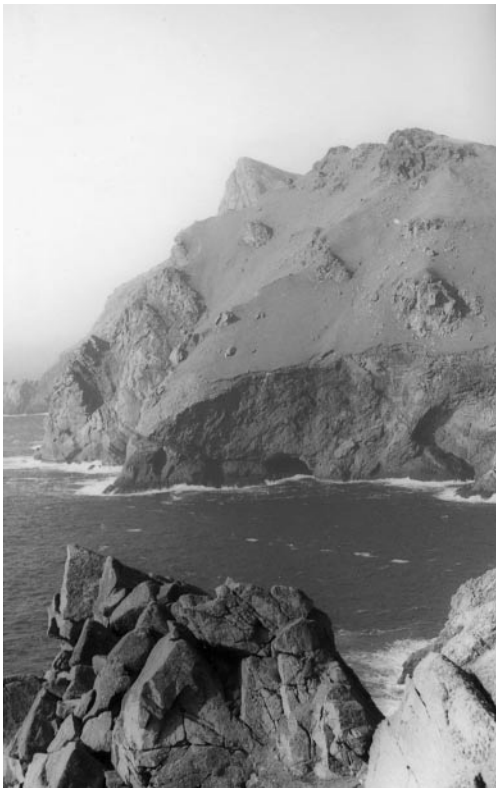


Figure 36: The south-west coast of Hirta, the main island in the St Kilda group, where cliffs tower to over 1100 feet and many wrens *(Troglodytes troglodytes hirtensis)* nest among the boulders.

working on glaucoma. We termed the glaucoma team the 'B' team, which rather irritated Archie.

Professor Estlin Waters: After I completed my house jobs in February 1960 my next job was as a Senior House Officer at the Pneumoconiosis Unit. I took that job because there was supposed to be, by reputation, lots of time to read and work for other things; it wasn't a very busy clinical job. My job was to clinically care for the patients in the pneumoconiosis ward, although I was employed by the Medical Research Council. The thing I remember most from that seven months is the tea breaks. I can't remember whether there was butter on the menu or not, but I can remember the very stimulating conversations between John Gilson, Archie Cochrane, and Peter Oldham, particularly between Archie Cochrane and Peter Oldham. Those tea breaks, I suppose, changed my career, because I hadn't planned to go into research, but five years later I was offered a post in the Epidemiology Research Unit by Archie Cochrane. My credentials for that were probably even less than Archie's credentials for his job. At least he had had a paper published in a medical or a psychological journal.[77] My only publications were on seals and birds; I think Archie Cochrane was quite impressed that I got up at dawn for a whole week to count the number of wrens on St Kilda in the Outer Hebrides. I had hardly any experience in medical research when I started at the Epidemiology Unit in July 1965. I found the unit very friendly and was given responsibility at a very early stage, especially considering my lack of research experience. I started off right from the beginning working on a number of different topics with a number of different people. I worked on chest disease with Archie Cochrane himself.[78] Most of my time, especially in the first few years, was spent working with Peter Elwood on all the various aspects of iron deficiency anaemia. I also started some work with the people at the Cardiff Royal Infirmary, particularly Max Sussman and Bill

[77] See note 21.

[78] Professor Estlin Waters wrote: 'Ian Higgins flew over from the USA to supervise the 1966 follow-up study at Staveley, Derbyshire, but I was largely responsible for the day-to-day organization of this survey.' Note on draft transcript, 26 May 2000.

Figure 37: Fieldwork team for another anaemia study conducted by Peter Elwood (far left), Ferndale Clinic, May 1968, with Marion Jones (white top, front row) next to Fred Moore, Janie Hughes (in front row), next to Estlin Waters (far right).

Asscher[79] on urinary tract disease, especially bacteriuria. Peter Elwood suggested that I should develop a subject of my own and very kindly handed over a study that he had just started on headache and migraine.

I worked on migraine throughout my time in the Epidemiological Research Unit until September 1970 and for about the next ten years after I left for Southampton University, but I am very grateful to Peter for all that he did during the time that I was at the unit, but particularly for giving me the encouragement to start this topic on my own. I think this shows that there was no fixed pattern as to how the unit was working at that time. Some of the work was done in cooperation with clinicians and my work on urinary tract disease would be an example of that. Other work was almost entirely confined to people in

[79] Asscher A W, Sussman M, Waters W E, Davis R, Harvard R, Chick S. (1996) Urine as a medium for bacterial growth. *Lancet* **ii**: 1037–1041.

the unit and, as Peter [Elwood] has mentioned, to particular people in the unit.

A number of distinguished visitors came to the unit at about that time.[80] I can remember many of these people and it was an honour and thrill to take them up to the Rhondda to show them around. One of the things I remember was taking them to lunch in a café in the Rhondda Fach called Myrtles. At that time pit-head baths were not universal and when these eminent scientists from around the world came to sit in Myrtles very often they would be joined by miners up from their shift underground, their hands, face and clothes still covered in coal dust. It probably wasn't the sort of visit that they had anywhere else.

Figure 38: Janie Hughes (left) as receptionist in an anaemia survey, *c.* 1966.

Mrs Janie Hughes: I joined the MRC Epidemiological Research Unit in 1964 and, surprising to say, I must have enjoyed the time because I am still working for Dr Elwood now, even though I retired from MRC two years ago. Professor Cochrane was the Director when I joined, but I had very little to do with him. He was popular as an overseas speaker and he entertained us with the things that happened. I must say more things happened to Prof. Cochrane when he was abroad than to anybody else since. He got his passport stolen, he was accosted in lifts, he lost his luggage every single time he went abroad. I have always worked for Dr Elwood and we probably will be working together when we are both on our Zimmers. But we were a very happy unit. I think people are astonished when I say we were like a family, we were really very happily working together. Very recently I have been working part-time for a local health authority and apparently one of their criteria when they asked me to join them was that I was epidemiologically trained (whatever that might mean), and as Dr Tudor Hart said, I did have an interview when I joined, but I wonder now how I ever got the job. I had no training whatsoever in epidemiology or anything to do with medicine, but Dr Elwood was a great encourager as he likes to call it. I didn't call it that at the time, when just

[80] Professor Estlin Waters wrote: 'When travelling, there was a paradox between how little was known about the Epidemiology Unit in Britain and the mention of the unit or Archie Cochrane abroad – at least in the late 1960s and 1970s – was a passport to recognition, even envy. Abroad, it was amazing how many people one met had stayed in Archie's Rhoose home. But I met a selected sample of people!' Note on draft transcript, 26 May 2000.

Figure 39: L to R: Ann Chapman, a haematology technician from the local hospital, Janie Hughes and Estlin Waters above the Rhondda valley during the anaemia study in Rhondda Fawr, 1967.

after I had passed my driving test, I had to drive 40 miles along the coast road to this obscure little place to join a survey team, but I must say I have thanked him every day since. He 'encouraged me' to administer some horrible questionnaires to people, he encouraged me to knock on doors late at night. In those days though people still left their keys in the door – something that doesn't happen these days – and you'd knock on the doors in the Rhondda valleys and they'd just shout, 'Come in'. They all have burglar alarm systems attached to them now. I have had a very, very enjoyable work time and I think I can thank Dr Elwood for most of that.

Professor John Pemberton: We did perhaps benefit in those days from there being an absence of ethical committees. [**From the floor**: We were perfectly ethical.] In another study when we were getting interested in anaemia, Peter [Elwood] and I thought we were going to eliminate hypochromic anaemia from the world by adding iron to bread.[81] We started by persuading the director of the mental hospital to allow us to add iron to the bread of patients in various wards. So some got extra iron and the others who didn't were controls. We went on increasing this iron in the bread until it tasted so bad that we ourselves couldn't eat it.

Wade: One of the interesting differences between survey work with the byssinosis and other asbestosis work that

[81] Elwood P C. (1993) A clinical trial of iron fortified bread. *British Medical Journal* **i**: 224–225.

Peter Elmes and I did in south Wales,[82] and my later work in Belfast was the names. I don't think we realized how difficult it was going to be when surveying miners in south Wales where so many men had names like Jenkins, Jones, Thomas or Williams. Archie solved this by ensuring that every man X-rayed was also photographed holding a board with his X-ray number and his name. When the unit returned four or five years later to re-X-ray that pit, it was possible to identify and radiograph the right Mr Jones. Of course the miners all know each other by Jones 'longtuff' or Jones 'big nose' or some phrase of that sort, but that wasn't very useful to the survey team.

Kilpatrick: I think probably one of Archie's few failings was that he wasn't remotely interested in the career of epidemiology or epidemiologists. He wasn't interested in administration, he wasn't interested in academic medicine, he didn't enjoy the professorship as I told you, he didn't particularly enjoy being president of the Faculty of Community Medicine, and I think this is a great tragedy in a way, he could attract people to his unit, but he didn't see further than giving them any opportunity for further training. This I think was a pity and that was one of his few failings as far as I was concerned.

Doll: Dr Howarth, have you got any comments from the MRC side at all about this work?

Howarth: I don't think really I can contribute on this one, because I had very little to do with the unit during my time in the headquarters office. There is one question that I would like to ask, and that is whether the studies on hypertension in this unit led to controlled trials in the 1960s, just when the new drugs became available for the treatment of hypertension, because it was very strong letters from Archie Cochrane in the unit and from Colin Dollery at Hammersmith, which persuaded the Council to set up the working party, under the Chairmanship of Professor Peart, which carried out the mammoth treatment trial of mild to moderate hypertension, which Bill Miall in his spare

[82] Elmes P C, King T K, Langlands J H, Mackay J A, Wallace W F, Wade O L, Wilson T S. (1965) Value of ampicillin in the hospital treatment of exacerbations of chronic bronchitis. *British Medical Journal* **ii**: 904–908. Elmes P C, Wade O L. (1965) Relationship between exposure to asbestos and pleural malignancy in Belfast. *Annals of the New York Academy of Sciences* **132**: 549–557.

time is probably still analysing.[83] But I really don't know, and it's a question that I would ask from people in the unit, whether in fact there were any such trials, and whether this is what persuaded Archie to write his letter.

Weddell: Yes, we carried out a randomized controlled trial of the control of moderately raised blood pressure.[84] It was a combined trial, combined between the Cardiff unit and the medical unit at St Thomas'. Our numbers were much too small, but the data collected during that trial actually formed the basis of the calculation for the sample size of Bill Miall's subsequent MRC mammoth trial. There was no way we were ever going to get any results at all out of our tiny one, but it did pave the way.

Dr David Tyrrell: I wanted to ask a question and make an observation about the international impact of the unit. I came across the unit in a way first of all when I was in the USA and I met Ed Kass[85] who was starting to become interested in infections of the renal tract and possible relationships with hypertension. He had to base much of his work on patients coming into the hospital in Boston. He amused me really, because he assumed I knew everybody in Great Britain. He said, 'Do you know these people in Wales? There's a man called Bill Miall and he's looking at hypertension in a population'. Later, of course, he actually met and worked with Miall when they did the same sort of thing in Jamaica.[86] I think it was that people who couldn't do them were impressed with the power of studies done on whole populations, and that seemed to me to be something which drew them to study what was being done at the unit and the methods used and so on. I wonder whether I am right in that, because

Figure 40: Stories of iron tablets being fed to the Rhondda sheep are without foundation, despite this offering from Estlin Waters in the late 1960s.

[83] Medical Research Council Working Party. (1985) MRC trial of treatment of mild hypertension: principal results. *British Medical Journal* **291**: 97–104. Miall W E, Greenberg G. (1987) *Mild Hypertension: Is there pressure to treat? An account of the MRC trial.* Medical Research Council Working Party on Mild to Moderate Hypertension. Cambridge: Cambridge University Press.

[84] Barraclough M, Joy M D, MacGregor G A, Foley T H, Lee M R, Rosendorff C, Holland W W, Cranston W I, Rea J N, Saville Sneath J, Webster B, Bainton D, Cochrane A L, Greene J, Kilpatrick G S, Weddell J M, Kilpatrick G S (Mrs), Sweetnam P. (1973) Control of moderately raised blood pressure. Report of a co-operative randomized controlled trial. *British Medical Journal* **iii**: 434–436.

[85] Kass E H, Zinner S H. (1969) Bacteriuria and renal disease. *Journal of Infectious Diseases* **120**: 27–46. Kass E H. (1956) Asymptomatic infections of the urinary tract. *Transactions of the Association of American Physicians* **69**: 56–64. For bibliographic details, see page 133.

[86] See for example, Miall W E, Kass E H, Ling J, Stuart K L. (1962) Factors influencing arterial pressure in the general population in Jamaica. *British Medical Journal* **ii**: 497–506.

it was just an impression that I got. The people who saw the visitors and took them up the Rhondda might be the people who would know what they were really most interested in and about the way the unit ticked.

Doll: Can anyone answer Tyrrell's question?

Wade: There weren't quite so many visitors to the PRU when I was there in the early days. The work that attracted attention later was the system of grading chest X-rays, jointly developed by Archie Cochrane, John Gilson and Peter Oldham.[87] Each chest X-ray was graded by a team of at least three people against 'standard films'. There were four grades: normal, grade 1 pneumoconiosis, grade 2 pneumoconiosis, and progressive massive fibrosis (PMF). The standard films were in demand from all around the world.

Elwood: The iron deficiency studies that John Pemberton mentioned in Belfast[88] led to some questions about the government policy then of adding iron to flour. We found no evidence that the iron was being absorbed and that alarmed the Department of Health (the Ministry of Health at that time), and Dr Bill Berry[89] flew over to Belfast and interviewed us and

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[87] Fletcher C M, Oldham P D. (1949) The problem of consistent radiological diagnosis in coalminers' pneumoconiosis. *British Journal of Industrial Medicine* **6**: 168–183. *idem* (1951) The use of standard films in the radiological diagnosis of coalworkers' pneumoconiosis. ibid. **8**: 138–149. Ministry of Health, Joint Committee. (1952) *Standardization of Radiological Terminology in Pulmonary Disease and Standardization of Technique in Chest Radiography*. Report of a joint committee of the Joint Tuberculosis Council, the Faculty of Radiologists and the Society of Thoracic Surgeons. London: HMSO.

[88] See notes 75 and 81.

[89] Berry W T. (1968) Nutritional aspects of food policy. *Proceedings of the Nutrition Society* **27**: 1–8. Berry W T, Darke S J. (1968) Vitamins in health and disease. *Practitioner* **201**: 305–313. Greaves J P, Berry W T. (1974) Medical, social and economic aspects of assessment of nutritional status. *Bibliotheca Nutritio et Dieta* **20**: 1–9. Dr Peter Elwood wrote: 'Dr Bill Berry was a very good friend and enormously encouraging. He had an interest in all the nutrition work of the unit and very much against the procedures in government departments at that time. He obtained funding from the Ministry of Health for our two-year randomized controlled trial of iron added to bread, also for the trial of the effect of milk on infant growth and nutrition, including bearing the costs of the daily milk tokens given to half the mothers, their infants and their other children, and he provided funding for the school milk trial. The iron-enriched bread randomized controlled trial involved daily deliveries of bread to 300 homes. In order to enhance compliance we gave a 10 per cent discount to the women at intervals. This involved Janie Hughes and Marion Jones visiting the women and giving each a postal order, some for quite sizeable sums of money. A few of the women got wise to this and started purchasing extra bread for friends and neighbours, and keeping the refund themselves. Others got even wiser and refused to pay the bread delivery man, knowing that we would not put in the huge effort into the trial and just let them be lost to the trial. Sure enough, we told the bread firm and the delivery man that they must deliver the bread to these women and we would pay whatever bad debts accrued. When I submitted the accounts and explained this item to Bill Berry he was highly amused. However his accounts department was not amused at all. They had never before handled the item "bad debts" before!' Note on draft transcript, 27 March 2002.

visited various people involved and so on. He was very anxious to find some flaw in our work, because it was government policy to add iron to flour. Shortly after that I left the Belfast unit, but I never lost the contact with Bill Berry. He was head of nutrition within the Ministry of Health and we did a series of studies, paid for in part by the Ministry of Health. It was most unusual in those days for the Department to admit that they didn't know something and to pay us to find the answer, but the sad part was they never paid any attention to the answers that we provided. We did a series of studies, first of all on the absorption of radioactive iron and then a feeding trial in the Rhondda – one of the most ambitious studies I think that the unit ever did – where for two years we had a special bake of bread for 300 women and a little van went up and down the valley supplying the daily bread to 300 homes and we monitored the change in haemoglobin level over the two-year period.[90]

My interest in platelets is a long story, but it started in the middle-to-late 1960s. I became interested in ischaemic heart disease and one of the areas it seemed to me should be opened up was haemostasis, thrombosis, and within that I took a particular interest in platelets. Pathologists, including Michael Davies and others, were showing that in the vast majority of infarcts the head of the thrombus was composed of platelets,[91] so I went to a number of meetings, and I went round some haematology departments, talking to haematologists about how to measure platelets, so that we could set up an epidemiology study with tests of platelet function and see whether those predict ischaemic heart disease events. I couldn't get any tests that we could use in a large long-term study. The one test that I remember discussing in great detail was where one could take a glass slide, score it with emery paper, put a film of blood on, wash the blood off after a few minutes, stain it, and look at the platelets. If the platelets were active, then they had a lot of pseudopodia

[90] Elwood P C, Waters W E. (1969) The vital distinction. *Nutrition Today* **4**: 14–19. Elwood P C, Waters W E, Sweetnam P. (1971) The haematinic effect of iron in flour. *Clinical Science* **40**: 31–37.

[91] See, for example, a recent review of the subject in Flores N A, Sheridan D J. (1994) The pathophysiological role of platelets during myocardial ischaemia. *Cardiovascular Research* **28**: 295–302.

Figure 41: Serge Renaud's mobile laboratory at the Caerphilly Miners' Hospital, 1984–88.

going along these scores from the emery paper. If the platelets were not very active, then they didn't have those pseudopodia. That's not a test that you could do in a field study, but it was many years before we actually had a test that we could use there. I then became interested in publications on aspirin and platelets, and it occurred to me that as a second-best strategy, for an epidemiologist, we could alter platelet function in a number of people and see whether that altered the risk of ischaemic heart disease. So we planned the first aspirin trial and we started admitting patients, as far as I remember in 1968, after their first infarct, to a randomized controlled double-blind trial. Now if I can just make a remark about what happened later. Many years later in our Caerphilly study we did tests of platelet function, and we borrowed a mobile laboratory from Serge Renaud[92] in France. He motored it across, he brought it up to Caerphilly, and the hospital provided hard-standing, and within that mobile laboratory we did very detailed tests of platelet function, using platelet-rich plasma. Ten years later we evaluated those tests and we found that none of them were predictive of ischaemic heart disease. Now we had other tests which were done in a more recent phase of Caerphilly, but I often think back that if I had had my wish as an epidemiologist and I had got tests for platelet function such as those tests done in the mobile caravan, that whole area of research as far as we were concerned would have come to nothing, because none of those tests proved to be predictive of ischaemic heart disease. But fortunately we took up this second-best as I say and we set up a randomized controlled trial of aspirin. Our interest at that time was platelet function, not aspirin. We were using aspirin as a tool in an epidemiological inquiry. The trial ran for, perhaps, a year or 18 months and one day I had a phone call. Archie, by the way,

[92] Renaud S, Dumont E, Godsey F, Suplisson A, Thevenon C. (1979) Platelet functions in relation to dietary fats in farmers from two regions of France. *Thrombosis and Haemostasis* **40**: 518–531. For further work by the unit, see, for example, Elwood P C, Renaud S, Sharp D S, Beswick A D, O'Brien J R, Yarnell J W G. (1991) Ischaemic heart disease and platelet aggregation. The Caerphilly Collaborative Heart Disease Study. *Circulation* **83**: 38–44. Elwood P C, Renaud S, Beswick A D, O'Brien J R, Sweetnam P M. (1998) Platelet aggregation and incident ischaemic heart disease in the Caerphilly cohort. *Heart* **80**: 578–582. Elwood P C, Beswick A, Pickering J, McCarron P, O'Brien J R, Renaud S R, Flower R J. (2001) Platelet tests in the prediction of myocardial infarction and stroke: evidence from the Caerphilly study. *British Journal of Haematology* **113**: 514–520.

always told the story that he took the phone call, but I believe that it was me that took that call, one Saturday morning. Martin Vessey, who had been working with you, Sir Richard, had gone out to the USA to a pharmacological unit with Hershel Jick.[93] They had been looking at unexpected effects of drugs and what they were doing was questioning patients who had come into hospital and on their third or fourth day after admission they questioned them about the drugs they had been taking during the week before coming in, to see if they could spot any harmful associations between drug taking in the week before coming in and conditions they came in with and complications that they developed having come in. In their first analysis, the one thing that stood out like a sore thumb was a negative effect of taking aspirin. The number of patients with myocardial infarction [heart attack] who had taken aspirin in the week before admission was very, very low, their relative risk was about 0.3, suggesting one of two things, and therein lay the dilemma. Either patients who took aspirin in the week before infarction died and didn't get into hospital to be questioned, so aspirin could actually be increasing mortality, or patients who took aspirin didn't get a myocardial infarction to come into hospital. These two alternatives were rather different, but they could both explain the data that had been collected by Hershel Jick and his team. So Martin Vessey told Hershel Jick that there was a randomized controlled trial in south Wales and I took this phone call on a Saturday morning, and I immediately recognized that it was essential that we break our code even though it was very early on in the trial. It was such a dangerous situation to run on and then perhaps find that our aspirin was increasing mortality. We discussed it with a number of people and I think it was then that you became involved, Sir Richard. I think we saw you, or at any rate talked to you, but we decided to break the code. My memory is that there were 11 deaths on placebo and eight deaths on aspirin, and those were trivial numbers, but they

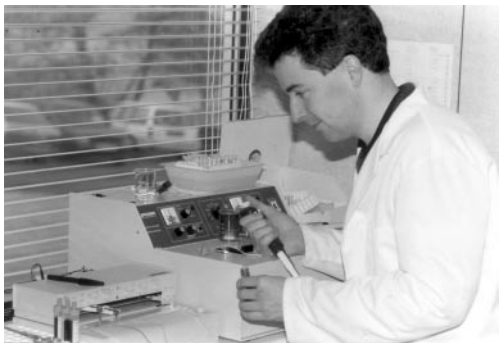

Figure 42: Andrew Beswick doing platelet aggregometry in the Caerphilly study, *c.* 1989. Reproduced by permission of Dr Peter Elwood.

[93] Boston Collaborative Drug Surveillance Programme, co-directed by Hershel Jick and Dennis Slone, started in June 1966. See Jick H, Miettinen O S, Shapiro S, Lewis G P, Siskind V, Slone D. (1970) Comprehensive drug surveillance. *Journal of the American Medical Association* **213**: 1455–1460.

gave us sufficient confidence to feel that we should continue our trial. You [Doll] and others at MRC headquarters were sufficiently excited by these preliminary results and with the potential of aspirin, that we were given extra resources, which was most unusual in the MRC. We set up satellite trials, in Oxford, Manchester, and Swansea. We had already set 1000 as the number to be randomized in that trial, but we did go beyond that and actually randomized 1400 patients and about 18 months later we analysed the results. And the results showed a 24 per cent reduction by aspirin in the number of second infarcts or ischaemic heart disease deaths, and we published that alongside a paper from Hershel Jick's unit in the USA, the observational study showing the deficiency in aspirin taking by myocardial infarction patients. We were somewhat disappointed at the time, because the *British Medical Journal* delayed and delayed before publishing and they published our trial under the heading, 'For debate',[94] but looking back I think that was extremely wise. We learnt, and Archie certainly emphasized, that clinical practice should never be altered because of one trial, however convincing, however exciting. There should be a number of trials, trials should always be replicated, and later of course we think in terms of overviews. But those days were the most exciting.

After we broke the code, I was invited over to National Institutes of Health (NIH), and I met a number of very prominent people in America working on heart disease and I presented the results of our trial, these 11 deaths and eight deaths, and it was so exciting. The Americans set up their trial on the survivors of their coronary drug project, and that was published a few years later. We then set up a second trial and within a few years six trials had been published, and an overview of those by Richard Peto in the *Lancet* was I think the first overview and really paved the way for the tremendous growth of

[94] Elwood P C, Cochrane A L, Burr M L, Sweetnam P M, Welsby E, Hughes S J, Renton R. (1974) For Debate: A randomized controlled trial of acetylsalicylic acid in the secondary prevention of mortality from myocardial infarction. *British Medical Journal* **i**: 436–440. Boston Collaborative Drug Surveillance Program. (1974) Regular aspirin intake and acute myocardial infarction. ibid. 440–443. Jick H, Elwood P C. (1976) Aspirin and myocardial infarction. *American Heart Journal* **91**: 126. Elwood P. (1981) Trial of acetylsalicylic acid in the secondary prevention of mortality from myocardial infarction (letter with results). *British Medical Journal* **282**: 481.

interest in overviews.[95] We went on to conduct two more aspirin trials which perhaps I might talk about later,[96] but I think it is a very exciting situation now, because there have been over 170 trials throughout the world of aspirin and vascular disease and the consistency of those trials is really quite remarkable. If I might just add something of particular interest to me, coronary heart disease is rising in incidence in the Far East and in developing countries and I have been invited out to the Far East and to India on a number of occasions to lecture on heart disease and aspirin, and I can honestly say that aspirin has enriched my career enormously, even in retirement. I would like to pay tribute to Nick Henderson, of the European Aspirin Foundation,[97] who has been enormously encouraging to me personally, and, I think, to you [Doll] and Richard [Peto] in your doctors' trial,[98] but also in spreading the message in the Far East and other countries, that aspirin is an exceedingly beneficial drug and highly cost effective. The drug firms are not interested in it, it makes no profit, and it takes the Aspirin Foundation and a few enthusiasts to get this message across. It really is marvellous to be associated with it.

Doll: This has been one of the major developments in clinical medicine in the last 30 years and we do owe it to a very large extent to the work of Peter Elwood and that unit. The Medical Research Council had an Epidemiological Committee at the time, which I was chairing, and of course other people were aware of the effects of aspirin on platelets and we were asked to consider what we could do to test whether aspirin was of any significant clinical value, and our committee in its wisdom decided that myocardial infarction was too

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[95] Peto R. (1988) Representation of the people? *Lancet* **i**: 1346. For a more recent discussion of aspirin, see Mann C C, Plummer M L. (1991) *The Aspirin Wars: Money, medicine and 100 years of rampant competition.* Boston, MA: Harvard Business School Press, particularly 263–271, 293–310.

[96] See the unit's second aspirin trial, Elwood P C, Sweetnam P M. (1979) Aspirin and secondary mortality after myocardial infarction. *Lancet* **ii**: 1313–1315. See also discussion on page 74.

[97] For example, see Elwood P, Hughes C. (1997) *Aspirin and Cardiovascular Disease*. Cardiff: Centre for Applied Public Health Medicine, University of Wales. Also available on the European Aspirin Foundation website (www.aspirin-foundation.com/mainpage.htm, visited 12 November 2001).

[98] Peto R, Gray R, Collins R, Wheatley K, Hennekens C, Jamrozik K, Warlow C, Hafner B, Thompson E, Norton S, Gilliland J, Doll R. (1988) Randomised trial of prophylactic daily aspirin in British male doctors. *British Medical Journal* **296**: 313–316.

rare a condition to enable us to do a decent study, so we thought we would have to test whether aspirin prevented venous thrombosis. And we laid on a study to test if it would prevent venous thrombosis and it didn't seem to have any material effect on that.[99] It subsequently has been shown to have an effect, but as Sir Richard Peto, if he were here, would immediately leap up and say, 'You didn't have anything like enough numbers'. But we were frightened of trying to test its effects on the prevention of myocardial infarction. When I say it was too rare, I mean too rare a condition per 1000 people per year to be able to lay on a prophylactic study, which Peter Elwood had the courage to do.

There's one other comment I'd like to make. You talked about people advising you after you had broken the code, and found there was benefit in reducing the morbidity, not just the mortality, not just your eight and 11 deaths, and that you really must enlarge the study, and of course it so happened that the effects were much greater in the grouping of centres that you had first started with. I forget where that was, in Cardiff. Overall, the 24 per cent reduction was exactly what subsequent research has shown that aspirin does produce. But Archie never forgave us for having said you must extend to the other centres, because he said the other centres didn't ensure the treatment was carried out properly and they didn't get any significant reduction, when the Cardiff centre was getting a 40 per cent reduction.

Elwood: It demonstrated what we all know, that Cardiff is the place for good epidemiology!

Doll: Anyway he was very cross about it, but I believe the combination of the four centres did in fact give you the correct answer. There is Mr Henderson. He must have some contribution to make on this, because many of us have been grateful to him for the energy he has had in persuading us to do research on aspirin.

Mr Nick Henderson: The Foundation has been going for 25 years and most of you will also be aware, I am

[99] Medical Research Council, Steering Committee. (1972) Effect of aspirin on postoperative venous thrombosis: Report of the Steering Committee of a trial sponsored by the Medical Research Council. *Lancet* **ii**: 441–445.

sure, that this is the 100th anniversary of the development and production of aspirin as a product for treatment. I doubt if there are many products that have lasted 100 years and have been so widely researched and, if anything, it is gaining increasing interest. I want to return the compliment, if I may, to Peter Elwood. He is a tremendous enthusiast for aspirin and I think his conviction is totally correct, but he's too modest to say that he has personally visited the Far East, Indonesia, Hong Kong, Singapore, the Indian continent and Pakistan, he has spoken about aspirin, and enthused an awful lot of doctors about its use, and all from that very early work he has described to us today and I think he certainly should be remembered as the parent of aspirin in myocardial infarction. The work goes on, and shortly, I hope, he is going to South Africa. There is now an American Aspirin Foundation, and Southern African Aspirin Foundation, a Far East Foundation based in Delhi, and perhaps as a sort of *quid pro quo* I had a letter the other day from the Pakistan Aspirin Foundation, so it's growing and will continue to grow.

Wade: Very interesting hearing about Hershel Jick. I knew him quite well. After the thalidomide disaster, that was 1962 [thalidomide was withdrawn in 1961], Peter Elmes and I looked at what drugs people coming into hospital had,[100] because I think in Belfast at that time 5 or 6 per cent of admissions were related in some way or other to drug taking. I know that at this meeting in 1966 at Geneva Jick was there and we discussed this, and I don't think I had published my paper at that time but we were talking to him about it. He must have started the study then, but I didn't know that, and I lost touch with him too.

Doll: Who else wants to contribute to the discussion of aspirin?

Elwood: Can I just add that aspirin, of course as everyone will know, is of growing interest because of growing evidence that habitual aspirin takers have a very low risk of bowel cancer, gastric cancer,

[100] See Elmes *et al* (1965), note 82.

oesophageal cancer. It's also been noticed that habitual aspirin takers have a very low risk of cataract. But the one that excites me and perhaps a few others in the audience, is that there is growing evidence that aspirin may delay cognitive decline and dementia. My children, observing me taking an aspirin, or half an aspirin a day, say, 'Dad, it's too late!'

Doll: There can be little doubt, I think, that the aspirin work of this unit has been of outstanding importance, but it's so outstanding clearly that everybody recognizes it and we know all about it. There is nothing to say except that it is very much to the credit of the unit that it had the imagination and energy to do this work.

Tyrrell: Did you do any work on the relation with cerebrovascular events?

Elwood: We didn't, but, of course, other units did and the effect on stroke and on TIAs [transient ischaemic attacks] is quite in keeping with its effect on other vascular conditions and the evidence on that is every bit as convincing as in myocardial infarction.

Tyrrell: Let me add a trivial point to fill this thing out. I got a letter from the Chairman [Doll] some decades ago asking if I would please take part in a trial of aspirin and myocardial infarction, and I said I was already taking regular aspirin, having had a TIA and he said, 'Oh well, that lets you out of my trial then'.

Thomas: I remember the first scientific meeting I sat in on, knowing Peter Elwood from church connections and other people there. We sat very gentlemanly at the table and ladies talking and so on, and I almost sat forward at the end of the meeting, expecting them to close in prayer, it's a sort of Welsh tradition really, that we were almost like that. It sounds like another generation, which it was, we are talking 1972–73. But there was a civility and a general enthusiasm.

At the unit we had a wide range of students, some dieticians from Guildford, the annual MSc students down from the London School [of Hygiene and Tropical Medicine], and applied biology students from

Bristol. Students were taking part in projects and being encouraged to do so and I think George [Davey Smith] has indicated that he was in that category early in his career. It's that enthusiasm and the ability to get out and change things [that makes epidemiology attractive]. I think most of us come into medicine thinking that people know the answers all the time, but the longer you spend in medicine, clinically, you begin to realize how uncertain are even the apparently firm foundations of medicine. That's what is good about the unit, it's been challenging them [accepted medical ideas], having to define things [concepts].

I was just going to give some of my experiences of working in the unit. It's been said what encouragers Peter Elwood and Archie Cochrane were. I went along there in 1972, finishing a BSc project on air pollution and chronic bronchitis, and I just happened to be very enthusiastic reading the documentation that they had at the Pneumoconiosis Unit. Archie was approaching retirement but Peter Elwood mentioned to me it might be worth reading *Effectiveness and Efficiency*, which I did and I found it very interesting. I had a totally non-medical background: I finished my public health degree and was a health inspector for a few years and then did an MSc in occupational safety and hygiene. Peter Elwood and Archie, as I understand it, were thinking about further research, a follow-up of the flax workers,[101] and they drew me in on that project, initially with a research grant, and then working as a technical officer, at the MRC Epidemiology Unit. I worked there on a range of projects really. What impressed me was the sheer range of projects that were going on for a relatively small staff and medically trained staff. I was looking at environmental aspects there. We did a fair bit of work on lead, which Peter Elwood was very enthusiastic about. We looked at water lead, we looked at air lead, we travelled round and we really did field epidemiology, which was the forte of the unit, high response rates, hitting an area very intensively. I always used to think from the early days when I would be

[101] See note 74.

collecting the water samples or whatever, and Peter Elwood would be persuading the ladies that their children ought to give a little blood sample for us and so on, that maybe kissing the blarney stone was a thing that we all ought to learn in epidemiology. There were respiratory studies that we followed up, not only flax workers, but we followed up the asbestos workers and in fact recently we were also following up the slate workers that were seen in the 1980s. Having been a public health inspector, I took a little bit of interest in pesticides, and here I must thank Sir Richard Doll for encouraging me in an early study I did on following up pest control officers and their use of a possible bladder carcinogen called ANTU (alpha-naphthylthiourea).[102]

I do remember Peter Elwood's encouraging role. I had known him from church connections almost since I was aged 14, and I remember even as a student he used to say, 'I am going to a meeting at such and such a town, would you like to come along for the ride?' Going from Cardiff to have a look around Oxford was quite a day out for a Welsh boy in those days. He got back in the car, I remember, after the meeting with Sir Richard [Doll], and he was obviously quite pleased with the way that it had gone, and he said, I think in Sir Richard's summary of the meeting, that there was as much evidence that aspirin was beneficial as there was for half the drugs in the British Pharmacopoeia.

Later on, I'd finished my research there and I was always keen to study medicine and I applied every so often – Peter Elwood must have got fed up writing me references – but I was fortunate in 1981 to get a place at Leicester and I went there. I was also able to come back for my elective in about 1983–84, and from 1994 onwards to 1999 finishing the Caerphilly study. But in my time at the unit as well I shared for several years the attic with Archie Cochrane and I was really quite unashamedly his tea boy. He was a bit shaky on his legs as time went on, and we were at the top of the building and to be honest, if Archie ever offered to make it,

[102] Davies J M, Thomas H F, Manson D. (1982) Bladder tumours among rodent operatives handling ANTU. *British Medical Journal* **285**: 927–931.

there was normally cigarette ash in it and various other things, so we took it as a healthy way to make it ourselves. But he used to be working away, he was writing his obituary there,[103] he used to let us read it, which we young people all thought was a bit odd, but he was working on his autobiography as well, and he always said, 'What shall I call it?' I always said, 'Why don't you call it 'Archieology – The study of Archie Cochrane', because he was in a sense rather unashamedly self-interested.[104] Archie was always interested in talking about the distinctions between applied and pure research and, in his view, his job was to educate people like myself and others in the attic. He was very interested in the Rothschild report about applied research then and I see things have gone full circle now with the very great interest in applied and commissioned research.[105] At that time Archie had implied that researchers were not under an obligation to do applied research, and it had been said when he was younger that 'gentlemen' did not do applied research. I think Archie thought the truth was somewhere in between, that there should be some benefit to mankind from what he was doing. But my own impression was, as the quinquennial reviews came around, that the world of epidemiology was changing. I got the impression that in Archie's day you could be like Indians, roving wherever you liked, attacking whatever you liked, but as time went on people were getting pinned down on reservations and they were being told in strong terms not to stray off too widely, that they had to develop programmes of research, and that is why I could see that things like Caerphilly and other projects coming on later, were trying to develop more of a programme pattern. Archie was trying to educate me about life and and showed me the proposals for setting up the MRC Environmental

Figure 43: Archie Cochrane in retirement with *The Times* crossword puzzle, *c.*1981.

[103] See ALC/9/1 in the Cochrane Archive, Llandough Hospital, Penarth, Cardiff. See also biographical note on page 133.

[104] See note 20.

[105] Lord Rothschild's report, 'The Organization and Management of Government R&D', along with that of Sir Frederick Dainton, 'The Future of the Research Council System', were published in 1971, with the preface being a memorandum by the Government. See the Lord Privy Seal. (1971) *A Framework for Government Research and Development.* Cmnd 4814. London: HMSO.

Selwyn St Leger

There's one anecdote that I can repeat to you. This was told to me by Archie, I wasn't there at the time. As you know there were those with commissions during the war, and then they were reservists afterwards, and when the Korean War came and the Government decided that the reserves would be called up, or at least put on standby. At the time two letters arrived at the PRU, one addressed to Captain Archie Cochrane, and the other to Major Fred Moore. Archie used to tell me that with relish. Fred, of course, was a wonderful raconteur about his experiences. He was with the Desert Rats. Once, explaining to me why he never washed his mug – I supposed it was a tin mug that he never washed – other people washed theirs and they all went down with the Ds and Vs. He never washed his, because they had limited water supplies, therefore there was contamination.

Figure 44: Captain Fred Moore (b. 1915), a member of the Epidemiology Unit from 1950 to 1985.

Epidemiology Unit[106] on his desk and he said, 'What do you think about these?' and I said, 'This is very interesting, Archie', and Fred's comment was, 'It looks like a great big fishing expidition, but it might catch some big fish.' Again, I think this is a fairly good assessment of the situation. Fred Moore and he were always discussing and arguing about things. People have said that Fred was a bit of an old woman, really, and I know on my leaving card he wrote in inverted commas, 'Is there anything that I have forgotten?' because I used to be very paranoid. If Fred passed it [a paper], I knew

[106] The Medical Research Council Environmental Epidemiology Unit was established at the University of Southampton University in 1979 directed by Sir Donald Acheson to carry out research on the occupational and environmental causes of disease and to investigate geographical variation in disease rates within the UK. The current director, Professor David Barker, was appointed in 1984. See www.mrc.soton.ac.uk/generalinfo.asp (visited 5 September 2002).

that most of the facts and figures were right and that things were drawn correctly. Fred and Archie used to argue, but Fred, rather like a good NCO in the services, would have that polite way of saying 'Professor' or 'Sir' at the end of what he had said to him, which took away the insult. I remember them coming back into the door one day after they had been to a funeral, and he said 'I have said to Prof., the next funeral you go to, Archie, err Professor, won't be anybody else's'. It was always a joke, privately, in fact, as to who would be more wealthy when he passed on, Fred or Professor Cochrane, because Fred had investments and was, reputedly, part-owner of a local brewery.

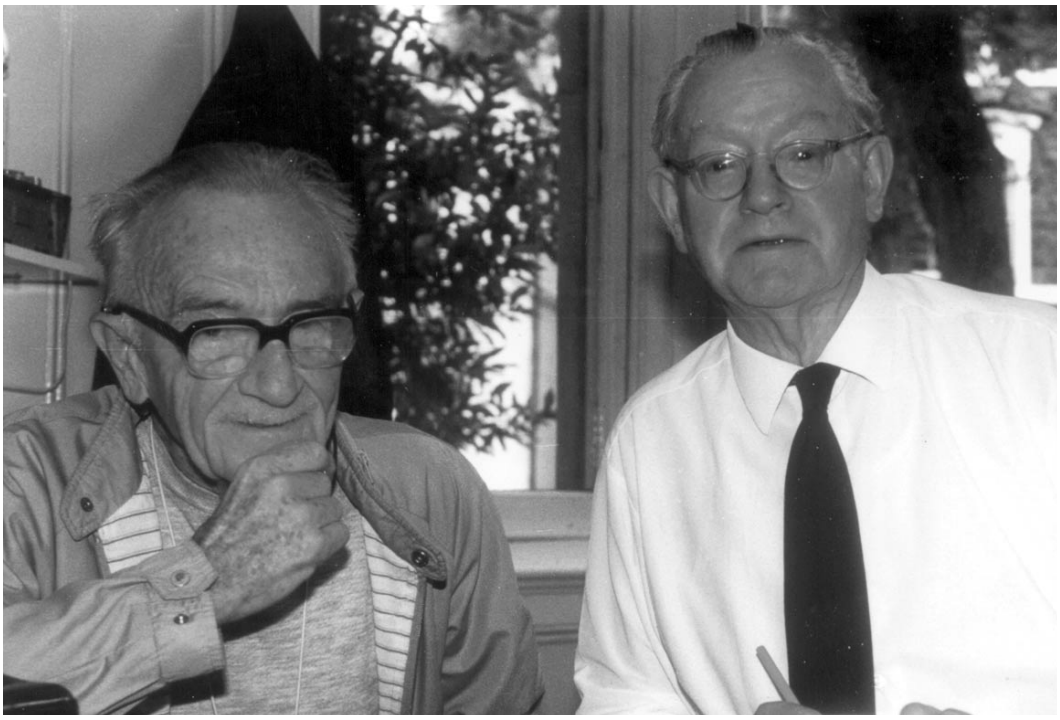

Figure 45: Archie Cochrane and Fred Moore at Richmond Road, Cardiff, *c.* 1981.

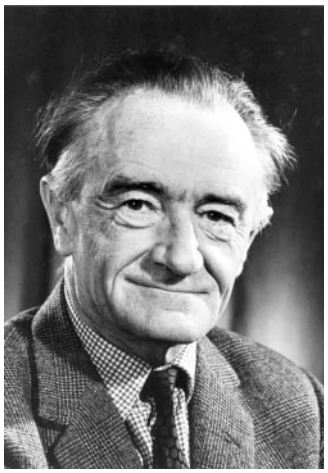

Figure 46: Archie Cochrane.

Archie Cochrane

Your letter was about the first thing that I saw when I got back from a very pleasant holiday in Davos. My immediate reaction naturally was to return to Davos at once, as there was little point in my staying here! [107]

Dr Joan Faulkner and Dr Dick Cohen

Dr Cochrane's attitude was very much more reasonable than we had anticipated. He was prepared to discuss amicably and rationally the staff he would need in his new unit and the accommodation that would be necessary for them.[108]

Julian Tudor Hart

I realized that epidemiology is really a democratic subject, high response rates means one man one vote, everybody in a community is important. We need everybody's blood pressure, we don't just need the blood pressures of people who have come along to see you about their blood pressure or have coronaries, we need the whole distribution. This wonderful discovery of Pickering's, that blood pressure was continuously distributed, so we no longer had to label people as having diseases or not having them, but could interest ourselves in how much they had and whether it was useful to call high blood pressure a disease. So de-deifying disease, getting distributions and combinations of distributions, was a new thing. I could see straight away that the debate between Pickering and Platt it wasn't a scientific debate, it was a social debate.

Mary Thomas

I was only going to the unit as a temporary worker in the Rhondda Fach study, between two other plans that I had. And I stayed for probably two years – it wasn't that long. It was not a happy place to work if you weren't in the scientific staff room. I don't know how happy it was in the scientific staff room, but it was terrible – infighting, backbiting – you know, professional jealousies. I presume they were professional jealousies. I was very much younger than I am now and was an innocent in most of that. It taught me a lot though. Archie was very nice to me, good to me. I was in the peace movement at the time and he defended me when I was arrested in London, and was a couple of days late back for work and the personnel manager wanted to get rid of me. Mr Cory[109] *was quite ready to say that my services were to be dispensed with, but Archie said, 'Oh, just leave it to me, there's no question'. And there was no more heard of it. We were extremely badly paid, very badly paid, so badly paid that that's the real reason that I left, frankly. I just was not making ends meet, transport costs and living costs. I was all right while we were getting overnight subsistence out on the Rhondda Fach survey, as we were most of the time. But when we were back in Llandough or in Cardiff in Richmond Road, then the money was absolutely pitiful. I just couldn't afford to live. Archie was so generous, because he was a rich man. Rumours were going around all the time that he was paying for this and paying for that, and I just didn't want to be part of it. I did tell him that I couldn't afford to stay there. I learnt all the skills of field work in Rhondda with Fred Moore and the team, the obsessional nature of data collection, I will be eternally grateful for those skills that I learnt and have never forgotten.*

Peter Elwood

The unit then began, shortly after I came [1963], to expand. Archie was brilliant to work under, but he had limitations. He had the occasional brilliant idea and will always be remembered for these, but he didn't do an awful lot himself. Now that's not a criticism, he operated at a very high level and spent most of his time travelling, meeting people, going to meetings. He stimulated an enormous amount of work, but he left me to run the unit. There was money available in those days, and so the unit gradually expanded. We took on an assistant epidemiologist and then another statistician, and then another epidemiologist, and so on. Archie of course had set up the glaucoma survey with two ophthalmologists and that was a very, very fine piece of work, it really set a lot benchmarks in

[107] Confidential letter from Archie Cochrane to Dr R H L Cohen, 13 January 1960, PRO FD7/1046. See page 40.

[108] Note for File D.5028/1, 'Visit to Pneumoconiosis Research Unit by Dr Cohen and Dr Faulkner, 19.1.60'. PRO FD7/1046.

[109] Dr Peter Elwood wrote: 'Geoffrey Cory was the administrator and finance officer at the PRU, but he also served the EU and paid us a weekly visit.' Note on draft manuscript, 27 March 2002.

ophthalmology, but when that came to an end there was very little follow-up, and so I inherited one or two people from that team who joined the unit and had no other work to do.

Peter Elwood

The Government had asked the Department of Social Medicine at Queen's University, Belfast, to investigate whether or not byssinosis occurred in the flax industry and if so, what disablement did it cause? Richard Schilling had established that cotton workers' byssinosis was prevalent in the cotton mills,[110] *so we did a survey of all the flax mills in Northern Ireland, about 24 of them. Incidentally, the one mill that would not give us permission to do the survey was owned and run by the then Minister of Health from 1963–64, a man called Anthony Barber. I interviewed all the people, described this study that we were doing, used the MRC questionnaire on respiratory symptoms, asked them for employment history, and I think I measured height and weight. Another person did lung function tests and someone else made dust measurements in very great detail throughout the mills. Eric Cheeseman, the first professor of medical statistics in the UK, was in the department, a very prickly character, but one who gave me enormous encouragement, and I owe a lot to him as well as to John Pemberton. We saw about 2500 people in the flax industry, and confirmed that byssinosis does occur. I was left with some questions, and I very nearly wrote a minority report in the official report of the study, because I felt that there was doubt about disablement from byssinosis. When the men went in on the Monday and the Tuesday, if they were exposed to high levels of dust, they got quite severe symptoms. In my analysis I found that it was really the smokers who got the severe symptoms. Non-smokers got very mild symptoms. But I was very concerned whether or not there was permanent disability, and so I set up a little study on my own, to follow up some past workers, and I travelled all over the north of Ireland seeing these past workers, trying to estimate whether or not they had any continuing disability.*[111]

Peter Elwood

John Pemberton was very good to me. He offered me a job as 'the boy', the junior member of a small team of four people, to look at flax byssinosis. I have always said that somebody who was into research should be fascinated by the process, not by the answers, and the process was absolutely exhilarating, because we were able to put limits on the degree of confidence. The statistical estimate of the confidence interval was the thing that really stimulated me. Clinical medicine was just a fog about this and dealt with single cases, you never knew whether you had any effect or whether any association was real. Whereas dealing with numbers, and with pretty basic statistics in those days, we were able to put levels of confidence on our answers. I can remember walking home reading Moroney's Facts from Figures,[112] *practically walking into lampposts. It was such a revelation to me that you could have a degree of confidence within medicine. This was way back in the middle-to-late 1950s.*

Estlin Waters

Certainly in my case there was an overlap between counting birds and epidemiology. I had been interested in birds from a very young age when I was in Canada, but I was also interested in the scientific side of birdwatching, especially bird migration and bird numbers. When I was on St Kilda[113] *I wrote about a dozen papers and short notes for ornithological journals and for the* Proceedings of the Zoological Society of London *on various aspects of birds and on the grey seal. I was interested as a naturalist. At that time I didn't have any real knowledge of statistics. It was my birdwatching that kept me scientific during my medical student days. I used to read some of the bird journals, the medical journals were too heavy to read as a student. I don't know how some of our medical students now manage, but they can and do. I*

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[110] Schilling R S F, Hughes J P W, Dingwall-Fordyce I, Gilson J C. (1955) An epidemiological study of byssinosis among Lancashire cotton workers. *British Journal of Industrial Medicine* **12**: 217–227.

[111] Dr Peter Elwood wrote: 'This issue of permanent disability was debated for a further 20 years and it was only settled by later studies of the respiratory health of ex-textile workers, and their mortality. See Elwood P C, Thomas H F, Sweetnam P M, Elwood J H. (1982) Mortality of flax workers. *British Journal of Industrial Medicine* **39**: 18–22. Elwood J H, Elwood P C, Campbell M J, Stanford C F, Chivers A, Hey I, Brewster L. Sweetnam P M. (1986) Respiratory disability in ex-flax workers. ibid. **43**: 300–306. Elwood P C, Sweetnam P M, Bevan C, Saunders M J. (1986) Respiratory disability in ex-cotton workers. ibid. 580–586.' Note on draft transcript, 2 April 2002. See page 116.

[112] Moroney M J. (1953) *Facts from Figures.* Second revised edn. London: Penguin Books.

[113] Waters E. (1964) Observations on the St Kilda wren. *British Birds* **57**: 49–64.

Figure 47: Dust sample taken from a child's hands for lead pollution studies, 1970s.

felt the teaching we had at London was not very scientific, it was more of an apprenticeship: I do this, so you do this. The birdwatching kept me critical of the scientific side of things. When I joined the MRC it was very much the other way round. It was the epidemiology that was the scientific side and I think I have been able to apply a bit of it to my birdwatching. The two have run together, one perhaps ahead of the other, but the two are related. I think that someone who wants to count wrens on St Kilda has got something in common with someone who measures the haemoglobin level in a population. My experience of working alone on St Kilda and writing papers on natural history probably helped me when starting in medical research.

Janie Hughes

When I first started in April 1964 the job was mostly office based. I got to know what sort of research the unit was involved in and then I started to do some fieldwork. My first field job was Trehebert at the top of the Rhondda valley, where Dr Elwood had started some work on anaemia and I started to work in the clinics there and also doing a bit of door-knocking, but not very much to begin with. After that I worked on studies of lead pollution. Near motorways we took blood from people who lived there and swept pavements in cul-de-sacs away from them. I never took blood, Dr Elwood did, but he always had to have a chaperone and somebody to do the admin. We've worked in north Wales, taking blood from very young children, looking at blood leads. We worked on studies of hard and soft water – for example, a hard-water area in Gloucester and perhaps a soft-water area in south Wales [Llanybydder, a big horse-breeding area]. We collected children's teeth, cut their hair, and took finger nail clippings.

Peter Elwood

It was my decision to withdraw from the Rhondda, which was in those days about an hour's journey away and it was really very wasteful. The origin of course was the studies of pneumoconiosis and Archie actually got money to put up a very nice clinic in Ferndale in the middle of the little Rhondda [see photographs on pages 45 and 47], which we used as a headquarters. We had about four rooms and we could do a certain amount of technical work and did quite ambitious surveys there. But it was an hour's journey away. I also felt that the Rhondda was a selected population and when we began to study conditions other than those of mine workers, it was quite obvious that there was a social class-biased movement out of the valleys. So I made a conscious decision to go somewhere else and we chose Caerphilly, which we felt was a fairly stable population, relatively close, and the health authority there and GPs and so on seemed to be very cooperative and have proved to be. I think the first study that we set up was a study of the elderly and Michael Burr really took over that area of research,[114] but I did the study of folate levels and B_{12} levels as well as haemoglobin in Caerphilly.[115] And we looked at a number of things in relation to that. Then Michael Burr arrived and he set up studies on vitamin C and on the health of the elderly and respiratory symptoms. He then set up studies on asthma and Caerphilly proved to be very, very suitable.

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[114] Elwood P C, Burr M L, Hole D, Harrison A, Morris T K, Wilson C I, Richardson R W, Shinton N K. (1972) Nutritional state of elderly Asian and English subjects in Coventry. *Lancet* **i**: 1224–1227. Burr M L, Elwood P C, Hole D, Hurley R J, Hughes R E. (1974) Plasma and leukocyte ascorbic acid levels in the elderly. *American Journal of Clinical Nutrition* **27**: 144–155.

[115] Hughes D, Elwood P C, Shinton N K, Wrighton R J. (1970) Clinical trial of the effect of vitamin B_{12} in elderly subjects with low serum B_{12} levels. *British Medical Journal* **i**: 458–460. See also Cochrane A L, Moore F. (1971) Expected and observed values for the prescription of vitamin B_{12} in England and Wales. *British Journal of Preventive and Social Medicine* **25**: 147–151.

Julian Tudor Hart

I was hoping to develop a practice that was purpose built to be a research department, and then I thought Archie and Ian Higgins, and Peter Elwood could come along and they would use my population. So I went to Glyncorrwg, which was an isolated population easily defined. I found gross pathology there, and a shambolic state of the practice. I couldn't contemplate any kind of research for at least five years. About the third year I was there Peter Elwood had been doing haemoglobin studies on anaemia prevalence and so on. I had been very struck by each time I had taken over a new practice, I found a clutch of women with really severe anaemia, haemoglobins of 3 or 4 grams, for whom it was a deliverance, you topped them up with iron and corrected it, and then the effect was fantastic. So I bought myself a haemoglobinometer and I started systematically collecting data, eventually aiming at 100 per cent coverage. After I had got about half way to that target, I went down to Richmond Road [to the EU] and talked to Peter Elwood about it, hoping to get some help from him. He was very scathing about what I was doing, he obviously thought it was terrible half-arsed stuff, which it was. But he didn't seem to have any idea of the circumstances I was working in. He went on at me about whether I had weighed menstrual loss, whether I had collected sanitary towels and weighed them to assess their menstrual flow (which we now know to be a grossly inaccurate way of measuring menstrual loss). And then, he said, 'Are you sure that your measuring instrument is accurate?' Well, I hadn't done anything to it, I had just assumed that it was. When I did, I found that it was absolutely awful, and I didn't know whether it had always been awful from the beginning or whether it had become awful. So there was just no way I could depend on it. I had to throw away all the data. I lost everything. But it was a good elementary lesson, which I needed. I had learnt all about this before, but you don't really learn it if you are not doing it. It has to be your own work.

Figure 48: Janie Hughes testing haemoglobin (Hb) levels on a haemoglobinometer, 1967.

1964–69 Iron deficiency anaemia studies

Peter Elwood

The study of the effect of iron in bread on haemoglobin level in the Rhondda Valley surveyed, as I remember, about 8000 women. We identified those who had haemoglobin levels below 11 grams, I think it was. We gave them a month's treatment to bring their haemoglobin level up and then we put half of them on bread fortified with an iron salt, and half on ordinary bread, and we watched the fall in haemoglobin level over the next two years. We wanted to look at prevention, not treatment, with iron in bread. So we raised their haemoglobin levels, knowing that they would slowly return to what they had been over the next year or so, and we gave half of them bread. We estimated that the absorption of iron from the bread was only about 4 per cent. When I submitted the paper to journals they all refused it, and said, 'This cannot be right, we all know that iron is absorbed from food at the rate of about 30 per cent in women with low haemoglobin levels, this cannot be right'. I had great difficulty publishing the paper. In the end we did publish it and over the next five, ten years, it gradually became apparent that iron absorption from food stuffs is about 4 per cent, so we were shown to be right in the end[116] *But that was another fascinating set of studies and again I just valued the opportunity to follow through an idea and look at the distribution, the association with indices of morbidity, look at mortality, and then to run randomized controlled trials to look at prevention.*

The iron studies with South Asian women are perhaps the most fascinating story of my life. The studies of the absorption of iron from bread were radioactive studies, done immediately after I came to the unit in 1963. I set up these studies using radioactive iron, because such precise measurements of iron retention could be made. I got friends and colleagues to come to the medical school (on Newport Road in those days) and have a special breakfast, in which we had two forms of iron. One was given as a control. We had baked some iron 59, radioactive iron, into bread and people received a slice of bread with this, and then a fortnight later, we asked them to go to Harwell [the UK Atomic Energy Authority, Harwell, Didcot, Oxfordshire] and have whole-body measurements of the iron that had been absorbed from the bread. The absorption was almost nil. I got a bit of publicity because of this, both in this country and in the USA, and I was asked to join the WHO Committee on Iron Deficiency. The Committee said there was undoubtedly a real problem where chapattis or tortillas are eaten and bread is not and wanted to know what fermentation did to the iron and would I repeat this study using chapattis? So I set up a study to look at radioactive iron absorption from chapattis.

In order to mimic real life as closely as possible, I got an Indian woman to help make about 200 chapattis. We measured the amount of radioactive iron in each and stored them in a deep freeze. I went up to Coventry where there was a fair-sized Asian population with the help of the health authority and one selected GP. We did rough power calculations (on the back of an envelope in those days), and we estimated that the method was so precise that we could get very accurate measurements from a quite small number of women. So we selected 20 women, all over 50, not suffering from any important disease, but no one who might become pregnant. Tom Benjamin, one of the fieldworkers, and I took the chapattis up to Coventry and we asked the women to include one chapatti with a meal each day for one week. Each day Tom Benjamin would deliver a chapatti on dry ice to each of these women, who would defrost it and eat it as part of her meal. A fortnight later they were driven to Harwell, and Tom Benjamin arranged a visit to Oxford, took them round one of the colleges, and took them for tea, with breaks on the way there and back, and really I think I made 20 friends on that project, they were so friendly to us.

We found that iron was no better absorbed or absorbed no differently from bread.[117] *This study was a seven-day wonder, and everyone forgot about it. Twenty, perhaps 25 years later, I was telephoned by a reporter making a television programme on the uses of radioactive iron in medical investigations. 'Yes,' I said, 'I did look at the absorption*

[116] Elwood P C, Newton D, Eakins J D, Brown D A. (1968) Absorption of iron from bread. *American Journal of Clinical Nutrition* **21**: 1162–1169.

[117] Elwood P C, Benjamin I T, Fry F A, Eakins J D, Brown D A, De Kock P C, Shah J U. (1970) Absorption of iron from chapattis made from wheat flour. *American Journal of Clinical Nutrition* **23**: 1267–1271.

of iron from bread, and I was also asked to look at it from chapattis'. The television programme blew up this story of the radioactive chapattis in an incredible way. They interviewed one of the women and a relative of another, who made extraordinary claims that a research worker from the MRC (they didn't name me) had given them chapattis and they had eaten a chapatti each day and were then driven in secret to a military establishment where they had a whole lot of measurements made. One woman said, 'My hair fell out, I began to get pains and cramps, I became arthritic, I am now diabetic, and if only I hadn't touched those chapattis I am sure I would be fit and healthy'. A relative of the subject who had died, said, 'My mother's health failed from that day on and she would be alive now were it not for those chapattis'.

The health authority set up an enquiry at the request of the Asian community and I went up to Coventry. I had prepared over the weekend a very full account of what we had done and I had clipped to it an account of the original study published in the American Journal of Clinical Nutrition[118] *and I asked the chairman of the meeting if I could give an account of what I had done before there were any questions. Well, the meeting was exceedingly hostile. The health authority were obviously keeping neutral, but one or two there were not. Over the subsequent weeks I was accused of all kinds of things. For example, an Asian health visitor had been with me on this study and she could testify to the fact that I had explained all about the study to these women, but she refused, saying she had never met me, had never had any part in the study of chapattis, and knew nothing about it. Janie spent a day or two in the basement, going through all the letters, and she dug out one from the health visitor saying how much she had enjoyed the study, how well the people had been handled, and how delighted they were to take part, refuting many of the things that had been said. She also found a letter that I had written to the son of one of the women giving a complete description of the study. Another was from the physicist who had prepared the radioactive iron, which had been submitted independently to a number of experts, who said that it was an extraordinarily low dose. That was why we had used Harwell, which had the most sensitive counter in the whole country. So the thing took a long time to die. One little codicil to that. I was in India a few years ago and one of my contacts told me the radioactive chapatti study had been raised in the Indian Houses of Parliament and in all the Indian papers.*

Another accusation was that I had purposely chosen these women because they were illiterate. We found letters from three of them thanking me for the most interesting study, written in perfect English.

Peter Elwood

I had an idea in the car about the randomized control trial of iron in bread [started in 1964]. I was chatting to somebody about the problem of anaemia, as I thought it was at that time, and how we could do something that was relevant to it. Giving tablets through GPs was obviously achieving very little, what could we do? And so the fieldwork, which lasted about ten years and ended with the radioactive chapattis, all started with an idea in the car as I was chatting to somebody about the work on anaemia, which at that time had only extended to symptoms and realtionships with cholesterol level and blood pressure.

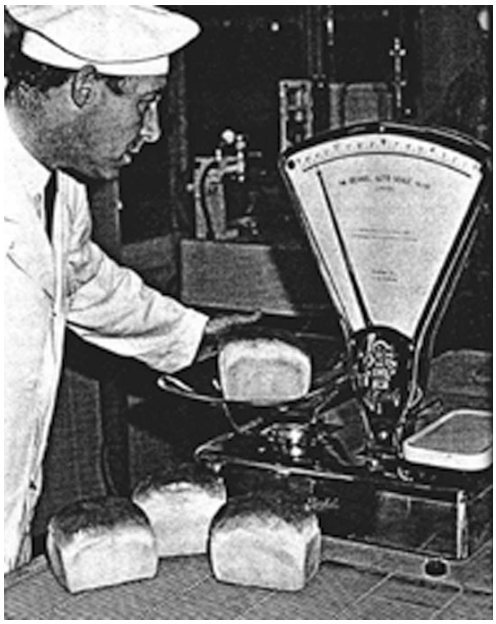

Figure 49: Special bread made from flour containing iron labelled with a radioactive isotope.

Figure 50: The medical researcher as a baker's man, delivers bread from the Epidemiological Research Unit.

[118] See note 116. See also Elwood P C. (1968) Radio-active studies of the absorption by human subjects of various iron preparations from bread. In Ministry of Health. *Iron in Flour*. Reports on Public Health and Medical Subjects No. 117. London: HMSO, 1–30.

1968–72 Headache and migraine studies

Estlin Waters

Although Archie Cochrane suggested that urinary tract infection would be a good subject for me to get into, and I did write a lot of papers and attended conferences on that, I was working in a team. It wasn't my own thing, so I wondered what else I could do that really would be mine, in the same way that Peter Elwood had 'got' anaemia. I was helping him, but it was his subject. Again I think it was probably Archie Cochrane who suggested headache and migraine, because Archie himself suffered from migraine. At that time Peter Elwood had actually started the first survey that the Epidemiology Unit did on headache and migraine.[119] *He had just got to the stage of collecting the questionnaires and he very kindly said that if that was the subject I wanted, it was mine. He very generously handed it all over to me, and really that was the subject, headache and migraine, that I did on my own then. I did lots of surveys of various sorts, including randomized trials of treatment of ergotamine tartrate.*[120] *I spent a long while on headache and migraine, both at the Epidemiology Unit and later when I went to Southampton.*

One of the problems of migraine is how you define it. Definitions were not satisfactory and varied widely. It quickly became apparent to me that all the definitions were really just descriptions. Typically migraine was usually unilateral, sometimes accompanied by nausea or vomiting, and sometimes with a warning that it was coming, but very few of the definitions stressed how often this had to happen, and whether it had to happen in every attack or whether all the features had to be present. What I did was work out the prevalence of headache, and the prevalence of each of these symptoms, without making up my mind whether individuals had migraine or not. So I would say of all the headaches, what proportion were unilateral or sometimes unilateral?

Archie Cochrane was very keen, I am sure he was right, that any questionnaire needs a clinical validation. So we had Paddy O'Connor (later Air Vice-Marshall Patrick O'Connor CB), who was in the RAF, to see people who had completed our questionnaires. His job, or one of his jobs as the chief neurologist in the RAF, was to decide if people had migraine or not, and if they had migraine they were not allowed to be a pilot or a navigator. So as far as he was concerned they either had it, or they didn't have it. We got leave of absence for him from the RAF so he came down, and he lived in my Cardiff house. He used to go round houses in the Rhondda seeing people who had completed my questionnaires, and he did this blindly, not knowing what they had said on the questionnaire, and he decided whether they had migraine or not. He more or less put them into two camps, migraine or not migraine. He did a little group of GOK (God only knows), but I think it was only a few cases in 120, where he couldn't make up his mind. Because I had given him randomly selected people, I was able to work out the prevalence of migraine as if he had seen everyone in the Rhondda and this created quite a stir, because it really hadn't been done in this way before. At that time the Migraine Trust, with Princess Margaret as patron, had started up and was active, having a symposium every year. So I think I got quite well known for the migraine studies.[121] *I did the randomized trial for ergotamine tartrate on people who had completed the headache questionnaire, because one neat definition was 'migraine is a headache that responds to ergotamine'. It's such an unpleasant drug that if you didn't have migraine, you wouldn't take it. So I did this randomized trial between ergotamine and a placebo, and found no benefit of ergotamine*

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[119] Waters W E. (1970) Community studies of the prevalence of headache. *Headache* **9**: 364–367. *idem* (1968) Research in the Rhondda. *Migraine News* **6**: 3–4. The Migraine Trust supported this research by the Epidemiological Research Unit, as it was known then. See also Waters W E. (1986) *Headache*. London: Croom Helm.

[120] See Waters W E. (1970) Controlled clinical trial of ergotamine tartrate. *British Medical Journal* **ii**: 325–327. See also Tansey E M. (2001) Ergot to ergometrine: An obstetric renaissance? In Hardy A, Conrad L. (eds) *Women and Modern Medicine*, Clio Medica 61. Amsterdam and New York: Editions Rodopi B V, 195–215.

[121] See, for example, Waters W E, O'Connor P J. (1971) Epidemiology of headache and migraine in women. *Journal of Neurology, Neurosurgery, and Psychiatry* **34**: 148–153. *idem* (1975) Prevalence of migraine. ibid. **38**: 613–616. O'Connor P S, Tredici T J. (1981) Acephalgic migraine. Fifteen years experience. *Ophthalmology* **88**: 999–1003.

at all. At that time the only two other randomized studies on oral ergotamine had also shown that it had no effect, but it was widely used as the main drug for the treatment of migraine. It was supposed to be specific, if the attack responded it was migraine. For the trial we used ergotamine only, which was widely used, but a lot of ergotamine was combined with caffeine and other drugs. Of course caffeine could have an effect on ordinary headache as well as migraine, so we didn't use it. But it has subsequently been shown that caffeine increases the absorption of ergotamine, so maybe the pharmaceutical industry was ahead of the evidence at that time by putting caffeine with ergotamine. For a long time many headache researchers never accepted the finding of my ergotamine trial.

Then I tested various hypotheses about migraine, whether it occurs more often in higher social classes, more intelligent people, in people with higher blood pressure, and whether it ran in families. We did studies on all these hypotheses, and almost all were completely negative. For example, when testing the hypothesis that migraine people were more intelligent, we found that in the population as a whole there was no link between intelligence (nor social class) and having migraine. But the higher social classes, classes 1 and 2, and the more intelligent people, were much more likely to go to their doctors with their symptoms. Many people with migraine, including many that Paddy O'Connor had clinically diagnosed, had never in their life been to their doctor for their headaches. So what really interested me was that doctors managed to pick out this association between intelligence and social class and those attending for migraine. This was true in patients who went to see doctors. But they drew the wrong conclusion in saying that migraine was more common in these groups than in the general population. So I was quite impressed how doctors could spot a relatively small difference, but nevertheless the material they had was biased.

Incidentally it is actually true that after I wrote the paper showing that migraine wasn't associated with intelligence and higher social class,[122] *I left Archie Cochrane's unit. He was a well-known sufferer from migraine, and he often told the story: 'Look what happened to people who don't get the right answers!'*

Figure 51: The Rhondda Valley in 1968.

[122] Waters W E. (1971) Migraine: Intelligence, social class and familial prevalence. *British Medical Journal* **ii**: 77–81.

1969–79 Aspirin trials

Peter Elwood

I remember one meeting in America where I heard somebody talking about the role of platelets in heart disease, which was not well established in the mid-1960s. I came back and talked to Professor G V Born and others about methods of estimating platelets. Really there was no way. The literature had an occasional letter from John O'Brien, a haematologist in Portsmouth, and Harvey Vice, a haematologist in the USA. One [letter] said that aspirin had a very marked effect on platelets, which were much more active when the patient had taken aspirin. John O'Brien showed that aspirin was so active that one tablet a day was enough to reduce platelet activity.[123] *So I felt, well, here is a way of testing the role of platelets. One would like to use a conventional epidemiological model, measuring platelets and following up the cohort to see how it relates to vascular disease. But I felt there was another approach. We could clobber the platelets of a group of men and see what their experience is. I got in touch with one of the drug firms, Astra Nicolas, long since absorbed by another firm, and they were very encouraging. So we set up a study and in order to make it efficient, we took patients who had had an MI [myocardial infarction] and thought we would give half of them one aspirin a day and see what the mortality was. And we decided to use mortality, that the identification of a second event was too uncertain and there could be bias in it, because aspirin, even at one tablet a day, might reduce their pain, and we might not ascertain as many infarcts in the group on aspirin as on the placebo. We decided to use an index of death or survival. We had great difficulty admitting patients, because the consultants were very, very reluctant – they thought this a madcap scheme, absolutely daft. I well remember some of the patients saying to me after I had explained it all, 'Oh, of course, doctor, I am all for research, I will help you, but tell me what's really in these tablets? You are not serious that it's aspirin. Tell me, what's in it?' I had great difficulty in setting up the trial.*

Hershel Jick of Boston University School of Medicine had previously set up a fishing expedition, where he asked every patient what drugs they had taken in the week before coming into selected hospitals, eventually about six hospitals in six countries. He linked these 40 or 50 drugs with diagnoses, looking for interactions, harmful side-effects, that people taking a rhubarb tablet came in with liver disease, where this had never been expected, that kind of thing. He produced a whole battery of tables with ten or 20 diagnoses, and 30 or 40 drugs, and just risk ratios or some index like that across for admission with that drug compared with all the other patients with that diagnosis. The one thing that stood out like a sore thumb on this table was a risk ratio of about 0.3, as I remember it, for aspirin and myocardial infarction, an extraordinary deficiency far greater than almost any other. He was looking for the unexpected, and this was certainly unexpected.

Peter Elwood

Doll was very, very worried about one tablet a day. He said, 'That's homeopathy. Why don't you start giving a big dose?' But I stuck to my guns and said that one tablet was enough, but I gave in on the next trial. We set up a second trial, and we gave three tablets a day, but I certainly wasn't willing to change the protocol for the first trial, despite a lot of pressure. And the MRC just said, 'Ask for whatever resources you want and we will give you them, expand the trial as much as you can.' So, looking back, I should have been much more ambitious, but I asked for three nurses, and I got a nurse in Swansea and we started admitting patients. We got one in Manchester and one in Oxford and we boosted the number of patients in the trial.

Peter Sweetnam

First, the aspirin study was expanded greatly and in a hurry because of Hershel Jick's findings.[124] *Because of Jick's work the study ended up with, I think, 1600 or 1700 individuals. Whether it would really have been much better if it had been 3000 or 4000 is a moot point, because if you had looked at aspirin and ischaemic heart disease, say, in the late 1970s, I think you would have found*

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[123] O'Brien J R. (1968) Effects of salicylates on human platelets. *Lancet* **i**: 779–783.

[124] See note 65. See also Wood L. (1972) Treatment of atherosclerosis and thrombosis with aspirin. *Lancet* **ii**: 532–534. *idem* Aspirin and myocardial infarction. ibid.: 1021–1022. Jick H, Miettinen O S, Neff R K, Shapiro S, Heinonen O P, Slone D. (1973) Coffee and myocardial infarction. *New England Journal of Medicine* **289**: 63–67.

something like five or six sizeable randomized controlled trials, all of which (bar one) showed really quite similar sorts of results. Typically there's about a 25 per cent benefit. None of these trials, by and large, were statistically significant in themselves, and one, the AMIS (Aspirin Myocardial Infarction Study),[125] *which showed next to nothing, was by far the biggest of the lot. I have always felt that I would much rather have five separate, disparate trials of 10 000 individuals rather than one of 50 000. Taking the aspirin example, if AMIS had been the only one that was done, the big one, aspirin might have disappeared forever from the face of the medical earth, in terms of thrombotic disease. There's a great advantage to having large samples, but if it came down to a choice between one large and rather more medium ones, I would go for the rather more medium-sized ones every time, with different people doing it, slightly different designs or different subjects. I think it is much safer.*

Janie Hughes

I think the most rewarding thing of all that we have ever done is the aspirin studies. I know it took 20 years to convince consultants that this cheap little tablet could be beneficial, but it really was worth it. The first aspirin studies were hard, hard work, trying to recruit people by cold calling. I think because we didn't have a reputation as yet. We were visiting hospital wards and taking names of men who had been discharged after an MI. In those days if you had had a heart attack you were considered a real invalid by your family and it was hard to convince people that a simple little aspirin tablet could be of benefit to them. Whereas now I think people have been brainwashed and they know of the benefits. Lots of papers have been written, but those were real pioneering days then in the early 1970s. Not that I was the principal person who persuaded them, but I usually chaperoned somebody or other who was doing it.

Peter Sweetnam

Peter Elwood's first aspirin trial which was published I think in the British Medical Journal *in 1974.*[126] *In the basement here [in Canynge Hall, Whiteladies Road, Bristol] you will find my hand calculations for the life tables and, literally, they were done by hand. There are sheets upon sheets of data, because we still didn't have access even then to a computer on which you could easily have done a life table. It's so difficult to try to get things chronologically correct, because I am sure that by then the university had an ICL System 4, and we used it for a few years by going over to Park Place in Cardiff, sitting down at the punch-card machines and punching out programmes and control cards etc. We first started doing that around about the same time as I was doing the analysis for the aspirin trial. Writing a programme for a life table analysis then was not the easiest thing in the world to do.*
[See also page 77]

Figure 52: John O'Brien, haematologist, St Mary's Hospital, Portsmouth, at a unit dinner following a scientific meeting for the Caerphilly study in the1970s. Seated on his left is Margaret Elwood, and Ian Baker on his right.

[125] Schoenberger J A. (1979) Recruitment in the Coronary Drug Project and the Aspirin Myocardial Infarction Study. *Clinical Pharmacology and Therapeutics* **25**: 681–684. The Aspirin Myocardial Infarction Study research group. (1980) The aspirin myocardial infarction study: final results. *Circulation* **62**: V79–84.

[126] See Elwood *et al* (1974), note 94.

1972–79 Barry–Caerphilly child growth study

Peter Elwood

I had had a lot of contact with the Department of Health, or Ministry of Health as it was then, following the work on iron deficiency, and one of the committees that I got on to was on child nutrition and child growth. So in collaboration with the Department of Health, we set up a study of child growth. We selected 1000 pregnant women, 500 in Caerphilly and 500 in Barry, a fairly stable town, not too far from Cardiff. We followed them during their pregnancy and then we followed their infants to the age of five. We made very detailed measurements of growth in the children and administered questionnaires on nutrition, on health generally, on their psychological state, and a whole lot of other things. Again the point that I made earlier, the ability in epidemiology and particularly in an MRC unit, to go back to a study or a cohort, is unrivalled in a long-term unit with secure funding. We went back to those children and looked at their school records and their accidents when the children were aged about seven and administered a few questionnaires to them to see if their early growth and so on had affected their situation later. We also went back at 11 years and looked at accidents in children, in relation to a number of things we had at baseline, but the real value of that cohort is now being shown by the Bristol group.[127]

Janie Hughes

In the early 1970s we worked in Caerphilly on the child growth and nutrition study. That was a very popular study, because we were giving out free milk to half the women on the study and we monitored their children until they were five years of age, so we were known. We weren't known terribly well, but we were known, and when we started the Caerphilly cohort studies in the late 1970s – 1978, 1979, I think – our reputation went ahead of us and people seemed to be very keen to join the study and cooperate. We just worked from there. And I mean these men, now 20 years later, look on us as friends. They have even been known to ring up just to chat. And we are still seeing them, still monitoring their progress, still doing tests on them, so I think we have established a really good rapport with these men.

John Yarnell

Peter Elwood had started off doing some work in the Rhondda, both he and Michael Burr had built up a relationship with the Caerphilly general practitioners and also practitioners in Barry as well. David Bainton had been at the unit and he had done quite a lot of work on the prevalence of gall stones using the Barry population.[128]

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[127] Dr Peter Elwood wrote: 'The Epidemiology Unit was to close on my retirement in 1995 and all the records, data, blood and other samples had to be re-housed. The value of these was recognized and in particular the Caerphilly Study of Heart Disease had enormous potential. The unit's work was well known to Professors Stephen Frankel and George Davey Smith in the Department of Social Medicine at the University of Bristol – Davey Smith had actually worked with the unit earlier. This department seemed an obvious repository for the records from the unit and the MRC agreed to finance the refurbishment of the basement of Canynge Hall in Bristol. All the unit records were transferred there in 1998, with an MRC Committee under the chairmanship of Professor David Strachan to encourage and control access to the data.' Letter to Mrs Lois Reynolds, 27 March 2002.

[128] Bainton D, Davies G T, Evans K T, Gravelle I H, Abernethy M. (1973) A comparison of two preparation regimens for oral cholecystography. *Clinical Radiology* **24**: 381–384. Bainton D, Davies G T, Evans K T, Gravelle I H. (1976) Gallbladder disease: prevalence in a South Wales industrial town. *New England Journal of Medicine* **294**: 1147–1149.

Statisticians and technical preoccupations

Peter Sweetnam

It was mainly analysis of data. The work was put in front of you until one got a lot more experienced when one got invited along to join the discussions about the design of the study in the first place. The analysis in those days was hard work, because we only had electromechanical calculators, punch-card sorters (Hollerith machines), so that even to do a multiple linear regression with two or three variables, if you had 200 individuals, was extremely time consuming. If you looked at the statisticians' office then you would have found mountains and mountains of paper with numbers on and sums of squares on the ends of all the columns and rows. And then one checked them, double-checked them, cross-checked them, trying to make sure that you had actually got it right, because of course it was terribly easy to get them wrong. There were also purely practical things, such as the electromechanical calculators, which would jam regularly as clockwork if you tried to be a bit too quick with them.

An electromechanical calculator would be about 18 inches square, with a moving carriage on top. The keyboard had long rows, of 0s, 1s, 2s, etc. You could enter a two-, or perhaps three-digit number at the left-hand end of the keyboard and another at the right-hand end. An instruction to multiply that number by itself would then produce, on the moving carriage, the square of the left-hand number, the square of the right-hand number and twice the cross-product. These squares and cross-products could be accumulated. This could work well, provided the original numbers weren't too large and provided there weren't too many of them, when the sums could overlap. But it was fairly easy to get this wrong. The only electrical assistance was to drive the carriage up and down, the rest of it was basically a mechanical operation. Very, very time consuming. I can't actually date this. Later we had what was probably the very first purely electrical calculator with a programming capacity, called a Monroe Epic. It consisted of a box that was rather like the electromechanical calculator, and another larger box that contained four large printed circuits. There were two versions of the Epic, one with 14 programming steps and another with 42 steps. We, I think, had the former. The machine had four registers in which numbers could be stored, but all arithmetic operations were done between registers 1 and 2. Registers 3 and 4 were simply non-accumulating stores. The calculations that could be done even with the 42 programming step machine were thus very limited as many programming steps were used to switch numbers between registers. These Monroe Epic calculators would have appeared around 1967–68.

Computers were beginning to appear at about this time. I don't remember whether the unit sent me, or whether I went of my own volition to what was then Newport Tech and did a FORTRAN programming course on an Elliot 803. That must have been in the late 1960s. At that time the only computer in the university as far as I know that was available for people like me to use was a Stantec Zebra, which was actually a valve machine and where all the data and the programmes were inputed on paper tape, a real nightmare of a problem to handle. It was a very time-consuming business and you were really very restricted in the analysis that you could do by the sheer practical limitations. It could take days to do a multiple regression with this equipment, unless there were very few subjects, and just one or two variables.

Figure 53: Litton Monroe Epic 3000 keyboard and printing unit with free-standing calculating unit, introduced in 1967 as the first programmable printing calculator. © Nigel Tout.
www.vintagecalculators.com/

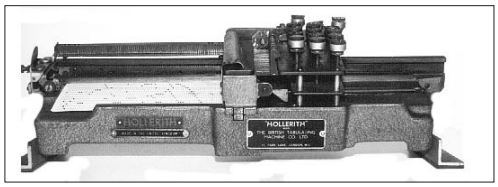

Figure 54: Hollerith manual card punch, *c.* 1930. Herman Hollerith patented a census machine in 1884, first used in the 1890 US census. He established the Tabulating Machine Company in 1896, later part of the Computing, Tabulating and Recording Company, the basis of the International Business Machines Corporation formed in 1924. © Computer Museum of America.
www.computer-museum.org/

Peter Sweetnam

[Data arrived] usually on bits of paper, sometimes it was decks of [punch] cards. We had some hand punches in the unit, the nearest equivalent was the old individual credit card machines, with a block of metal and a little keyboard, and you would just slide the card in and type away and the card came out punched with the appropriate holes. There was also another machine, a verifier, whereby you'd put the same card in and you would type the same stuff in again, and it would stop if you hit a key that was different from the hole that was actually punched in the card. Staff like Janie [Hughes] used to do that. Those machines must have been available when I started, because I am pretty sure we would have used those on a Hollerith counter-sorter machine. The Hollerith could be set to look at a particular column and it would then run all the cards through and sort them physically into piles according to what was punched in that column. It was far from foolproof, although a slick operator like Fred Moore, the person who mainly used the counter-sorter to sort the cards in piles, would pack them all all together and lift them up and check that he could actually see through the hole to make sure that the machine hadn't sorted any into the wrong place. The early machines just sorted the card, they didn't count. Having counters on a machine was a later addition. I think the one we had when I first arrived would have had counters on it as well.

I didn't do much of the actual data punching. I don't think that we ever had a large, half-electronic card punch machine like they used to have over in the university, banks and banks of them. I don't know whether Janie [Hughes] used to go over to the university and punch cards over there or up to the Heath. At a later stage we used the university department of what was then called Medical Statistics and Computing, of which Hubert Campbell was initially senior lecturer and later professor, when they actually appointed a professor, as there wasn't a professorship associated with the department originally. They had a sizeable department of punch card operators and at some later date and for most of the Caerphilly data we would actually pay them to enter the data for us. In the early days it would mean putting data onto punch cards and later we used direct entry, putting them onto files on the computer and then later on the floppy discs. People like Janie were expert at it, she was very, very fast. I got to the stage where I was quite fast on these machines, I could cope with probably 7000 or 8000 key depressions an hour. Janie would probably be 50 per cent quicker and the ones who were doing it all the time probably double that speed. A lot of data could be punched in a short period of time.

The counter-sorter could do cross-tabulations between variables. You could also make cross-tabs between three variables. If you imagine that you have got three variables, each with just three values each, then you got 27 different possibilities, which means you have got 27 different piles of punch cards. If another variable is added with four values, you are beginning to get yourself in one hell of a mess. Fred Moore was the obsessive one who could do that, because it really required somebody very orderly, very meticulous, to do it. Cross-tabs were about as far as you could go on a counter-sorter.

Then you would do the analysis – electromechanical calculator, pencil and paper. And it would be up as far as doing multiple linear regressions with two or three variables. If you look at the papers from that date, that's very much the limit, because that was the limit of what was do-able. Correlation coefficients weren't not too bad if you had 50 subjects, but by the time you had 200 to enter and to calculate the correlation coefficient, my memory is that you could put on the electromechanical calculator you could put the x value down the left-hand end of the keyboard, the right-hand value down the right-hand end and if you multiplied that number by itself, looking it as a whole number, you could get on the moving carriage the sum of squares of x at one end, the sum of squares of y at the other end and twice the cross product in the middle. Provided the numbers weren't too large and provided there weren't too many numbers, because eventually they would start overlapping each other. There was enough distance separating the numbers, providing the numbers weren't too large or too many. But by the time that you get to 200, 300 or 400 numbers, you not only had the problem of overlap on the carriage, but to enter all those numbers correctly, is a tedious task to put it mildly. Again one has to be a bit of an obsessive really.

Figure 55: Peter Sweetnam during the Caerphilly–Speedwell study, *c.* 1990.

THE MRC EPIDEMIOLOGY UNIT, 1974–90

Elwood: I intend to talk about the community studies. There were a number of strands in our thinking about the Caerphilly study. One was our increasing contact with John O'Brien,[129] a very, very bright and active platelet expert at Portsmouth, who is still working and publishing on platelets well into his eighties. Another strand was that David Bainton, who unfortunately isn't here, left the unit after working on gall bladder disease and went to Bristol to set up the Speedwell study. You will notice in our publications, it is very often Caerphilly and Speedwell.[130] He set up the Speedwell study and the initial hypothesis was to look at HDL (high density lipoprotein) cholesterol and the incidence of ischaemic heart disease. Very shortly after that we set up the Caerphilly study and they were set up as twin studies. I often call them that and people ask, 'Where did you get 2500 twins living in Bristol and in Caerphilly?' Well, of course, that's not what I mean. We set up these two studies in parallel, with the same methodology, the same laboratories, with the aim of comparing variables between the two areas, one with a high incidence of ischaemic heart disease, the other with a slightly lower than average ischaemic heart disease, or of combining the two cohorts and having almost 5000 subjects. I think the success of the Caerphilly studies, and they have been enormously

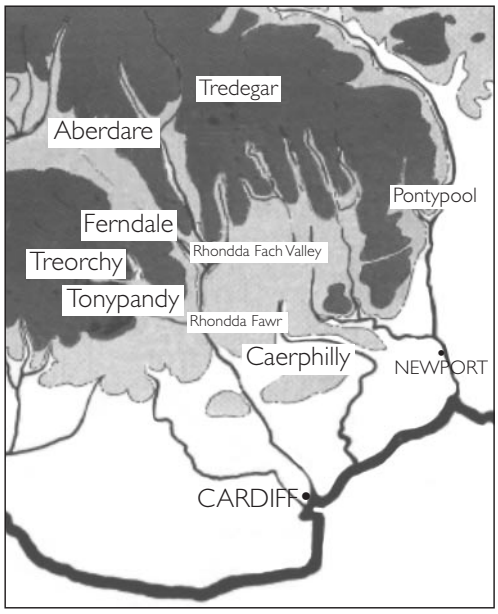

Figure 56: South Wales.

[129] See note 123, page 74, and photo on page 75.

[130] The Caerphilly Prospective Study, the fifth prospective study of cardiovascular disease in the UK and the second population-based study after the British Regional Heart Study, started in 1979. For further details of the study, including phases, see www.epi.bris.ac.uk/mrc-caerphilly/ (visited 25 February 2002). See, for example, The Caerphilly and Speedwell Collaborative Group. (1984) Caerphilly and Speedwell collaborative heart disease studies. *Journal of Epidemiology and Community Health* **38**: 259–262. Baker I A, Eastham R, Elwood P C, Etherington M, O'Brien J R, Sweetnam P M. (1982) Haemostatic factors associated with ischaemic heart disease in men aged 45 to 64 years. The Speedwell study. *British Heart Journal* **47**: 490–494. Bainton D, Burns-Cox C J, Elwood P C, Lewis B, Miller N E, Morgan K, Sweetnam P M. (1982) Prevalence of ischaemic heart disease and associations with serum lipoproteins in subjects aged 45 to 64 years. The Speedwell study. ibid. **47**: 483–489. Yarnell J W, Patterson C C, Sweetnam P M, Thomas H F, Bainton D, Elwood P C, Bolton C H, Miller N E. (2001) Do total and high density lipoprotein cholesterol and triglycerides act independently in the prediction of ischaemic heart disease? Ten-year follow-up of Caerphilly and Speedwell cohorts. *Arteriosclerosis, Thrombosis, and Vascular Biology* **21**: 1340–1345. Greenwood R, McCarron P, Elwood P, Shlomo Y B, Bayer A, Baker I, Frankel S, Ebrahim S, Murray L, Smith G D. (2001) The incidence and aetiology of stroke in the Caerphilly and Speedwell Collaborative Studies I: methods and incidence of events. *Public Health* **115**: 4–11. *idem.* (2001) The incidence and aetiology of stroke in the Caerphilly and Speedwell Collaborative Studies II: risk factors for ischaemic stroke. ibid. **115**: 12–20.

Figure 57: Janie Hughes, *c.* 1968.

Figure 58: Marion Jones, *c.* 1968.

successful, depends on a number of factors. One was the teams that we had, and I would like again to pay tribute to Janie Hughes and Marion Jones, who were meticulous in getting a high response rate and in the quality of the data that were collected, and then Peter Sweetnam, in the meticulous analyses that he performed. They were set up 20 years ago and we are still seeing the men. The men in the Speedwell study are being seen currently and no doubt plans will shortly be formulated to see the Caerphilly men again. We published some 120 papers on ischaemic heart disease[131] and we've looked at a whole range of things from homocysteine, to haemostasis, to lipids, to lifestyle factors, to psychological factors with John Gallacher and Stephen Stansfeld.[132] A tremendous range of data was collected and looked at in a predictive way. Then in the last two to three years Janie Hughes and I have identified every stroke and TIA (transient ischaemic attacks) as completely as possible in the Caerphilly study and with help from people in Bristol, we have done the same in the Speedwell study. We now have a complete list of strokes and TIAs and we will be able to examine prediction by all of these risk factors which were originally collected in relation to heart disease. We will be able to look at them as predictors of stroke and TIA. I see this study as making a tremendous contribution over and above what we have already published on ischaemic heart disease. I mentioned one of the reasons for its success and that was the team that we had and their dedication to these studies, but in addition we set out to enlist collaboration as widely as possible, and there is a tremendous number of people in this room and elsewhere, who have received either data from the studies, or who have given us ideas to work on, in collaboration with them, or have actually come down and collected data with us, like Stephen Stansfeld.

[131] Dr Peter Elwood wrote: 'By March 2002 there are 166 published papers and about 17 with journals. The early papers were on heart disease, but now many are on stroke and cognitive decline.' Note on draft transcript, 27 March 2002.

[132] See, for example, Gallacher J E, Yarnell J W, Sweetnam P M, Elwood P C, Stansfeld S A. (1999) Anger and incident heart disease in the Caerphilly study. *Psychosomatic Medicine* **61**: 446–453. Stansfeld S A, Sharp D S, Gallacher J E, Yarnell J W. (1992) A population survey of ischaemic heart disease and minor psychiatric disorder in men. *Psychological Medicine* **22**: 939–949. Stansfeld S A, Gallacher J E, Sharp D S, Yarnell J W. (1991) Social factors and minor psychiatric disorder in middle-aged men: a validation study and a population survey. ibid. **21**: 157–167.

Stephen came down repeatedly to Cardiff and collected data on psychosocial factors and I think the level of collaboration that we enlisted for that study was really quite remarkable. Its value lies not just in what the epidemiology unit put into it, but I listed over 40 collaborators in one of my summaries of the study, all of whom had put a substantial amount of work into either the ideas, the collection of data, or the analysis of the data.[133] Our policy, certainly under my direction, was to enlist as many collaborators as possible, and to be as free and open with our data as possible. We collaborated with David Strachan who gave us some marvellous ideas on chronic infection and we released stored serum samples for that and a number of papers have come out.[134] This is the story again and again of the Caerphilly and the Speedwell studies, and again if I may pay tribute and express my thanks to Stephen Frankel, George Davey Smith, Andy Ness, Yoav Ben-Shlomo, that all those data are going over to Bristol and will continue to be worked on and exploited, but that's after 1990.

Dr Stephen Stansfeld: I'd like to follow up Peter Elwood's comments on collaboration in the Caerphilly study. I first became involved in the Caerphilly study in 1983 when I was working with Professor Michael Shepherd at the general practice research unit in the Institute of Psychiatry. I was becoming interested in the relationship between psychological disorders and coronary heart disease and he told me, 'Go and see Peter Elwood in Cardiff,' which I did and Shepherd actually accompanied me at that time. Thus began an involvement with the Caerphilly study that I have had ever since. I was always impressed with the very high standard set by the Epidemiology Unit in the collection of data in the Caerphilly study, and as Peter has mentioned but underplayed, his generosity in allowing the data to be used by others. He always, I feel, had a

[133] See Appendix for the list of collaborators provided by Dr Peter Elwood.

[134] See, for example, Strachan D P, Carrington D, Mendall M A, Ballam L, Morris J, Butland B K, Sweetnam P M, Elwood P C. (1999) Relation of *Chlamydia pneumoniae* serology to mortality and incidence of ischaemic heart disease over 13 years in the Caerphilly prospective heart disease study. *British Medical Journal* **318**: 1035–1040. Strachan D P, Mendall M A, Carrington D, Butland B K, Yarnell J W G, Sweetnam P M, Elwood P C. (1998) Relation of *Helicobacter pylori* infection to 13-year mortality and incident ischemic heart disease in the Caerphilly prospective heart disease study. *Circulation* **98**: 1286–1290.

Figure 59: Receptionist takes survey details, *c.* 1965.

real respect for the cohort, he wasn't just going to allow the data to be used willy nilly. He always made it quite clear that one had to come up with very clear scientific ideas, some clear hypotheses to test before one was going to be allowed any access to the cohort and I think that this was particularly so if one was going to be measuring things like mental illness. There was a certain amount of suspicion, I think, that had to be overcome, perhaps understandably, before I was going to be allowed to go out and do some psychiatric interviews on cohort members, which I subsequently did. But I have overwhelming gratitude to Peter and the team for allowing me to be involved. It has allowed me to look at all sorts of interesting things, like the relationship between coronary heart disease and psychological disorders. Also, at that time one of the variables being considered as a potential risk factor for coronary heart disease was noise exposure, and that's allowed me to piggy-back on to that study,[135] to look at road traffic noise exposure and psychological disorder longitudinally, there have been very few opportunities to do so. Altogether, I am very grateful to Peter and I hope that there will still be opportunities for collaboration with this wonderful team and data set.

Doll: We have plenty of other things to discuss, so let's go on to another subject. Dr Burr, I think you have done some work on asthma[136] that you might like to comment on.

Dr Michael Burr: I joined the unit in 1970. Peter Elwood was not at that time Director, Archie Cochrane was, but Peter Elwood saw me first and advised me at the interview to be sure to bring in the word 'randomized' somehow, somewhere, so I duly did and was appointed, for which I am very grateful. And we did some work on asthma, surveys of asthma, and randomized trials of asthma, particularly in relation to

[135] Stansfeld S, Gallacher J, Babisch W, Shipley M. (1996) Road traffic noise and psychiatric disorder: prospective findings from the Caerphilly study. *British Medical Journal* **313**: 266–267.

[136] For another example of postwar developments in asthma treatment, see Reynolds L A, Tansey E M. (eds) (2001) Childhood asthma and beyond. *Wellcome Witnesses to Twentieth Century Medicine,* vol. 11. London: The Wellcome Trust Centre for the History of Medicine at UCL.

elimination of house dust mites from the bedding.[137] The early trials of that were not particularly good, looking back, and not surprisingly we didn't get rid of the mites, and therefore we didn't improve the asthma. Later on we did randomized cross-over trials, with new bedding versus old bedding, which did show an effect, and I have had an interest in asthma ever since.

Elwood: That's even briefer than the talk about aspirin. Michael did some beautiful surveys of asthma in schoolchildren over time,[138] and I think his evidence of the recent increase, recent doubling and more, of the prevalence of asthma among school children is among the best in the whole country and perhaps internationally. He has also gone on to do studies of asthma in different countries, so the unit made quite a big contribution. But my disappointment is that there are no new hypotheses to test and so although one can continue the work, we really need some fresh thinking on asthma and I don't know of any.

Burr: I think there are new hypotheses, all right. They are coming out all the time as David Strachan can support me in saying. I think the one I like the most is that it's all due to being too hygienic for our own good,[139] I think that's quite an attractive hypothesis, but there are plenty of others, indoor air pollution and other things. We did a survey in 1973 of asthma in school children, which I was able to repeat again in 1988 in the same area, using the same methods, questionnaire and an exercise challenge test, very easy to do, great fun to do, and over an interval of 15 years it did demonstrate an increase, as others have shown since.[140]

Professor David Strachan: I guess that I am representing the respiratory epidemiology community as much as

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[137] Burr M L, Neale E, Dean B V, Verrier-Jones E R. (1980) Effect of a change to mite-free bedding on children with mite-sensitive asthma: a controlled trial. *Thorax* **35**: 513–514.

[138] Burr M L, Eldridge B A, Borysiewica L K. (1974) Peak expiratory flow rates before and after exercise in schoolchildren. *Archives of Disease in Childhood* **49**: 923–926.

[139] Strachan D P. (1989) Hay fever, hygiene and household size. *British Medical Journal* **299**: 1259–1260. Cookson W O C M, Mofatt M F. (1997) Asthma: an epidemic in the absence of infection? *Science* **275**: 41–42.

[140] Burr M L, Butland B K, King S, Vaughan-Williams E. (1989) Changes in asthma prevalence: two surveys 15 years apart. *Archives of Disease in Childhood* **64**: 1452–1456.

anything. I think what impressed me when I first met Michael [Burr] in 1985 was that at that stage it was clear that people were having a great debate about how to measure asthma. Asthma epidemiology was becoming dominated by clinicians who had a great interest in measuring precisely, but in a rather cumbersome manner, the reactivity of the airways to various compounds, many of them pharmacological. What attracted me about the work that Michael had done was that here was a very simple, acceptable, free-running exercise test, which was not only measuring something that was easily applied in a population survey, but was also measuring a natural stimulus to asthma which was actually a relevant challenge to the child and a relevant challenge in terms of the burden of public health. I think the intervening decade has vindicated that general approach of using a simpler tool in larger numbers rather than more complex tools in smaller numbers.[141] We are seeing now with asthma epidemiology a tendency to revert to measuring physiological challenges as much as pharmacological challenges, partly for ethical reasons and partly because we feel that they can be applied in more representative population samples. I would very much like to see a third survey of children in south Wales to see whether asthma has increased further over the period since 1988. I always say there's a prize awaiting the person who shows that asthma is not increasing any more and decides that it is on the decline. No one has yet published a paper to say so.

Wade: Can I just ask a question about the further history of those children that you saw in the first survey. Does their asthma get worse as they get older or does it get better? Or does it not change?

Burr: We did follow them up, though we never published the results, and I believe the questionnaires are still in existence. They did in fact get better individually. I am speaking now from memory, not having done a formal analysis, but it was clear at the time they were getting better, 12 is about the sort of age from which you

[141] See, for example, Asher M I, Keil U, Anderson H R, Beasley R, Crane J, Martinez F, Mitchell E A, Pearce N, Sibbald B, Stewart A W, Strachan D, Weiland S K, Williams H C. (1995) International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *European Respiratory Journal* **8**: 483–491.

tend to improve. That was not a follow-up study, though I have done follow-up studies since of a cohort of children and we are actually analysing one now,[142] which was set up when I was with the Epidemiology Unit.

Wade: Why do they get better?

Burr: An interesting question. Airways get bigger with age, but that's probably not the only reason.

Elwood: My contact with the Ministry of Health was Bill Berry from the iron studies, and they [MoH] asked us later when school milk was stopped [1972] if we would evaluate the benefit of school milk, welfare milk. We set up two studies actually.[143] Welfare milk in those days was supplied to all pregnant women and all children under five and to all school children, but it was very severely curtailed, it wasn't actually stopped, but it was very severely curtailed [in 1972]. We set up randomized controlled trials in both those groups. We selected 1000 pregnant women and arranged for the tokens to be issued to them and to all their children under five – at Ministry of Health expense. The 'index child' from that pregnancy was followed to the age of five, half were supplied with milk tokens and half were not, and we monitored growth in those children and we collected a lot of further information. At the same time, we ran a trial in school children where we selected schools by a number of well-defined criteria to get the most nutritionally vulnerable children and we set up a randomized controlled trial in something like 600 children, seven to nine years of age. Half of them were supplied with school milk and half were not. Just to

Figure 60: Janie Hughes, *c.* 1966.

[142] Lowe G L, Burr M. (2001) Undiagnosed and untreated wheezing in a cohort of adolescents with a family history of allergic disease. *British Journal of General Practice* **51**: 664–665.

[143] In 1968, the provision of free milk was abolished in secondary schools, and in 1971, Baroness Margaret Thatcher, Education Secretary from 1970 to 1974, introduced legislation to end free school milk for children between the ages of seven and 12. By 1980, free milk for five to seven year olds had also come to an end and welfare milk for those on Family Income Supplement/Credit ceased in 1988. European countries managed to block an attempt by the EC to end its subsidy in the early 1990s. See Baker I A, Elwood P C, Hughes J, Jones M, Sweetnam P M. (1978) School milk and growth in primary schoolchildren. *Lancet* **ii**: 575. Baker I A, Elwood P C, Hughes J, Jones M, Moore F, Sweetnam P M. (1980) A randomized controlled trial of the effect of the provision of free school milk on the growth of children. *Journal of Epidemiology and Community Health* **34**: 31–34. Elwood P C, Haley T J, Hughes S J, Sweetnam P M, Gray O P, Davies D P. (1981) Child growth (0–5 years), and the effect of entitlement to a milk supplement. *Archives of Disease in Childhood* **56**: 831–835.

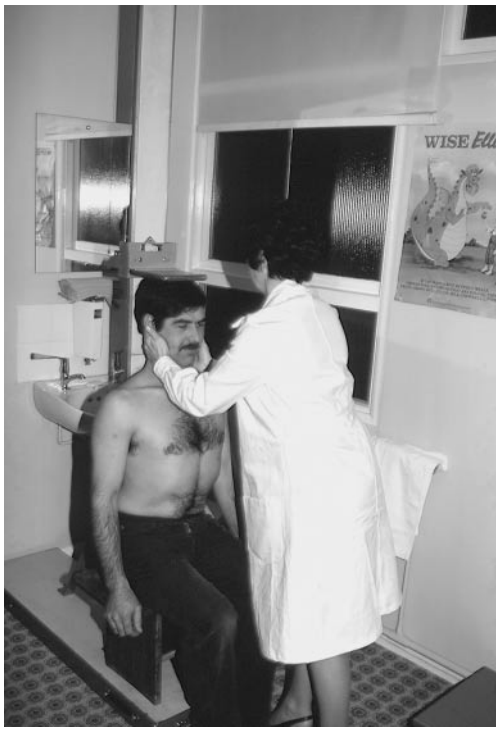

Figure 61: Marion Jones measures sitting height with a Holtain stadiometer in the Caerphilly study, *c.*1980.

make a point in passing about the Department of Health's response to our answers, we had shown that iron added to bread was of virtually no benefit, but it is still added to white flour in this country. We later showed that school milk was of benefit to the most vulnerable children, but it was never reintroduced, so the effectiveness of that research can be called into question.

Here I must pay tribute to Janie Hughes and to Marion Jones, who is not here, and other members of the unit. Those data were collected, filed and coded meticulously, and all those records have gone over to Bristol now. One very exciting development of that work is that the team in Bristol is picking up a number of our surveys, including those surveys on children, growth and nutrition of children, and are doing further studies on the children. The children who were seen while they were intrauterine until the age of five are now aged 27, and a survey is just about coming to completion.[144] Early markers of diabetes and heart disease are being sought in those young adults and they no doubt will be surveyed in another ten, another 20 years to see the development of ischaemic heart disease. It is just one of the greatest thrills that virtually all the data, thousands of stored blood samples, serum and plasma samples, are all going over to Bristol, and I would like to take this opportunity to thank Stephen Frankel, George Davey Smith, Yoav Ben Shlomo, Andy Ness, and others back in Bristol, that they are taking over our surveys and basic studies and are continuing that work, it's tremendously thrilling.

Doll: We have purposely decided that the discussion today ends in 1990, so we won't have any extended discussion of the great contribution that's being made in Bristol now by taking over the ERU studies, but it has been nice to hear this recognition by Peter Elwood of what is being done in Bristol now and his gratitude to them. I am sure we all feel the same.

Hughes: As Dr Elwood said, I kept all the records, I didn't actually do any of the visiting of the children and their mothers, but what I did do is that at the end of the

[144] Montgomery A A, Ben-Shlomo Y, McCarthy A, Davies D, Elwood P C, Davey Smith G. (2000) Birth size and arterial compliance in young adults. *Lancet* **355**: 2136.

study I measured every single child with a Holtain stadiometer[145] and this is my claim to fame, this is the one thing I was trained in. I was sent to St Thomas' Hospital to be trained how to measure the children properly. And similarly in the milk supplementation study in schools I measured the children with a stadiometer, also skin-fold thickness. I was actually shown how to do it properly. In those days we didn't just work Friday afternoons and Monday mornings on survey, if we had 2000 people to see, we just worked every single day until we had seen the whole lot, there was no let up. We worked very hard and very long hours, and we just continued seeing people, until we had seen the whole of the population or the cohort, whatever it might be.

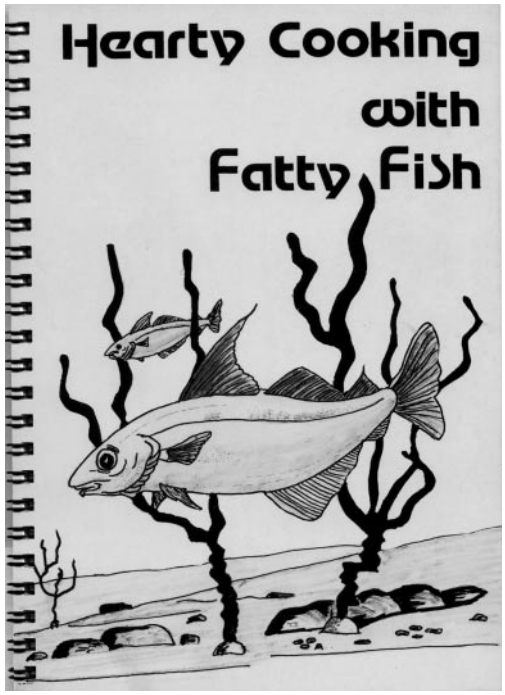

Figure 62: Cookbook issued to subjects in the diet and reinfarction trial (DART), prepared by Elaine Vaughan-Williams, Senior Dietician, no date, *c.* 1990.

Burr: The DART study arose as part of a number of studies on diet and heart disease. Not all of the unit studies were in the Rhondda or in Caerphilly. For example, we set up a cohort of 10 000 people who were health food shoppers, a somewhat eccentric group, but they are still being followed up in Oxford and interesting findings are coming out of that. We also conducted a number of small randomized controlled trials on subjects like fish, fibre, alcohol, vitamin C, coffee and decaffeinated coffee, looking at short-term end-points in relation to various physiological indices of heart disease. Then out of that we embarked on what was a very ambitious trial, looking at men who had just had a myocardial infarction to see whether secondary prevention could be undertaken by means of dietary change. In the end we enlisted 2000 men who'd just had a myocardial infarction. They were randomized in a factorial design, so that there were three separate factors that they could have any combination of, or none at all: advice to eat less saturated fat; secondly, to eat more cereal fibre; and thirdly, what was then quite a new idea, advice to eat oily fish.[146] I should say that this

[145] Dr Peter Elwood wrote: 'The Holtain stadiometer was a highly accurate instrument for measuring standing or sitting height, later with a digital readout. Along with other Holtain instruments including skin-fold and bone calipers, it was made by an engineering firm in west Wales.' Note on draft transcript, March 2002. See Figure 61 page 86.

[146] Dr Michael Burr wrote: 'DART was a single study. We conducted eight small randomized controlled trials on various dietary/nutritional factors, but it would be incorrect to describe them as "in DART".' Comment on draft transcript, 8 April 2002. See Burr M L, Fehily A M, Rogers S, Welsby E, King S, Sandham S. (1989) Diet and reinfarction trial (DART): design, recruitment, and compliance. *European Heart Journal* **10**: 558–567.

Figure 63: Ann Fehily, *c.* 1980.

idea came out of a meeting that Ann Fehily (who was then a nutritionist with the unit) had attended, and she came back saying that people were talking about the importance of oily fish and this seemed a rather cranky idea, but we thought that if we were going to set up a trial, we might as well test something new, and be a bit original. So we set up this trial and 2000 men were admitted to it. The advice to eat less saturated fat fell on deaf ears, the south Wales men were addicted to their fats and wouldn't change. Advice to eat more cereal fibre was taken up, but sad to say, it did them no good. In fact, to our dismay, the results went in the wrong direction. Mercifully they did not achieve statistical significance, but it caused us some anxiety. But oily fish was the right stuff to give them, because it produced a 29 per cent reduction in all-cause mortality within two years of starting.[147] I have always felt that that was something worth doing, as oily fish is pleasant to eat, you don't have to live on it, just two good meals a week is sufficient, as long as you eat the right sort of fish, not the stuff you get from fish and chip shops.

Doll: I think you should tell us the 95 per cent confidence limits of your 29 per cent reduction.[148]

Burr: I am sorry I don't have them with me. In those days that was not quite so important as it is now, but I assure you they were quite respectable.

Wade: I think it has made quite an impact on some of my cardiological colleagues anyway. Brian Prichard spent a whole lecture on it. My short-term memory is badly affected. I need whatever it is that is good for Alzheimer's.

Burr: Excuse me, oily fish may do that as well you know!

Elwood: Aspirin is even better!

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[147] Burr M L, Fehily A M, Gilbert J F, Rogers S, Holliday R M, Sweetnam P M, Elwood P C, Deadman N M. (1989) Effects of changes in fat, fish and fibre intakes on death and myocardial reinfarction: diet and reinfarction trial (DART). *Lancet* **ii**: 757–761.

[148] See Fehily A M, Burr M L, Phillips K M, Deadman N M. (1983) The effect of fatty fish on plasma lipid and lipoprotein concentrations. *American Journal of Clinical Nutrition* **38**: 349–351. Fehily A M. (1985) Dietary fibre, fish and blood lipids. *Nutrition Bulletin* **10**: 36–42. Rogers S, James K S, Butland B K, Etherington M D, O'Brien J R, Jones J G. (1987) Effects of fish oil supplement on serum lipids, blood pressure, bleeding time, haemostatic and rheological variables. A double blind randomised controlled trial in healthy volunteers. *Atherosclerosis* **63**: 137–143. Burr M L. (1990) Oily fish and heart disease. *Practitioner* **234**: 398–401.

Burr: Oily fish is good natural stuff.

Figure 64: Ann Fehily, Michael Burr and Elaine Vaughan-Williams during the randomized controlled dietary trials, *c.* 1989.

Waters: We are asked to try to say in the Witness Seminar what was the achievement of the unit, and obviously at face value, the achievement of the Epidemiology Research Unit was to conduct a large number of population studies, in a wide variety of diseases that were all fairly common, or common enough to be significantly represented in random samples of the general population. The unit wasn't the first to do that, there were a number of other studies done earlier,[149] and the technology that was required to do these studies was available to anyone at that time. The situation was, of course, changing, data handling, computers and so on, were evolving during this period of time, but I think the achievement of the unit was not just to do this variety of studies, but to back them up with scientific credibility. Many people have mentioned the high response rates that were necessary. We have also heard the examples of the reproducibility of chest X-rays, the validity of measurements and eliminating bias,[150] and bias was one thing I was very conscious of, at the unit, throughout the time that I was there. Everything that was done must be done to a very high standard, and I think it would have been quite easy, with different personnel at the unit, to have used the technique of random samples of the general population, but done rather sloppy research, with smaller numbers and lower response rates, creamed off all sorts of areas, but in a second-rate way.

I think that the achievement of the unit really was this very critical attitude to all the data that it collected and particularly to the elimination of bias. This was due to Archie's attitude and to the inclusion of statisticians on the unit's staff.

Tyrrell: Can I just add that as Charles Fletcher's arrival

[149] For example, the Framingham Heart Study of the US Public Health Service. See Dawber T R, Meadows G F, Moore F E Jr. (1951) Epidemiological approaches to heart disease. *American Journal of Public Health* **41**: 279–286. The Framingham Heart Study started in 1948, recruited 5209 men and women aged between 30 and 62 years in Framingham, Massachusetts, USA, and was directed by the National Heart Institute. The subjects returned every two years for further tests and a second generation group of 5124 children of the original sample was recruited in 1971. See www.nhlbi.nih.gov/about/framingham (visited 4 September 2002).

[150] See Last J M. (1983) *A Dictionary of Epidemiology*. Oxford: Oxford University Press, 10.

at the unit has been brought up, that I worked with Charles Fletcher in a small way much later and I could see then something that he had brought from the unit which was his great respect for first-class statistical work, and I remember him saying to me once, 'There's this young man, he's very clever with numbers, and he'll actually be able to work out what all these data that we have collected means'. This was in connection with a bronchitis survey,[151] and I had been pumping in data along with other people, and it had just become a mountain of data. This bright young man was Richard Peto. So he not only appreciated his skills, but he spotted another man with potential.

Thomas: We ought to pay tribute to Peter Sweetnam, he can't be here today. He's the statistician at the unit, he has been at the unit from 1966 up to now, as we are finally decommissioning the unit, and officially closing next week. Peter [Sweetnam] has worked on virtually all the major projects that we have been involved in. [See table on page 38]

It has been alluded to by David Tyrrell that doctors very often are good at collecting data and then rather slide up to the statisticians and say, 'Well we have got this, can you look it?' 'What does it all mean?' Well, we haven't been like that at the MRC but in a sense, like many research units, I think it is always hard to get the amount of statistical back-up that you would like for a lot of the projects. There are often competing researchers, collecting a variety of data, and in a sense we are all subject to the different fashions of ways of looking at data and though it might be very easy for us to suggest another way of reanalysing the data, it can involve them in a lot of work. And Peter Sweetnam has got on with this determinedly over the years. He has been thorough, and I think for many of us, as doctors, we are not used, very often as clinicians, to dealing with such errors in such detail and such exclusive definitions

[151] See Fletcher C M, Elmes P C, Fairbairn A S, Wood C H. (1959) The significance of respiratory symptoms and the diagnosis of chronic bronchitis in a working population. *British Medical Journal* **ii**: 257–266. The questionnaire is reproduced on pages 265–266. See also Medical Research Council. (1966) *Questionnaire on Respiratory Symptoms and Instructions for its Use.* Dawlish, Devon: W J Holman. Fletcher C M. (1975) The natural history of chronic bronchitis. *Community Health* 7: 70–78.

and so on, and statisticians can be very helpful in getting us to think rigorously and logically about what we are doing. Peter Sweetnam has done that and I think all of us who have worked with him would agree. He is co-author on around 100 papers from the unit, including the early aspirin studies. It is interesting to look at the early analyses, they were virtually worked out long-hand on sheets of paper with long lines, as was the asbestos follow-up, because some of these early analyses were done without the benefit of the modern computing systems and packages and so on, and it took a lot of very detailed calculating and often, as most statisticians complained, of tidying up our data before they could analyse it.

Elwood: Perhaps I am anticipating, but if I may just say here that one of the things that I find very interesting is the totally different styles of management that Archie and I had. Archie almost never called a unit meeting, whereas I had a weekly unit meeting.

Archie seemed to give tremendous encouragement to individual people in the unit to get on with their work and their ideas and develop them, but I always took the view that the whole unit had combined responsibility for everything that was done within the unit. So the style of management was totally different, but Archie had this marvellous ability of just coming round occasionally and seeing me and then seeing others at different times and he would just put his finger on a weakness or on an opportunity that we hadn't already spotted. He was enormously stimulating in that way.

Weddell: I actually differ from Peter when he said that Archie wasn't a good manager. I think he was a very good manager. He wasn't in the unit a great deal as Janie [Hughes] has just mentioned because he was away so much, doing so many things, but the days he was there he used to come in and see all of us, in our rooms, in his own time, and so if you had a problem, you could actually talk to him, there was never any question of queuing up to see Archie, he came round and saw all of us.

Figure 65: First meeting of the International Corresponding Club (renamed the International Epidemiological Association in 1959), held at the Hotel Noordsee, Noordwijk, The Netherlands, 1–6 September 1957. In this selection, L to R: Back row: (Sir) John Brotherston, Henry Makoveu, Xavier Gellé, Charles Fletcher, John Lee, Maurice Backett and Alice Stewart. Second row: George Reader, Richard Doll, R Hitchens, Lester Breslow and R F L (Bob) Logan. Sitting: William Pickles, Joan Faulkner and Herman Hilliboe.

Pemberton: I was a contemporary of Charles Fletcher and Archie Cochrane, but I didn't have anything directly to do with that unit, but we did meet at the International Epidemiological Association (IEA) meetings.[152] I remember that Charles Fletcher, for example, gave a paper on his bronchitis questionnaire,[153] which so many people afterwards adopted in epidemiological studies of bronchitis. We used that in the flax byssinosis survey that Peter Elwood referred to just now. I know Peter was glad when I introduced him to Archie Cochrane, but when he went to south Wales to work with Archie it was a great loss to us in the Department of Preventive and Social Medicine at Queen's University, Belfast. He took to epidemiology like a duck to water and I remember coming into the department one morning when he told me that he had been out knocking on doors in a street off the Grosvenor Road, saying to the ladies who answered the door, 'Could I come and take some blood please?' and he got away with it. I was a bit alarmed when he told me this. I said, 'Well, Peter, you may be accused of assault, rape and goodness knows what' and suggested he should take a social worker with him.

Elwood: The study had a 97 per cent response rate.[154] It represented a sample of women on the electoral role of Belfast, and Archie was very impressed, and I am sure that was one of the reasons that he agreed to give me a job.

Tudor Hart: We really have to think about collective organizations and how you enlist the support of a population and the sort of thing that Owen [Wade] was talking about as these sort of studies eventually became

[152] See Pemberton J. (1998) Social medicine comes on the scene in the United Kingdom, 1936–1960. *Journal of Public Health Medicine* **20**: 149–153. See also the Society for Social Medicine website, (www.socsocmed.org.uk/HistoryPhoto.htm) for a photograph of the 1958 IEA meeting in Dublin, provided by Professor John Pemberton, which includes Sir Richard Doll and Dr Joan Faulkner among the original members. The *British Journal of Social Medicine* was founded in 1947 and became the *British Journal of Preventive and Social Medicine* from 1953, edited by Lancelot Hogben, Thomas McKeown and Ian Taylor (1953–59); and by Archie Cochrane, John Knowelden, and Alice Stewart (1959–78). It took its current title, the *Journal of Epidemiology and Community Health,* in 1978. See Murphy S, Smith G D. (1997) The *British Journal of Social Medicine*: what was in a name? *Journal of Epidemiology and Community Health* **51**: 2–8.

[153] Chronic bronchitis was one of the special subjects reviewed in the *Report of the Medical Research Council for the Year 1959–1960* (Cmnd 1422. London: HMSO, 1961, 22–26). See also note 162.

[154] See note 75.

the General Practice Research Framework (GPRF)[155] studies, we found that when we did the pilot studies in Glyncorrwg using Owen Wade's methods and Archie's methods – public meetings and explanations and answering these really very sensible questions about 'Why me and not him?' – we found that nobody else would do it. None of the other GPRF practices thought this was a sensible way to go about things and they thought that miners and mining communities were a special environment and nobody else could do this, and that's not so. So it isn't only a matter of these anecdotes. I think the truth is that the most telling anecdotes are really very characteristic about what it is that motivates people to take part in studies. I wanted to end up with what didn't happen, but could have happened, from this foundation which was laid in the 1960s. The Rhondda Fach had a population of around 10 000 at that time, and the repeated studies, particularly where the samples were large and overlapped, meant that you were accumulating a more and more complex profile of all sorts of different social and clinical problems and you were accumulating them over time. And had the unit staff persisted with that, we could have ended up with a population that was very much more completely described, where all the different studies would have fed into one another and been multidimensional, and it could have linked up with clinical care and it could have linked up with a periphery of excellence, of clinical excellence. That never happened and the studies moved out of the Rhondda Fach over to Caerphilly and I do suspect, because at the time I was there fatigue was beginning to set in in the population, that researchers were beginning to find that they were getting lower responses, as people repeatedly found themselves in the samples. So the answer was to move house and start with a new population, and I don't think that would

Figure 66: Eleventh scientific meeting of the International Epidemiological Association, Helsinki, Finland, August 1987. L to R: Professor John Pemberton, Dr Joan Faulkner (Lady Doll) and Professor Sir Richard Doll attended the first meeting in 1957.

[155] The Framework was created for the mild hypertension pilot study in 1973, which led to a full-scale trial from 1977 to 1985. See Medical Research Council Working Party. (1985) MRC trial of treatment of mild hypertension: principal results. *British Medical Journal* **291**: 97–104. Miall W E, Greenberg G. (1987) *Mild Hypertension: Is there pressure to treat? An account of the MRC trial. Medical Research Council Working Party on Mild to Moderate Hypertension*. Cambridge: Cambridge University Press. For the growth of research in general practice, see, for example, Reynolds L A, Tansey E M. (eds) Research in General Practice. In Tansey E M, Christie D A, Reynolds L A. (eds) (1998) *Wellcome Witnesses to Twentieth Century Medicine*. vol. 2. London: The Wellcome Trust, 75–132.

have been necessary if we'd found a way to link up clinical care, primary care, in the Rhondda Fach with research studies. I think a failing that Archie had, and that really was common to practically everybody associated with the unit at that time, was a feeling that there was a completely unbridgeable gulf between the data requirements for epidemiology and the data requirements even for very good clinical medicine. In view of the appallingly low quality of clinical medicine when you were seeing people at two- to five-minute intervals in the Rhondda it was just unthinkable that this could be incorporated into the research design, but I don't think it was unthinkable, and I think we ought to be starting to think like that now.

Dr Andy Ness: One point. The story of the shillings. D'Arcy Hart describes how the MRC sent shillings [half crowns, 2s.6d., 12½p] on the train to the miners in, I think it was, the 1937 survey.[156]

Wade: Can I say that I agree very much with what Julian [Tudor Hart] said, and I can't remember ever paying any miners. We worked up enthusiasm for the surveys. The older man would bring in the younger man, that's what I remember, because we had taken a lot of trouble about the survey publicity that we did in these areas.

One other comment that I would like to make about the interviews of these patients. We really learnt an awful lot. I remember John Gilson, I think it was up in Whitehaven, or perhaps up there on the coast in north-west England, one of the pits that goes right under the sea and we, Gilson and Philip Hugh-Jones, somebody else and I, all had to interview the people before they were X-rayed. They would have a short ten-minute interview. One of the interesting things was that three of us, when we asked the question about whether they had ever worn a gas mask underground, we only had about 1 per cent who told us that they had worn a mask, but John Gilson had about 8 or 9 per cent in his lot, and the reason for it was that John had worked in

[156] See discussion on page 11. See also MRC Special Report No. 243 (1942), note 5, page 35 for a description of the tuberculin test. The three special reports were published before Archie Cochrane was repatriated by the British Army shortly after VE Day.

the RAF during the war, was interested in gas masks and obviously he put over this question in a slightly different way from us. He said, 'Have you ever worn a gas mask?' and there was obviously something in the way he said it or the influence he had. So he got chaps that would say, 'Oh yes, I did wear one for a day, last Christmas time' or something like that. He got positive results, while we got negative results. I think the accuracy of such questions are very interesting, from the point of view of survey work.[157]

Weddell: Tudor Hart was mentioning the factor of survey fatigue and this particularly affected the Rhondda, and I am sure someone else is going to tell this story, but there was a Mr Jones who came up for the fifth time in a survey and he saw Archie because he was one of the refusals, and he said, 'How is it that my name has been drawn so many times?' and Archie said, 'Well we put all the names in a hat, and we shake them up very, very well, and then draw out a certain percentage at random'. 'Oh I see,' said Mr Jones, 'A bloody funny hat!'

Figure 67: Marion Jones does an ECG in the Caerphilly study, *c.* 1989.

Strachan: I am interested in asking a question of those who were working with the unit in those relatively early days as to whether there was a concept of a career in epidemiology? This is a question that has really posed a lot of problems over the last 20 years; whom do we wish to recruit as epidemiologists, how do we encourage them to acquire a set of skills, and is there a career structure that they can pass through? I would be interested to hear the perspective of those working for the unit, and perhaps people from the MRC who were interested in overseeing the units, whether they feel there was a career structure, whether the unit offered stepping stones to a career and what the concept was at this time of the epidemiologist in training for the 1970s and 1980s?

Waters: I was thinking of that very point when I was considering this meeting and my recollection is that I enjoyed the work there and thought that it was important. I didn't have any particular view about

[157] For further details on observer error, see note 37.

where it was leading me; I just stayed on, for over five years, because I found it stimulating and exciting. I was not aware of any career structure in epidemiology and was surprisingly unconcerned.

Doll: Professor Pemberton, would you like to comment on that? Or can I tempt you to comment on something else?

Pemberton: In the International Epidemiological Association (IEA), we met a lot of these people each year, and that sort of mixing and meeting of people helped them to transfer these ideas and to inspire each other.[158]

Dr Shaun Murphy: Could I ask the general question about the fact that obviously during the war years and the immediate postwar years, the MRC emphasis on occupational health research was a very important directional influence, but into the 1960s, the 1970s and the 1980s, to what extent was government policy and MRC policy influencing the choice of subjects for surveys?[159] Peter Elwood has mentioned the Department of Health's interest in the milk studies and the iron studies, but were most of the projects that were undertaken the result of an individual's research interests, or were there examples of the Government, government bodies or the MRC influencing the choice of subjects?

Elwood: I would say it was very unusual for a statutory body of any kind to influence research helpfully. I think one of the things we all set ourselves was to watch the literature, to go to meetings, and to pick up ideas that were not only worth researching but feasible, and these were difficult criteria to apply. Usually government bodies saw questions that were either not worth answering or were not feasible to answer. I often refer to those two areas of work, the iron deficiency and the school milk, but I always add the outcome of them, that iron is still added to your white flour, and most of our deprived children do not get school milk although they

[158] See note 152.

[159] Murphy S. (1999) The early days of the MRC Social Medicine Research Unit. *Social History of Medicine* **12**: 389–406. See also discussion on page 26.

would benefit from it. The Ministry of Health, or whatever department, paid no attention to the results.[160]

Doll: I can't resist following up the lead given by Peter with an experience of my own. Following the Rothschild recommendations when so much money was taken away from the MRC and given to the Department of Health for commissioning research, I was phoned by the Chief Scientific Officer of the Department of Health, 'Would I be interested in having under this commissioning system a cancer epidemiology unit?' Well I had quite a lot of support for my department, but I thought a little more support wouldn't harm so I said, 'Well, yes, all right if you give us the money'. So they gave me quite a lot of money, and then that was that, they didn't say anything about doing any work. The whole time I had that unit, I had two requests from the Department of Health to do work, one of them was so obvious that I had been doing it already for the past two years, and nearly had the answer, and the other was impossible to do. After some time, because the Department of Health refused to give career appointments to scientists, I succeeded in getting the unit switched from the Department to the Imperial Cancer Research Fund. But I think some other people may wish to provide some personal experiences in response to the question that we were asked.

Booth: Well, as somebody who sat on the Medical Research Council in the post-Rothschild years I can tell you exactly what happened at MRC level. There was, if I remember, a biennial meeting, maybe annual, but what happened was that the chief chap at the Department of Health, who in those days was Sir Patrick Nairne, came to a meeting of the MRC and they had a list of things they had been provided with by the MRC, which the MRC was already doing. They went down to the meeting and said, 'Right, under the money paid over by the Department of Health, we'll have this, we'll have that, and this, that and the other'.[161] It was

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[160] See discussion on page 85.

[161] For further discussion on funding changes, see Reynolds L A, Tansey E M. (eds) (2000) Clinical Research in Britain, 1950–1980. *Wellcome Witnesses to Twentieth Century Medicine*, vol. 7. London: The Wellcome Trust, 48–60.

already happening, it wasn't the Department of Health making a plea for certain things to be done, it was the Department of Health choosing to fund what the MRC was already doing and saying, 'We'll put it under the budget we support'. Now there are two very distinguished MRC administrators [Faulkner and Howarth] behind me who might wish to comment on that. Knowing them, I don't suppose either will wish to, but the pressure on them to speak is considerable.

Faulkner: I remember one or two things that were suggested by a group of medical officers from the Department of Health when we had a meeting with them to discuss commissioning research. One was that they said beds were being used a lot in the National Health Service to look after people disabled by disseminated sclerosis, multiple sclerosis, and would we do research on that, please. And so we told them that we already had a unit in Newcastle that was devoting most of its time to research on that subject[162] and also that people all over the world were hoping for a Nobel Prize by solving the problem of multiple sclerosis, so we couldn't really think of anything else to do. The other was research on incontinence, which was also a great problem. And they said we had to set up a committee, I don't remember what the outcome was, but we set up a committee on research on sphincters. Do you remember any more about that, Sheila?

Howarth: No, I don't think it went much beyond having a couple of conferences on the subject. We had various recurring chestnuts, didn't we? Tonsillectomy was one. It was a great expense to the NHS and the health departments, so would the MRC do a trial to decide whether tonsillectomy in children was worthwhile? Low back pain was another, wasn't it? And how to stop children smoking, that was another one. Those are just three I can think of off the cuff, and they were recurrent.[163]

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[162] See Thomson A L. (1975), note 31. For details of the Demyelinating Diseases Research Group, later Unit, established in 1961, see page 365.

[163] See, for example, Department of Health and Social Security, Working Group on Back Pain. (1979) *Working Group on Back Pain: Report to Secretary of State for Social Services, Secretary of State for Scotland.* London: HMSO. A L Cochrane, Chairman. Office of Population Censuses and Surveys. (1983) *Smoking among Secondary School Children.* London: HMSO.

Booth: If I could just comment, because the only man I knew who took seriously the MRC's consideration of incontinence was Tom Meade at Northwick Park and Tom Meade for my money is an epidemiologist who managed to put mathematical certainty on to events that I would never even have dreamed of thinking about in that sense, he really is quite remarkable. What he did over low back pain was to set up a study in which he compared the success at dealing with low back pain of the chiropractors in the local neighbourhood and he compared them with what the doctors in the hospital were doing.[164] If I remember rightly, the chiropractors came off best.

Tyrrell: They were the physiotherapists doing the physical therapies that the doctors had prescribed, as against the chiropractors using their methods.

May I raise another possible example of this pressure from government? It was the use of vitamin C in the prevention and treatment of colds. In that example there was a mixture of forces on the Common Cold Unit.[165] One was the literature, both newspaper publication, and the publicizing of a double Nobel Prize winner from California,[166] who said that vitamin C would cure colds and cancer as well. And there were also then questions asked in the House [of Commons] about why weren't we issuing vitamin C to everybody in the country? We did limited trials that showed no effect, and I got a letter from the said Nobel Prize winner saying that we hadn't proved it beyond doubt, we'd used too small numbers. I just wondered whether Peter [Elwood]

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[164] For biographical details, see page 133. See also Meade T W, Dyer S, Browne W, Townsend J, Frank A O. (1990) Low back pain of mechanical origin: randomised comparison of chiropractic and hospital outpatient treatment. *British Medical Journal* **300**: 1431–1437. Meade T W, Dyer S, Browne W, Frank A O. (1995) Randomised comparison of chiropractic and hospital outpatient management for low back pain: results from extended follow up. ibid. **311**: 349–351. Fairbank J, Davies J, Coupar J, O'Brien J P. (1980) The Oswestry low back pain disabiity questionnaire. *Physiotherapy* **66**: 271–273.

[165] See, for example, Tansey E M, Reynolds L A. (eds) (1998) The MRC Common Cold Unit. In Tansey E M, Christie D A, Reynolds L A. (eds) *Wellcome Witnesses to Twentieth Century Medicine*. vol. 2. London: The Wellcome Trust, 209–268.

[166] Pauling L. (1976) *Vitamin C, the Common Cold and the Flu*. San Francisco: W H Freeman and Co. See also Moertel C G, Fleming T R, Creagan E T, Rubin J, O'Connell M J, Ames M M. (1985) High-dose vitamin C versus placebo in the treatment of patients with advanced cancer who have had no prior chemotherapy. A randomized double-blind comparison. *New England Journal of Medicine* **312**: 137–141. Goertzel T, Goertzel B. (1995) *Linus Pauling: A life in science and politics*. New York: BasicBooks.

was subjected to any of this sort of pressure when he set up a clinically based study in a natural population?

Elwood: We actually ran two trials, one on the amelioration of the symptoms of a cold and the other on the prevention of cold during two winters. We actually set those up as piggy back research. I've already mentioned the study of 1000 pregnant women and their infants up to the age of five [the milk study].[167] That was an intensely boring study because the nurses made the same measurements again and again and again, so we added in a lot of other research projects. We did work on sleep and we did work on vitamin C in the mothers just to keep the interest up and to hopefully improve the quality of the data. We were using a gram of vitamin C a day throughout the winter in one trial, and in the other trial a gram once they had their first sniff [of a cold] in the other trial, telling them to take a gram a day to see how long the symptoms lasted. Neither trial showed any effect at all.[168] But that wasn't a response to any request from any official body, that was just our reading of the literature and perhaps the papers.

Tyrrell: Maybe I can come in there, because Tom Meade did take on a 1000-, or was it 800-person study based in Harrow and in Salisbury, which showed very clearly that there was no measurable effect of a large dose vitamin C and the possibility of statistical error was much reduced by the larger numbers.[169]

Doll: Well, if we think over all the things we have heard this afternoon and what we have known ourselves beforehand, what conclusions can we come to about the main contributions of the ERU and what criticisms do we have of its work? In what way did it fail to achieve the objectives for which it was set up that would be of use to

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[167] Elwood P C, Haley T J L, Hughes S J, Sweetnam P M, Gray O P, Davies D P. (1981) Child growth (0-5 years), and the effect of entitlement to a milk supplement. *Archives of Disease in Childhood* **56**: 831–835. See also pages 86 and 123.

[168] Elwood P C, Hughes S J, St Leger A S. (1977) A randomized controlled trial of the therapeutic effect of vitamin C in the common cold. *Practitioner* **218**: 133–137. Elwood P C, Lee H P, St Leger A S, McLean Baird I, Howard A N. (1976) A randomized controlled trial of vitamin C in the prevention and amelioration of the common cold. *British Journal of Preventive and Social Medicine* **30**: 193–196.

[169] Tyrrell D A J, Craig W, Meade T W, White T. (1977) A trial of ascorbic acid in the treatment of the common cold. *British Journal of Preventive and Social Medicine* **31**: 189–191.

other people in the future? I think it would be helpful in the closing minutes of this discussion to see if we can draw anything out in relation to those two points.

Tudor Hart: Well, I am taking aspirin and eating oily fish twice a week, so I will still be around in five years' time, when you can have another of these meetings with the survivors of this cohort, if the Going for Gold project[170] takes off in the south Wales valleys, which is modelled entirely on what Richard [Doll] has just said, lessons from ERU and the PRU. You can't get primary care doctors any more in south Wales valleys. Primary care doctors are small business men, that's what they have to be, and anyone who has set up a small business in the south Wales valleys now, prospectively, would need their head tested, so we don't have any volunteers. So at last we could start taking primary care as seriously as we have always taken secondary care, so we could have the integrated research and periphery of excellence that you have in clinical trials in hospitals, where you have centres of excellence and research. You would have the excellent data sets, but they would be applying to the whole population and you could start approaching things like they seem to be doing in Iceland, making the human genome available ultimately for the benefit of the human race and immediately for the benefit of shareholders. All sorts of extraordinary possibilities open up. It looks as though it actually might happen, because part 1 of that salaried service for GPs is having Welsh Office endorsement – the British Medical Association (BMA) is not opposed to it – for the valleys, not for fox-hunting practices, but for the valleys that they don't want to go to; they want them off their consciences. The rest of the bundle, the research part, meets some desperate needs of the universities serving the valley areas that need to prove to the medical school that you don't have to be a doctor to do research, in fact it might even be an advantage not

[170] Hart J T. (1999) *Going for Gold: A new approach to primary medical care in the south Wales valleys.* Third revision. Pontypridd: Welsh Institute for Health and Social Care, University of Glamorgan. Originally appeared in 1997 as a Socialist Health Association discussion paper. Dr Tudor Hart wrote: 'Going for Gold was officially endorsed by the Wales Assembly Secretary for Health and Social Services, Jane Hutt. In 2002 a primary care project along these lines was initiated in Ebbw Vale, jointly by the Gwent Primary Care Group and the University of Wales College of Medicine, directed by Dr John Watkins.' Comment on draft transcript, 18 April 2002. See www.wales.gov.uk/subisocialpolicy/content/comm_care_hutt_e.htm (visited 18 April 2002).

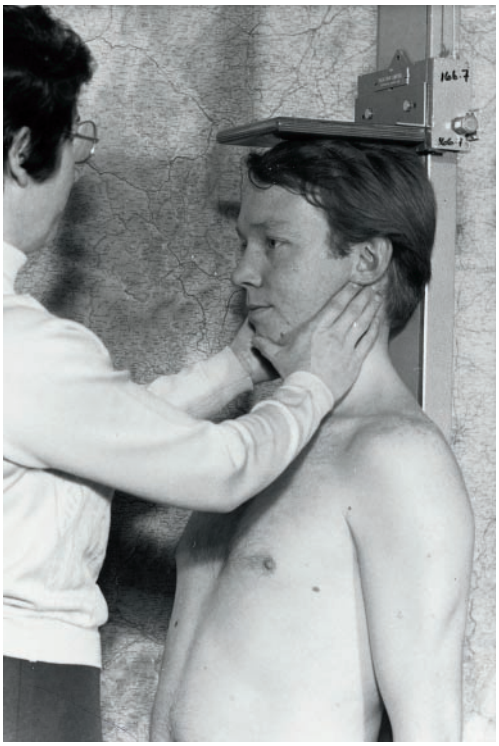

Figure 68: Hugh Thomas measured for standing height by Marion Jones, 1978.

to be a doctor because you don't have to go through the process of corrective learning to lose all the vanities of doctors. So I think it is going to happen and it is entirely based on these lessons, positive and negative, that Archie and company and Peter set in motion, and if it happens of course the Caerphilly population is going to be one component of it and another component – if the press isn't here and it can't get into print soon enough for it to matter – Dr Sengupta's practice in Ferndale, which was the birthplace of the Rhondda Fach studies. It's quite likely that the first, or one of the first, places that we'll be able to get our salaried doctors of the Going for Gold scheme operating in will be exactly there, which will have tremendous symbolic significance and the sort of people who take decisions about the real money are mainly thinking in symbolic terms. That is about as far as I can get. I am serious, I think if this comes off that will be about the time, in about five years, to see whether we can actually make this happen, but it has got extraordinarily wide backing from a remarkably diverse range of people, including quite establishment sort of people.

Thomas: Looking back to the period, I see one of the big contributions made by Professor Cochrane, and Professor Elwood later, is actually looking at a population and defining illness there and the extent of the illness. I am sure this is very important to general practice, because in the early debate about high blood pressure they'd been looking at hospital populations. In glaucoma they were looking at people who were presenting at eye out-patients, and so actually getting out there and seeing what was in the community has actually created a very valid view of why general practice research is so important and, as Aneurin Bevan pointed out, how much pathology is out there in the population that people weren't presenting to the medical practitioners because it was just too expensive for them to get treatment. The PRU and ERU have contributed to general practice research and our knowledge of disease.

Secondly, I think there are practical lessons. We did collect a vast amount of data, and it is always difficult in any unit to keep in step with the statistical analysis and the use of it, and it is good that sometimes this data can be reused and re-presented later on. Some people make

accusations of 'data dredging' and so on, but if the data is there and has the answers to questions then being asked, it is perfectly valid to go back and use it. I looked in fact at some of Peter Elwood's data from the byssinosis survey in Northern Ireland, he actually looked at rope workers, but didn't present it in a published form. I wrote it up virtually 20 years later and published it in a hygiene journal, because it was relevant to African countries that have a rope industry.[171] An important thing is to try to use the data effectively and have the statistical back-up when you have got it and statisticians are perhaps a more difficult breed to get hold of now, but constant dialogue with them was very important. I think the hours that the early fieldworkers worked, that if any of them were to decide to start suing the unit for having worked so long, they might have a case, but that wasn't the attitude then. There was a real sense of, 'There's a problem or there's a survey that we are going to do' and a real pride in their work. We're beholden to all their families as well, because there was a family price to pay for many of them who were out for such long hours all the time doing it. But it was through that leadership and that small team enterprise really, and I think perhaps a fourth lesson is when you are evaluating a unit, you can't always evaluate just on papers, on the analysis of the research profile and the impact of the publications and so on, there is also the evaluation of the people who are training there, coming on, being influenced. The unit touched many people and there are famous people right across the world who've been inspired through working in the unit, albeit for brief attachments. If we think in terms of value for money, there was a lot of good work in the ERU and also future work that will take place from it in terms of some of the local genetic studies, and from the long term follow-up of the different populations. These are such high-quality data they will be used well into the next millennium, and that has sort of added to the value the units (PRU and ERU, later EU) have given.

Waters: Probably the main contribution that the unit had is to the natural history of the disease, or prognosis,

[171] Thomas H F, Elwood J H, Elwood P C. (1988) Byssinosis in Belfast ropeworks: an historical note. *Annals of Occupational Hygiene* **32**: 249–251.

and it is because of such studies that the unit became interested in screening for disease, something that I don't think we have mentioned up to now this afternoon. I wonder if I am right in thinking, was it the interest in screening and whether it was effective that broadened Archie Cochrane's interest in health services research and 'effectiveness and efficiency'?

Elwood: I would like to comment and confess, because you [Doll] ask what are the failures of the unit. Well, I have thought a lot about why the unit was closed. It closed on my retirement and a small team was kept on and is finishing this month [March 1999]. But I would like to acknowledge that I think I failed the unit. Archie was an enormously high-profile figure. Somebody referred to his attendance at clinical meetings where he was enormously stimulating to a point of irritation, he made a lot of enemies, but he challenged clinicians.[172] I was not like that at all, I was very much a hands-on epidemiologist, out with the team, not going round the world, not collecting honorary degrees, I couldn't have kept up what Archie Cochrane did, but I do believe, if I may say and not be thought too modest, I think the quality of the data while I was director was very, very high indeed, and again I pay tribute to the team who worked with me and kept up a high response rate, very careful data, very careful coding, and storage of the data. I think the benefit of the unit has been immense but is going to continue because Stephen Frankel and his team have got all the data, all the samples, and are going to continue the work. I was hands on, I was out in the field, I wasn't going round meetings, boosting up the unit and so on, and I feel in some ways I let the unit down because it closed on my retirement.

Figure 69: Peter Elwood photographed in front of an Ordnance Survey map of Wales in the Caerphilly study, *c.*1989.

Wade: In rather similar thinking to yours, Dr Elwood, I don't think they set up the Pneumoconiosis Research Unit the right way. I think it was too isolated, and should have been established in close association with the Welsh National School of Medicine, but it wasn't. It was out at Llandough Hospital and was very separate and Charles Fletcher, although I was very fond of Charles and he did

[172] Hill G B. (2000) Archie Cochrane and his legacy: An internal challenge to physicians' autonomy? *Journal of Clinical Epidemiology* **53**: 1189–1192.

a tremendous amount for the unit, but he didn't really understand this Welsh community at all. One of the consequences was that we didn't get the support that the unit deserved and should have had from people like Jethro Gough, a pathologist.[173] He was one of the first people to show convincingly that coal dust really did damage people's lungs, and he did it by conducting a post mortem on all the trimmers who had died. The trimmers were the chaps who worked in the ships at Cardiff docks, and when they poured in their truckfuls of coal they stood round with great sheets of steel and bounced the coal into the four corners of the hold, otherwise there was the danger that a ship could tip over if all the coal went in one side only. It was Jethro Gough who convincingly showed that coal dust was toxic to people. Up until then it was always thought that it was the silicosis and the hard headers, the boys who cut the rock through to the coalface, who got silicosis. It was thought that they were the ones who were really in danger.

One of the consequences of the fact that the PRU was set up in isolation was that later on when it came to the time of closing it, it should have expanded 15 years earlier into other problems of occupational health, besides just the dust diseases. Let me say that it was because I knew that that Pneumoconiosis Unit was shutting down and there were so few occupational health units in universities, that I was able to persuade Robert Hunter, Vice-Chancellor of Birmingham University, to produce the money so that we could get Malcolm Harrington appointed, and to establish the Department of Occupational Health there.

Booth: Can I just say that I think what Owen Wade has just said is highly arguable. I don't want to say that I totally disagree with everything that he said. There are a lot of questions here. The question of the isolation of the MRC units have been of great advantage for some units and I think the Central Middlesex Hospital [London] is a very good example of that, it worked extremely well there.

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[173] Gough J. (1940) Pneumoconiosis of coal trimmers. *Journal of Pathology and Bacteriology* **51**: 277–285. Gough J. (1968) Fibrosis in coal workers. *Archives of Environmental Health* **17**: 836. Ryder R, Lyons J P, Campbell H, Gough J. (1970) Emphysema in coal workers' pneumoconiosis. *British Medical Journal* **iii**: 481–487.

I think that the PRU when it was set up owed a great deal to Jethro Gough, a pathologist who had advised the south Wales trades unions. The miners' trades unions and Jethro Gough convinced the Government and the MRC that something had to be done and that dust was not just silicosis but it was a big problem for coal miners.[174]

Wade: I'd agree with that but the trouble was that Jethro didn't really collaborate, he and Charles Fletcher didn't get on. I thought it was a great pity, this.[175]

Faulkner: I thought it was strange that Owen Wade said that Charles didn't get on with the local Welsh people and didn't understand people, but I have heard him address a meeting of Welsh miners and trade unionists in a brilliant manner and they gave him some sort of gold medal, but I can't remember exactly what it was. They were devoted to him.

Booth: I agree.

Doll: We heard one of the values of these seminars was to get contradictory statements made for the recording in history, so its has been interesting to have them. I have spoken too much and I don't want therefore to summarize my own views of what I think contributed to what went wrong in so far as anything did go wrong. I'd like other people to do it.

Tyrrell: I would like to think that the unit would be regarded as an example, particularly in the years that

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[174] See Industrial Injuries Advisory Council. (1973) *Pneumoconiosis and byssinosis.* Cmnd 5443. London: HMSO. Chairman H W Crane.

[175] Professor Owen Wade wrote: 'Despite Chris Booth's protest I know that both Charles Fletcher and Philip Hugh-Jones did brush up medical people, in Cardiff and in the Medical School, the wrong way, at any rate in the first five years or so of the unit's life. I know that Jethro Gough, a great friend of my father as our two families went on several holidays abroad together, was very upset by them. I think he felt that he was upstaged by them in some way and did not get the recognition he felt he deserved for his work. I think it might have helped if the unit had been set up with closer relationships with the Medical School and in particular with Gough's Department of Pathology. Outside the unit it was a difficult time for me. I had to listen to a lot of complaints about the unit from people in the Medical School who were colleagues of my father, the senior surgeon at the Cardiff Royal Infirmary. I often had to defend the unit against undeserved criticism – I fear not too successfully as I was regarded with suspicion as a sort of "apostate" because I had joined the Unit. What I wanted to say, before I was interrupted by Chris, was that I thought a lot more credit should be given to John Gilson, because he was a very wise and sensible person and he did a lot to improve the relationship of the unit to medical people in Cardiff and also with the trades union leaders and (important before nationalization of the industry) with colliery owners – and I think Charles Fletcher, if he was still with us, would be one of the first to agree with this.' Letter to Sir Richard Doll, 25 March 1999. This letter will be included with the documents deposited with Archives and Manuscripts, Wellcome Library, London.

Peter [Elwood] has been describing, of having a well-studied, well-understood cohort of people followed over a period of time. At times, I used to think of the Common Cold Unit as a resource like the Daresbury Synchrotron.[176] Such places can be a 'central facility' to which people with extra technical skills and understandings of pathology, chemistry, and so on, could come to answer different questions. They could use the corpus of understanding of the patients and their society to do a study to answer questions which on their own neither group could ever do. Probably the epidemiologists would not develop the high-technology unless they were in a high technology centre. Bringing the two together would, I think, be the way in which things should be done in the future. The other advantage of a cohort, I believe, is that cohorts followed up over a long period of time later yield information that you weren't thinking of originally. I am thinking perhaps of David Barker looking at cohorts who had been studied as babies decades before.[177] I would hope that people would continue to see the central importance of very well-studied groups of people in practically any problem in pathology and medicine.

Davey Smith: One short comment, following on from Peter's comment about the unit being shut, is that in the UK there is not now any similar outfit carrying out epidemiological studies on general population samples.[178] Many of the studies currently being carried out are in very special populations, civil servants for example, and the generalizability of the findings you then can make to other populations is in doubt. Also there is no central resource teaching field epidemiology that people go through to learn how to do field studies in the UK. From my short one-and-a-half-year connection with the unit in the 1980s, it was incredibly valuable to be able to go with people who could show

[176] Daresbury Laboratory in Cheshire is operated by the Council for the Central Laboratory of the Research Councils. See www.clrc.ac.uk/Home/ (visited 8 August 2001).

[177] Barker D J P. (1994) *Mothers, Babies and Disease in Later Life*. London: BMJ Publishing Group. Barker D J P. (1992) *Fetal Origins of Adult Disease*. London: BMJ Publishing Group.

[178] Hawthorne V M, Watt G C M, Hart C L, Hole D J, Davey Smith G, Gillis C R. (1995) Cardiorespiratory disease in men and women in urban Scotland: baseline characteristics of the Renfrew/Paisley (Midspan) study population. S*cottish Medical Journal* **40**: 102–107.

you how to do field epidemiology and I was rather surprised when I went to the London School of Hygiene and Tropical Medicine and did the then Rolls Royce Master's degree in epidemiology, after having worked with the unit, that the basic aspects of fieldwork just weren't covered in those sorts of courses. The best way of learning fieldwork is by being involved in those sorts of studies and understanding it in that way. Perhaps symptomatic of that is also the shift of epidemiology into something that is attached to the evidence-based medicine movement, which of course is very important, but maybe leaves this space, which the unit and similar places occupied, of work with representative population samples. There's no obvious replacement for the unit in Britain at the moment.

Strachan: The decision by the MRC to close the Epidemiology Unit begs a question of why the MRC wants to have an epidemiology unit or epidemiology units and I think you could come up with several answers to that question. One would be that there is a role for a community laboratory in which people with particular tests or particular investigational tools can apply them to a relatively representative sample of the general population, find out normality and abnormality, find out about prediction, find out a little bit about relationships over time and test a few aetiological hypotheses. So there is in a sense the model which was set by Framingham[179] and which has been to some extent followed with Caerphilly. Secondly, there is the role of hypothesis generation to 'fly the flag' for cause being as important as mechanism. Thirdly, there is the role of training and developing skills and (I would argue) creating some sort of career for people to become card-carrying epidemiologists. Those are three aspects which it seems to me, having heard the discussion, the MRC unit fulfilled in small ways over its period in office, but the question is whether the MRC views any of those three as being worthy of continued support in the future. That is a question that the MRC has to address, not just retrospectively in relation to the decision to close the unit in Cardiff, but also perhaps in

[179] See note 149.

its decision about the continuing support for epidemiology in relation to the other two units which are being reviewed at this moment. So I would like to put in a plea for some creative thinking about why it is we might need an MRC-supported epidemiology unit, as distinct, of course, from substantial programmes of investigation which the MRC would normally fund as projects and research programmes in their own right.

Weddell: I shall be very brief. I think one of the great benefits of siting the unit in Cardiff is that the populations both in the Rhondda Fach and Caerphilly are relatively stable and so you can do long-term studies of these populations. If you tried to do this in London, it would sink without trace, you couldn't do it. You do need relatively stable populations.

Doll: There's one study that the unit carried out in 1979, it was a correlation study which was initially set up to look at socioeconomic factors in relation to mortality from ischaemic heart disease in particular, but also mortality very widely, and this study came up with two findings. One was that in developed countries the infant mortality rate was inversely related to the number of doctors per 1000 of the population, a finding that I know intrigued Archie and which he often spoke about. It was statistically highly significant, but he never got a satisfactory explanation as to what it was due to. The other finding was an inverse relationship between alcohol consumption, or rather wine consumption, in this particular study, and the mortality from ischaemic heart disease.[180] I think we haven't discussed that study, because we now have an opportunity for putting its findings to effective use, and I would therefore like to thank all the speakers very much for their contribution, close the meeting and tell you that wine awaits.

[180] See note 202. See also St Leger A S, Cochrane A L, Moore F. (1979) Factors associated with cardiac mortality in developed countries with particular reference to the consumption of wine. *Lancet* **i**: 1017–1020. See Chart 2, page 121.

Archie Cochrane

In 1974 I retired to a desk in the attic at 4 Richmond Road and Peter Elwood became Director of the unit. It was largely as a result of his kindness that I stayed on. He was very encouraging, hoping that I would continue with two main lines of research: the 20-year follow-up studies of the various populations on which we had done cross-sectional surveys in the 1950s and the investigation of factors associated with mortality in 18 developed countries. For my part, I arranged for Peter to receive enough money from the Abbotshill Trust, with which I had a close association, to employ

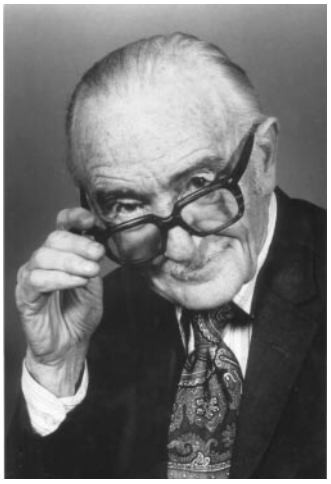

Figure 70: Archie Cochrane, *c.* 1970s.

an additional statistician for three years. I had not succeeded in persuading the MRC that an epidemiololgical unit needed as many statisticians as epidemiologists, with programmers to support them... Then came a dreadful day in 1977. It followed a routine MRC review of the unit that had not gone particularly well. There was something of a cloud over the place. Knowing a little about the review body, it was not difficult to suspect a degree of unhelpful personal bias in some of its reporting. Eventually Peter Elwood gained the necessary permission to show me the report, and to my horror it recommended that I should cease to work there. The committee felt that my presence was having a deleterious effect on the unit...The next few days were dreadful. I had, as far as I remember, a lot of silly ideas. I also drank too much. I considered selling Rhoose Farm House and buying a flat in Cardiff or Galashiels...Slowly the clouds lifted. The MRC finally ruled that I could continue working at 4 Richmond Road. I am very grateful to some unknown friends who gave me support at such a critical time. I am particularly grateful to all members of the unit who signed a letter supporting the view that I should be allowed to stay on.[181]

Peter Elwood

When I was appointed Director, I remember somebody said that I had fire in my belly, and that was one of the strands of thinking that allowed me to become Director of the unit after Archie Cochrane. Who could follow Archie Cochrane? Certainly the whole style of the unit changed very, very markedly, but I think one of the benefits was the on-going budget, the rolling budget. In the early days money was very free and I was asked if I needed any more staff, or could I do with some more money? I think we did things very, very efficiently, because while we were doing the Caerphilly study I was also running studies on lead, we were also doing the final follow-up of subjects in relation to byssinosis, and Janie and Marion would work on Caerphilly for three days a week and the other two days would be in Bolton and Oldham, or up in the valleys taking blood for lead studies. I think the cost of the various studies was very much less than if funding had been for the complete study on its own. We made very efficient use of time and resources. I think also that the unit attracted enthusiasts. Fieldworkers are rather a speciality, and to have a love of going out and meeting people and accepting the challenge of getting a high-response rate demands a certain kind of person and we seemed to get those people. We also could give them a career, and a career structure; the medical and the non-medical people, and the support staff, they all had careers structures within the MRC and permanent posts most of them. This was very beneficial to the development of an area of research, rather than just a one-off project. There was continuity, and I knew that when we followed up Caerphilly, we wouldn't have to start recruiting another set of staff for phase two and phase three. We would have the same people going back, who knew the area and were known by the men. That was a tremendous advantage.

John Yarnell

When I came to the unit it was rather interesting that Archie was sharing the same room as Peter Elwood. It was rather amusing at the time, as Archie was President of the Faculty of Community Medicine as well. Now Peter Elwood had just been appointed as unit Director [1974], Peter had a telephone with an intercom system there and Archie used to sit at the other end of the table in his old room, sharing this room with Peter Elwood, and he used the wall phone there. The MRC secretariat paid a visit and I think they saw this arrangement and they had 50 fits and they tried to expel Archie from the unit. We drafted a letter,

[181] See note 20, 253–255.

petitioned everybody to sign to request that Archie should be allowed to stay because he was not interfering with Peter Elwood's work and he was contributing his own expertise to the unit. They [MRC] did let him stay but on the proviso that he moved upstairs to the attic. So Archie went up to the attic at Richmond Road and carried on his work on the Rhondda follow-ups with Fred Moore, and others, who had mainly worked for Archie in the past. I should say that Fred Moore was an extremely valuable fieldworker. He was a trained nurse and did all the ECGs meticulously for the Caerphilly survey, at least for phases 1 and 2. He retired finally after that, well into his seventies I think. After this they [ECGs] were done by Marion Jones, another invaluable fieldworker.

Hugh Thomas

Working with Archie Cochrane when he was writing his biography there [at the ERU], it did always strike me, I am afraid, at how unfortunate a relationship he had with Jethro Gough. You could not mention that chap's name without Archie almost having a convulsion, but also there was his real sense of disappointment that the research did leave the MRC and go to the Coal Board and I just tried to listen dispassionately to him when he was talking about it. But in a sense, you can reflect historically, I suppose, that if Archie Cochrane had stayed entirely in the area of dust disease, we might have missed an awful lot of his other work in health services research and general epidemiology that he did in the Rhondda. So I think that, in a sense, his disappointment was actually turned to a very good advantage.[182]

John Yarnell

One of the first surveys of urinary incontinence that had been carried out in a population sample[183] *was done in the Caerphilly district and surrounding villages. We went up further towards the Rhondda, but not right into the valley. The Rhondda was a special coal-mining community and that was why Archie used it so much, because of course they were exposed to coal dust and he was interested in pneumoconiosis and then tuberculosis.*

Figure 71: John Yarnell during the Caerphilly study, *c.*1980.

Peter Elwood

It became increasingly difficult [to get posts approved], but I did manage to get a nutritionist, Ann Fehily, who put a superb amount of very high-quality work into Caerphilly, and that was a new post. I also got John Gallacher, with very great difficulty. Now he's a very, very bright original thinker and he put a marvellous slant on psychosocial factors into Caerphilly and later on cognitive function. He also set up a study of stress management within patients with angina, then the MRC pulled the plug on that. But it certainly became increasingly difficult to get more staff, but in the early years it was very, very easy, and I was asked whether I would like more staff and in the early days I said no I don't think I would want to cope with a bigger team. But later, I can think of one or two people that I would love to have appointed or to have offered an appointment to. And the MRC were just not willing at all.

Peter Elwood

Caerphilly was launched in 1979, and the first phase took until 1983, it took four years to see the men. John Yarnell chose the sample, using the electoral register, and some of the doctors lists, but we wanted to get a complete sample of men within a

[182] Hugh Thomas, speaking at the Witness Seminar, 'Pneumoconiosis in Coal Workers', 9 November 1994, unpublished.

[183] Yarnell J W G, Voyle G J, Richards C J, Stephenson T P. (1981) The prevalence and severity of urinary incontinence in women. *Journal of Epidemiology and Community Health* **31**: 71–74. Yarnell J W G, Voyle G J, Sweetnam P M, Milbank J, Richards C J, Stephenson T P. (1982) Factors associated with urinary incontinence in women. ibid. **36**: 58–63.

certain age range, 45–59 years of age, so a questionnaire was sent out, asking a few general medical questions, and asking the age of the respondent, and that was a key factor in identifying this particular age group within the community, and letters were sent out to virtually every male on the electoral roll, in order to pick the sample, and get a complete sample between those age groups. We set up the study in church halls, the YMCA and in doctors surgeries, moving around the town, and seeing people in the different areas. We had one dedicated person who visited the men and tried to persuade them to come to the clinic, and in the clinic we had six stations as we called them, where different tests were done. We piloted all this, timed everything and tried to envisage delays in the procedure so that the men went through as smoothly as possible. The record keeping and so on really developed ad hoc *as we went along, and one of the very, very big mistakes we made was that we used numbers going up from 1001 upwards and then we discovered later that Speedwell, the study in Bristol, had done the same, and so there was an overlap in the numbers, and that was bitterly disappointing. I had always suggested within the unit that each research topic had a unique number, and for instance our study on school children was, if I remember rightly, 32s, 33s, and 34s, and those numbers came first and then 01, 02, 03, for the different subjects. Janie and I developed this system and if we picked up a questionnaire we were able immediately to say which study it came from. But nobody thought much of that when Caerphilly was being set up, and we just used straight numbers, and then we got into a terrible situation where Caerphilly and Speedwell had been stored together and it has been very, very difficult to unscramble the two sets.*

Peter Sweetnam

Selwyn St Leger was the official statistician to the Caerphilly study when it initially started up. John Yarnell had done a variety of studies in Caerphilly, and this was essentially just another one. His initial study was the wide age range study of 700-odd men aged 30 to 69 years. My memory is that it was a unit review in the early 1980s, which said, 'Well, that's an interesting piece of work, but it's nothing like big enough, make it larger'. Hence it was expanded into the size that it became [2500]. It was about then that I probably started getting involved, I guess partly because Peter's aspirin work had finished. I think the paper on the second aspirin trial in the Lancet[184] *was some two-thirds of the way through the first phase in Caerphilly. I think that would be about the date of my first involvement with the study. My involvement with aspirin finished about this stage, and by then the cervical cytology had outrun its course. I think we had got about as much out of it as we thought we were ever going to.*

My work was almost always in tandem, particularly once Caerphilly got up and running and I got involved with that, but even before that, there was always more than enough to do. In the first few years, there certainly wouldn't have been from within the unit, which is why Hubert Campbell got me involved with the gastroenterologists at the Heath [Hospital] and others as well. But after that there were Peter Elwood's aspirin trials for which I did the analysis. There was always cervical cytology, which in one sense was entirely my pigeon. It wasn't really an epidemiology Unit project, although Archie was very interested, Peter and Michael Burr didn't want to know. I was interested in learning to handle these large volumes of data and learning how to use the computer. It was very useful from that end, but it was certainly extremely timeconsuming.

David Bainton

I came back to Cardiff, I felt that had been my stomping ground and I had good connections. We set up a partnership and I managed to get some money from ICI. Because we asked patients to fast, to come fasted, it was a two-stage observation. They would come to the clinic usually in an evening, and then we asked them to fast and come back for the blood sample [the following morning], and we then had to give them breakfast, and persuading the health authority, and justifying the packets of cornflakes and toast and so on. Yes, we provided patients with breakfast after they had given their blood samples. And so we got bits of money, and also we were sending samples to Portsmouth for various platelet function tests, so there was a Red Star carriage charge every week. I got soft money for that. So we put a package together based on the HDL hypothesis and you know, Caerphilly as well, but the trouble is Framingham had already got the data but never analysed it. Of course, within a very short time of the Lancet *publishing George Miller's hypothesis,[185] they could*

[184] See note 96.

[185] Miller G J, Miller N E. (1982) Dietary fat, HDL, cholesterol, and coronary disease: one interpretation. *Lancet* **ii**: 1270–1271.

Figure 72: Mavis Prentice, a field survey assistant in the Caerphilly study, serves breakfast to a subject who has just given a blood sample, *c.* 1989.

certainly publish cross-sectional data very quickly, and then they went back and looked at the incidence data. Anyway, there were various clinicians who got to hear about this ostensibly unselected population and wanted to ask whether there were opportunities for them to do some work. I would say, 'Well, we could slot this into Speedwell.' [186] *There was a Canadian gastroenterologist, who was interested in gallstones. What interested him in particular was the question, 'What was the normal bowel habit?' So we included that question and I said, 'Perhaps we could do our measurements first?' being a bit uncertain about quite how patients would respond to questions about their bowel habits. He appeared in a white coat and he was the last one to see them. So we slotted those questions in like that. And then we did the initial recruitment phase and several follow-ups. Ian Baker joined me in sharing the clinical work and we trained the clerk and the nurses in survey matters, trying to minimize bias and so on.*

John Yarnell

The Caerphilly Prospective Study really started out of this work in women[187] *in that we went back to these women to ask them for blood and we had this fairly elaborate theoretical structure looking for the determinants of HDL cholesterol, both dietary and physical determinants. We thought that it would be a good idea to do this in men as well. I had some encouragement and some disencouragement from other people. Peter Elwood was quite keen. David Bainton had actually just moved to Bristol and there had been the screening clinic. I am sure you know all about the beginning of the Speedwell study and I knew the chap who had actually run the original Speedwell clinic and I mentioned him to David, who had been away doing the MSc at the London School of Hygiene. I knew that David had previously been working with Archie, and he'd got this move to Bristol to start his work there and being at that time much more interested in epidemiology set up this Speedwell clinic, following and doing a much better job than the medical officer who had set it up in the first place. David was a friend of George Miller, who started up the work on HDL with his brother Norman Miller, and they were set up really to do another cohort study to look at whether HDL was truly an independent risk factor. That's what David set up his study to do and I started this small cross-sectional study in Caerphilly, encouraged by Peter Elwood to look at the determinants of HDL cholesterol and look at a number of lifestyle and physiological factors. I got interested in hormones although David wasn't especially. The work of Gerald Phillips*[188] *in the USA looked as though it should be followed up, so we did some pilot studies in the unit, measuring a small group of volunteers, staff and their friends, on five occasions to see what the biological variability of plasma testosterone, oestrogen and cortisol actually were, and whether they were stable enough to get away with doing single measurements. We thought we could possibly add this to David's work in Speedwell, but David felt he was taking enough blood, so he didn't want to take any more, and we wanted to make special effort on*

[186] For example, see MRC Epidemiology Unit. (1991) *Epidemiological Studies of Cardiovascular Diseases, Progress Report VII*: The Caerphilly and Speedwell Prospective Heart Disease Studies, Randomised Controlled Dietary Trials and Ischaemic Heart Disease, Vascular and other Determinants of Cerebral Ischaemia. Cardiff: MRC Epidemiology Unit.

[187] Yarnell J W G, Milbank J E, Walker C L, Fehily A M, Hayes T M. (1982) Determinants of high density lipoprotein and total cholesterol in women. *Journal of Epidemiology and Community Health* **36**: 167–171.

[188] Phillips G B. (1976) Evidence for hyperoestrogenaemia as a risk factor for myocardial infarction in men. *Lancet* **ii**: 14–18.

the hormones. So I did this cross-sectional study[189] *in a wide age range, which we hadn't looked at very much, but the men were 30 right up to 70 years of age. Encouraged by Peter Elwood, we decided to continue to form a Caerphilly cohort as well, looking at all the extra things that they weren't looking at in Speedwell, achieving a sample of similar size to that in Speedwell. Peter Sweetnam played a key role in the design of the original Caerphilly and Speedwell studies. One of the other things that we were quite interested in doing was measuring subfractions of HDL and we worked with Colin Bolton who collaborated with Norman Miller in setting up the method to do that in Southmead Hospital, Bristol. So it started from a cross-sectional study and grew into a cohort study when it seemed that we would get a lot of extra information.*

Janie Hughes

These men [from the Caerphilly cohort studies], now 20 years later, look on us as friends, and they have even been known to ring up just to chat. We are still seeing them, monitoring their progress, still doing tests on them, so I think we have established a really good rapport with them. I am following up some men from another study that was done in south Wales, some of it was Bristol and Gloucester, but mostly south Wales, and my response has only been about 50 per cent, whereas I could guarantee that if I sent out a similar questionnaire to the Caerphilly cohort men, my response would be about 85 per cent.

Janie Hughes

There were two units, the Pneumoconiosis Research Unit and the Epidemiological Research Unit, which became the Epidemiology Unit in the 1970s. Then 'Epidemiological' was dropped and it became 'Epidemiology'. Dr Elwood took over as Director in 1974. I think it was probably then that things began to change and you really had to justify why you wanted to do particular areas of research and your proposal was sent out to referees, as is the norm nowadays. Except that the MRC was still the grant-giving body as such, the money still came entirely from the MRC. If you look at the history of the unit, people who stayed, stayed for an awful long time, because we were basically a really, really happy family unit.

Peter Elwood

Archie was always very anxious that field epidemiology played a large part in the activities of the faculty [Faculty of Community Medicine, now of Public Health Medicine], and the original documents setting out the aims or mission statements or whatever it was at the beginning [in 1960], talked about statistics and field epidemiology being the basis of epidemiology. Only lip service was paid to that later, and all the training that the faculty introduced was [directed] towards community medicine, public health medicine, and the unit lost out very badly. In fact that was very noticeable, because a number of splendid people in the unit, like David Bainton, had great difficulty in getting their theses approved for their Part II Membership, and the view was taken that it hadn't a public health aspect. He [Bainton] looked at temperature and cardiovascular disease. He wrote a splendid piece. There were one or two others who got into the same difficulties.

Peter Elwood

I think perhaps it was me who didn't make a bid to [make training and career management] play a bigger part in this. But we used to get students visiting, and Cambridge used to send down their students, two days initially, and they stayed overnight, and we showed them the field studies going on and a view of the studies in progress. Several other groups used to send down people, and, of course, we still put a slot in the local teaching and training. But possibly if Archie had continued as Director we would have had a much bigger part to play within the Faculty and within the College of Medicine in Cardiff, we would still have been a significant part. But I just enjoyed fieldwork and testing hypotheses so much that I wasn't terribly interested in lecturing and training and so on. Let me say that most of the people who came to us and took up the training post of junior epidemiologist did extremely well, and it was almost a unique training in fieldwork, because we were so heavily involved in that, and practically nothing else.

Janie Hughes

I wouldn't say it was tension [between the clinical staff and the administrative staff], there was just a bit of a divide. It wasn't tension. I thought it was normal in a unit like that, that there were scientific staff and others, but I think looking back it was probably down to Professor Cochrane's leadership.

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[189] Yarnell J W, Fehily A M, Milbank J, Kubicki A J, Eastham R, Hayes T M. (1983) Determinants of plasma lipoproteins and coagulation factors in men from Caerphilly, South Wales. *Journal of Epidemiology and Community Health* **37**: 137–140. *idem* (1982) Dietary determinants of lipoproteins, total cholesterol, viscosity, fibrinogen, and blood pressure. *American Journal of Clinical Nutrition* **6**: 890–896.

He was a bit of a snob and we were the workers, and there was the scientists and the two didn't mix really. But that was my impression, but I think I probably was proved wrong later on. When he came back to work with us after he retired, some of the younger people, like Andy Beswick and Kim Neale, shared a room with him and he was an entirely different person. He seemed to love their company and they did The Times *crossword together. Had I been wrong about him? I think it was probably because he wasn't Director any more and the unit wasn't his concern and so probably it was because of the type of leadership he had that there was 'them and us'. That's our way of putting it. I mean it wasn't just my own personal view a lot of us thought this. Every Friday there was a scientific staff meeting and we weren't invited, so we never really were* au fait *with what was going on, we didn't know what studies other people were doing that we weren't involved in, which in hindsight I think was a bad thing. And it wasn't until Dr Elwood took over that we began to be invited. Perhaps not straightaway, but when he realized how we felt we began to be invited to the meetings. They were called scientific staff meetings, then they were just called staff meetings. And these continued right up until the time he retired, when we all used to meet in the conference room every Friday morning, whether there was anything to discuss or not, it was just to meet and to get together and know what other people were about, what they were doing. They were used as sort of rehearsals for papers that people were going to give at conferences. I think it helped both the speaker and the audience, as more often than not the audience had been part of the study that was being presented at conferences, and we had worked on these studies, so it was nice to see it being put together and talked about or given as a paper. And when there were 30-odd of us, we weren't always aware of what other scientific staff were proposing, so it was nice to keep up to date.*

Peter Sweetnam

I can't actually put a date on it [statisticians' involvement in the design stage of projects]. I think things slowly developed. Certainly when Peter [Elwood] took over the unit in 1974, he introduced a weekly staff meeting at which somebody would give a presentation, either of some analyses or some results, or a proposed piece of work etc., so that to some extent everybody got a little bit involved in the design of these things. I think actually over time we found that people tended to get a little bit overly critical and then others shied away from presenting things, because they didn't want to get cut to bits, which tended to happen. And I think probably after that, it then later evolved more into the people who were involved with a particular proposed project, literally sitting down and discussing it. But I suppose what also happened as well was that the size of the projects got larger and larger. There were some exceptions, even in the 1960s, some of Peter's anaemia studies are quite large numbers of individuals, but some of those were never even put on punch cards. The smaller ones were, but there were one or two that I think weren't. They might have been on edge punch cards. It's very difficult, I think to date changes in things, because the changes were usually gradual, rather than incremental, although certainly there was an incremental change, I think when Peter took over. He actually worked very hard at trying to decide how he was going to manage this unit and he talked a lot with a chap called Tony Johnson who was a lab manager from down in west Wales, who was very interested in the theory of management of organizations, and he introduced, in particular, these weekly staff meetings. We had staff meetings under Archie, but my memory is that they were much less regular and they were much more to do with routine things. There must occasionally have been presentations of planned bits of research and also results, but my memory is very hazy about these things, much less so for things like the arrival of the Monroe Epic[190] and what you could and couldn't do with it, than for the way the unit was managed. In a sense, it's probably partly me, but it's also partly the statistician's role, in that he didn't really manage the research (that was essentially the epidemiologist's job) and the statistician was there as adviser and essentially a calculating machine.

Selwyn St Leger

I think that we would have a staff meeting on a Friday morning, where, after dealing with the housekeeping matters, most of the time was spent discussing research proposals and ideas, batting them around, perhaps chucking them out as rubbish. We would have quite vociferous discussions, various camps would form and argue their points. And after that very often a research proposal or idea would arise. So Mike Burr might come and say he was interested in asthma and mites (as he was). All of us batted those ideas around,

[190] See page 77.

and then obviously the person who was leading on that day would go away with whoever was linking in, and work out proposals. They [these ideas] would still come back and be batted around.

Peter Elwood[191]

But the question of continuing disability from industrial byssinosis remained with me, and so about ten years later I went back to the north of Ireland, got the survival rate of all the men and women in the study, and worked out the mortality in the different departments. I showed that there was no excess mortality, even in the men who were exposed to the heaviest dust levels, provided we allowed for smoking and so on. I wrote a paper arguing that byssinosis was an acute condition, and although it led to men having to leave the industry, it did not cause permanent disability.[192] *Schilling clashed with me quite severely over that, but he remained a friend. I found a lot of these men felt very strongly about their research, but one was able to keep friends with them, and that added to the delight of medical research. There was a lot of controversy, but it was usually with friends. About ten years further on, I took the opportunity of looking at people who had worked in the flax industry, and we set up a similar study in the cotton area (Bolton and Oldham). We took random samples of people in towns in Northern Ireland where flax had been a major employer. We selected a large sample, I think it was about 2000 people, our estimate was that half of them would have worked in the flax industry, and half would not. We did exactly the same in Bolton and Oldham, and half of them it turned out had worked in cotton and half had not. And we looked at respiratory symptoms and respiratory function in some detail and we published two papers showing, I think, quite conclusively that whether or not there had been byssinosis, whether or not the subjects had worked in flax or in cotton, there was no residual disability.*[193] *There was a massive effect of smoking on respiratory function, but when we allowed for that there was no evidence of any respiratory disablement from textile dusts. Again, that led to controversy, but I think it did establish a very important fact, which sadly was of relatively little importance, because the flax industry died in Northern Ireland and the cotton industry died in Lancashire. So it was a very, very satisfying series of studies over a period of about 25 years, but of little ultimate consequence in this country. Whether or not other countries take account of it or not, I don't know. The results were so conclusive when we had finished that series of three studies, the prevalence study, the mortality study, and then the retrospective case control as it were, it really established that byssinosis was still a condition that caused acute disablement, could lead to people having to leave the industry, but was not a cause of permanent disability. It did lead to very, very great change in the attitude of companies towards compensation. They were able to stand up to them and say there is no permanent disablement. The size of compensation awards and the number of compensation awards fell away to almost nothing.*

Peter Elwood

In the early days of the MRC unit we were the sharp end and we were the reason for headquarters existing. Somebody has made that very point to me, that the work that we did secured the future of the whole organization, and so the whole focus was on facilitating and encouraging units. Then the board system was set up.[194] *I am not a politician, I don't understand a lot, but my thinking is that the universities became more and more jealous of MRC units, with their stable funding and secure careers, and people in the universities who were in research had to find their own money and had no stability, or at least not the same career stability. And the MRC boards came in and were very, very aggressive in the early days and the review process was certainly very, very threatening. This was*

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[191] See note 111 for a description of his earlier work on byssinosis.

[192] Elwood P C, McAulay I R, Elwood J H. (1982) The flax industry in Northern Ireland: twenty years on. *Lancet* **i**: 1112–1114. Elwood J H, Elwood P C, Campbell M J, Stanford C F, Chivers A, Hey I, Brewster L, Sweetnam P M. (1986) Respiratory disability in ex-flax workers. *British Journal of Industrial Medicine* **43**: 300–306. Elwood P C, Sweetnam P M, Bevan C, Saunders M J. (1986) Respiratory disability in ex-cotton workers. ibid. **43**: 580–586. See also page 67.

[193] See note 192.

[194] From 1 September 1974 three new research boards were introduced into the MRC's administrative structure: Neurobiology (later Neurosciences) and Mental Health Board; Cell Biology and Disorders Board; and Physiological Systems and Disorders Board, each with one or two grants committees. In addition were the Environmental Medicine (Research Policy) Committee and the Tropical Medicine Research Board. See House of Commons. (1974) *Medical Research Council Annual Report, April 1973–March 1974*. HoC224. London: HMSO, 156.

a total change and it led to changes in headquarters, which changed from being our representatives in negotiations with other bodies to become the executives of the boards. They came down to see us to put into effect decisions that had been taken by the boards and the whole atmosphere changed over a very short period of time. The review processes also became very, very threatening and initially very hostile. I submitted my first report on our first five years under the board system [c. 1980], and I was asked to appear before the board. One man, whom I won't name, attacked me most aggressively, hit the table, and almost shouted at me, because we had used a method that he disapproved of in one of our studies. I was told afterwards that because of his performance, it was decided that no Director would ever be called to give account in front of a board again. That was judged to be so discourteous, and it was certainly so threatening and so hostile. But that was the general atmosphere of the board and we never felt that we had friends at headquarters after the boards came in.

Peter Elwood

Certainly the foundation of epidemiology in those early years was the cross-sectional survey and I can remember lectures I received, and lectures I gave, focused on case-control study, leading onto cross-sectional surveys. Intervention trials were rarely talked about in epidemiology. There were drug trials, and a few prospective studies, such as Framingham, but these stood out as unique. Epidemiologists didn't tend to think in those terms, I think the value of the long-term prospective study was being slowly established and like the mustard seed it grew, but it wasn't the thinking in those days. I remember that my original department in Belfast set up one prospective study which was to run for a year to follow cholesterol level and blood pressure in, as I remember it, about 500 men and this was referred to as a rather unusual prospective study. The men were to be seen several times, rather unusual.

Janie Hughes

Fieldwork has changed enormously because people distrust you nowadays, whereas, perhaps even 20 years ago, working in the Rhondda, in particular, was easy because everybody left their keys in their door and you just turned the key and shouted, 'Can I come in?' and they would say 'Yes', without even knowing who you were. In the early days, I think I am right in saying this, we didn't even write to the people and say we were coming, we just cold-called, which we are not in favour of doing at present. We always announce our arrival by sending a letter. Nowadays in our studies we keep in touch with the population by sending them newsletters and keeping them up to date with what's going on. I don't think we did anything like that in the early days of studies in the Rhondda. I think in the X-ray study of the miners, for instance, notices were put up in workmen's halls, but perhaps it might have helped had we thought of putting an advert in the local press, or putting notices in doctors' surgeries. We mightn't even thank them, you know as a community, for what contribution they had made to our studies. So they probably might have ended up rather disgruntled and not wanting to cooperate in more studies.

Years ago people knew their neighbours, they knew lots about them, they knew the people across the road, they knew the people down the road. Nowadays no one wants to tell you anything about anybody, because they are always afraid of being accused of revealing things to agencies like the DSS, and so it's a closed shop. You can rarely get any information from neighbours these days. You cannot call at the corner shop, or the post office, which is what I used to do a lot, to learn about people's movements, that's out now. So now you have to rely on health authorities or ONS [Office for National Statistics], if you have flagged people, rather than by word of mouth with neighbours.

Valleys people stay valleys people, but in the big towns like Cardiff and even Caerphilly, they do move and change. I am a valleys person, so I suppose I am a bit biased, but valleys people are communities and they care about what goes on around them and they are very friendly, they are very warm, on the whole, whereas town people are cold, distant. Cardiff particularly is very cosmopolitan with lots of flat dwellers and you are not even knocking on a door, you are buzzing on an intercom at the bottom of the block of flats, so you don't get tremendous satisfaction from home visiting as we did years ago. And sometimes you can travel quite a distance and it's an absolute waste of time.

David Bainton

I thought we could try to evaluate some of the components of stroke care and I found a speech therapist who was prepared to concede that there might be some adverse consequences of speech therapy, so it became much easier to say, 'Oh let's do a trial, let's do a randomized trial'. You appreciate that at the worst, it was neutral, in ethical terms. It was difficult to get a balanced question. We very tentatively ran a pilot, wrote a protocol and we ran it for six months, without additional resources. We examined the question – 'What is the contribution of a professional speech therapist over and above a lay volunteer who is expressing

the same commitment and enthusiasm, without the particular skills of the speech therapist?' – and we randomized patients. The subjects had to have a sufficient degree of dysphasia. We applied for a grant, using our pilot data to furnish the application and we got a three-year grant from the Department of Health, which effectively paid for a full-time speech therapist to manage the study and also act as a therapist when required. I came back to the unit to help and got Peter Sweetnam to help as well, because I wanted to make sure, both for comment on the protocol (which I think he passed), and some power calculations, all the things you are supposed to do. What this illustrated was the dictum that 'There's nothing that makes a common disease so rare as starting to set up a randomized trial.' We got about 160 patients, I think it was, but by the time they were broken down into age, sex, level of dysphasia, intervention or control, there were quite small numbers. But what was quite clear was that, you know, volunteers were as good as – or actually they were better, but not statistically significantly better – than speech therapists. This raised, as always, lots of other questions. That was really my first major study and what I found is that you acted almost as a source of advice sometimes, and people would go off and do their own study and you weren't involved at all. Other times you would actually make various suggestions and almost help them write a protocol and maybe work with them. Other times there were studies that were initiated just from within the Department of Community Medicine.

John Yarnell

Yes, there were discussions about the size [of Caerphilly] and I think we had to balance this with the very intensive fieldwork which was very time consuming. I think both Tom Meade and Gerry Shaper [of the British Regional Heart Study][195] *had suggested that it should be larger and based on a fresh sample. We thought we would lose an awful lot of momentum to start again somewhere else. Peter Sweetnam did some calculations and we felt that we had just about got enough size and power to be satisfactory. One of the ideas was that at some stage things could possibly be tested out in the sister study in Speedwell or visa versa, so for some things we were going to rely on the combined cohorts whose total is close to 5000 men. But practically speaking, we just hadn't got the resources or the funding to do a larger sample with what we had. We did feel, and I particularly felt, that we could possibly overload it, ask too much of the men, but I was interested in getting as much as we possibly could out of the study scientifically. The second time round I think that in terms of what we were asking the men, we probably asked them quite a lot, two clinic attendances, the first visit a minimum of one and a half hours and the second visit included anything up to about 80 to 100 ml of blood which I don't think anybody else has ever asked for. We did take the advice of one of our consultant haematologists, Dave Hutton, who was working with us. He felt that for most people it was quite safe to have that amount taken.*

Selwyn St Leger

This is where I have views that many would find unacceptable. This is again looking back to this theme of mine about change promotion. I have now in my mind and in my writing drawn a distinction between what I call science and change-promoting research. Now science has a number of characteristics, one of which is that it is circular in the sense that it is scientist-to-scientist. The scientist decides what the issue is, largely what it is going to be, the peers decide whether the funding is going to be given and on the quality of the scientist and all that. Now change-promoting research, which I think all of R&D should come into, is actually externally referential – NHS priorities as specified by managers who decide largely what the research issues are although they are informed by the knowledge of researchers. The criterion of good work is not whether it has got published and gained brownie points, but whether it has brought about change or improvement. I won't go into all the details of that, that is in my book,[196] *but what I am saying is that if you have got*

[195] The British Regional Heart Study, administered from the Royal Free Hospital, London, recruited men from 1978 to 1980 to determine the factors responsible for the variation in ischaemic heart disease, hypertension and stroke in Britain. Three research nurses examined 7735 British men aged between 40 and 59 in 24 towns in the UK. The men were re-examined, aged 60 to 80 years of age, between 1998 and 2000. A female cohort from the same 24 towns was recruited in 1999 to the 'British Women's Heart and Health Study', directed from the University of Bristol. The original study was supported by the Medical Research Council (1975–85) and has been a British Heart Foundation Research Group since 1986, with additional support from the Department of Health and the Stroke Association. For a list of publications, see www.ucl.ac.uk/primcare-popsci/brhs/index.htm (visited 25 February 2002).

[196] St Leger A S, Walsworth-Bell J P. (1999) *Change-promoting Research for Health Services: A guide for research managers, R&D commissioners, and researchers.* Buckingham; Philadelphia: Open University Press.

fundamental scientific research, nobody has found a better way, including myself, of organizing it than the sort of MRC-type model, where you have got to give people quite a lot of freedom and leeway to get on with things, you may as well give them resources, but essentially it is the scientists themselves that are largely deciding what are the issues to be researched. When we comes to health services-type research, to which I would also put epidemiology, I think while they are not treating it as science in that sense, it's no less rigorous an activity, and it still has many of the trappings of science. The methods are the same. I think when you look at it in that context one is saying, 'Why? What for?' Now it may be that when you are at the level where aetiologic epidemiology is closer to traditional science, but even that needs a bit of oversight, because an awful lot of money goes into very large epidemiological studies and one wants to ask how they are going to inform future decisions or future research that leads to something practical. So I no longer believe in the idea of a unit of people given plenty of resources being left to get on with it.

I don't think the MRC will be able to sort that [epidemiology in the 21st century] out for itself, because it is in the culture of science, most of its study, all of its senior people on the scientific side and all these would call themselves scientists, and most of them are. I can only say – well again I will be provocative – if you consider something like the research assessment exercise (RAE), which is a driving force in universities in terms of their agenda and what they value, if you want to change it, as I do, to work that is actually for the most part useful in the health service. I am not talking about the pure sciences again, I am talking about the disciplines which do have a practical application. Well, you might ask, 'Why don't we go for a single stream of funding?' At the moment the funding you can get is relatively small, but some funding [is available] from NHS R&D, and that is the one thing which actually has an agenda, and you can get the prestigious larger beer from the MRC, for example, or the Social Science Research Council.[197] *My feeling would be that we actually take firstly, from the HEFC (Higher Education Funding Council) that proportion of their monies which is meant for medicine, then take from the MRC that proportion of its money which is meant for applied or directed research, and put that in with the NHS R&D and manage all of them through the NHS R&D structure. Instead of having RAE, in a sense, directing the funding, what you would do is to fund slightly differently. There's lots of pure science in the medical schools. Funding would be through the R&D stream, in a sense, of rolling projects, which would come with the infrastructure built in, not built on top of the existing infrastructure, so that would include the RAE component. I don't think it will happen in any short period of time and the reason I say that is that I don't think the MRC is capable of thinking along those lines, of things that are of interest to the NHS, linking with management interest. For example the concordat we have at the moment [between the Department of Health and the Medical Research Council] basically permits the MRC to do its thing and the health service will sort of step out of the way and let them get on with it. Now that's not sensible.*

Janie Hughes

I was very loath to move from the middle of town [Richmond Road] to Llandough Hospital [in 1990] for several reasons, but one of them was that it was further for me to travel and another was it was going to be different, because in Richmond Road [where the unit had been since 1962] we had been in a three-storey house and we were like little separate departments and in Llandough Hospital, we were going to be all in one corridor and I just couldn't envisage that working. As it happened, I was proved entirely wrong and it became an even nicer place to work in. It was just absolutely pleasant; it was wonderful. There were little factions every now and then, that disturbed the happiness, but on the whole I am sure we were quite unique. The building [in Richmond Road] was owned by the Welsh National School of Medicine and I think they gave it to us for a pittance which the MRC readily agreed to pay, but then the Welsh School of Medicine became the College of Medicine and I think they became a bit desperate for accommodation and money and they decided to sell the building. They gave us about two years' notice and we had to look for somewhere else. Dr Elwood hit on the idea of coming back to where the unit had originated, the pneumoconiosis block of Llandough Hospital, so that's how we came to be in this particular suite of rooms now. A lot of conversion had to be done,

[197] The Social Science Research Council (SSRC) was founded under a Royal Charter in 1965. In 1982 the Rothschild review recommended more attention be paid to empirical research and research related to public concerns. From 1983 it was renamed the Economic and Social Research Council (ESRC). See Rothschild V(ictor, Lord). (1982) *An Enquiry into the Social Science Research Council*. Cmnd. 8554. London: HMSO.

because most of these rooms weren't used as offices, they were laboratories, hence the hundreds of power points. There were laboratory worktops all around the place that had to be ripped out. Extensive alteration had to be done and the MRC agreed to pay. The rent for this place was quite hefty as well, so we were very fortunate. I didn't want to come and in fact I didn't pack my bags until the afternoon before we were due to move, I was going to stick it out as a sitting tenant. We got yearly visits from a subcommittee. I think I am right in saying this, that they had decided in 1990 that this was just a temporary move for the next five years and we were to wind down. In fact they were quite brutal in that they stopped what we considered quite a few extremely good studies and that was a disaster – DART2,[198] *that was one of them. And the stress management substudy*[199] *of DART2, and that was a really, really well thought-out study and everybody was terribly upset by this. As I say they were quite brutal, and they sort of said, 'Stop within three months', something like that. But we knew that there were about four or five of us who were due to retire or be made redundant in March 1997, and three more were to stay on until March 1999, so we knew exactly what the issue was. That didn't make it any easier, but I can honestly say that morale didn't get low. We had heard lots of tales about morale in the Pneumoconiosis Unit where there were 90-odd people working and they marched on Downing Street to no avail, and morale got really, really low and people got terribly bitter,*[200] *but it wasn't like that in the unit. Possibly because some of us who were due to 'retire' were coming to the end of our working lives anyway and it didn't matter too much. Of course, to people like Dr Elwood, you mustn't speak the word 'retire' – it's a dirty word.* [AN: Put 10p in the box.] *Yes. Every time you say it, it is a swear word.*

Janie Hughes

We knew five years before we [the EU] finished, it was called ERCS (Early Retirement Compensation Scheme). The unit was closing when I was coming up to 60 years of age. So they were making us redundant, but it was called early retirement and we were given a package.

Janie Hughes

Most of the training was on the job, but I did have some specific training. I went to St Thomas' to learn how to do anthropometric measuring properly and also I was privileged to work for other units, in that I was recruited to work for the UKCCCR (United Kingdom

Figure 73: The Epidemiology Unit's 25th anniversary at the University Hospital, Cardiff, 1985. A bust of Archie Cochrane, brought by Peter Elwood, is in the foreground, as he was too ill to attend the celebration dinner.

[198] Burr M L, Gilbert J F, Holliday R M, Elwood P C, Fehily A M, Rogers S, Sweetnam P M, Deadman N M. (1989) Effects of changes in fat, fish, and fibre intakes on death and myocardial reinfarction: diet and reinfarction trial (DART). *Lancet* **ii**: 757–761.

[199] Gallacher J E J, Hopkinson C A, Bennett P, Burr M L, Elwood P C. (1997) Effect of stress management on angina. *Psychology and Health* **12**: 523–532.

[200] For details of the closure, see Cotes J E. (2000), note 41.

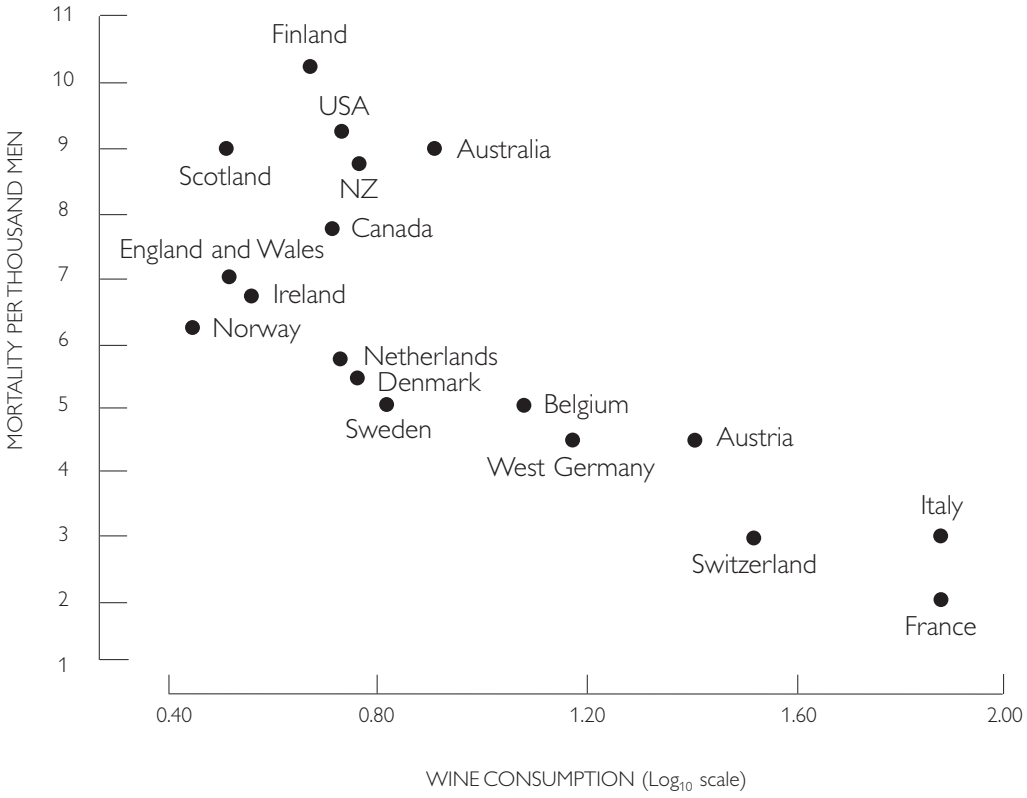

Chart 2: Relationship between ischaemic heart disease mortality-rate in men aged 55–64 years and wine consumption. See note 180.

Coordinating Committee on Cancer Research) on three studies, – a breast cancer study, a testicular tumour study [20 years ago now] and most recently, a child leukaemia study [1992].[201] *So I went to lots of training days for that: how to interview parents of children who were terminally ill; how to interview them in clinic situations; how to interview in their home situation; and how to treat sensitive data properly. I went on lots of courses, and I was often on away-days to Leeds or Oxford.*

Stewart Kilpatrick

But I think on the whole, the Welsh people benefited from the research work done, certainly the miners did, there's no doubt about that at all. And I think as you probably know even now there's a new scheme for the compensation of ex-miners who have bronchitis and emphysema and I am one of the assessors for that, so I know quite a lot about it, and that was all really based on a lot of the work that was done mostly in the Pneumoconiosis Unit, but mostly under Archie Cochrane, so I think the Welsh people have benefited from the presence there. Educationally, there's no doubt that the medical students have benefited from both these units and the research that they have done. And I was Dean of Clinical Studies in the University of Wales College of Medicine for 16 years, so I have had quite a lot to do with the education of medical students and the choosing of them at that time. At the same time I was Professor of Chest Diseases, so I really had rather a busy professional life.

Selwyn St Leger

We used to discuss lots and lots of things at Archie's court up in the roof, there was a good group of us, and that was the time when Brenner had been looking at mortality and unemployment and other people were trying to explain mortality patterns in other ways. We were just speculating, 'Well, look, if provision of health services and all the rest of it is so effective, shouldn't we find some correlation between service provision levels and mortality, perhaps in different countries?' That led us to think of doing an ecological study – of course we didn't use the word ecological study in those days, we called it a correlational study. Archie, Fred and myself took this forward, and we decided what we would

[201] See also UK Childhood Cancer Study Investigators. (2000) The United Kingdom Childhood Cancer Study: objectives, materials and methods. *British Journal of Cancer* **82**: 1073–1102. *idem* Childhood cancer and residential proximity to power lines. ibid. **83**: 1573–1580.

want, but not all of it was easily available, such as the economic information, and this is where Archie came into his own. He had contacts and he managed to get quite a lot of international information, which would be readily available now, but in those days it wasn't. Fred put the information onto big pieces of paper listing 18 countries, with all the variables along the top, such as ischaemic heart disease in different age groups. I am not sure if I transcribed the data myself, but we got a nice little database onto the computer. This led to the paper.[202] *We regarded that as great fun and didn't take it terribly seriously. What it did show was no particular link with health indices and, as you might expect, a very strong link with indices of wealth of the nation, such as gross national product. It also showed a curious little anomaly. If one standardized for everything else and then plotted the standardized residuals against provision of doctors per head for infant mortality, we found that infant mortality increased with doctors per head. We duly sent the paper off to Hubert Campbell, who accepted it and said that he would publish it, and when it was too late, he had dealt with the proofs himself, he was being a bit naughty I think, because when it was too late, I noticed that they had taken this lovely graph out of the paper. I was furious with Hubert, but it was too late, so we managed to persuade, I think it was the* Lancet *to publish the graph.*[203]

We sent a letter into the Lancet *with this graph in it, 'The anomaly that wouldn't go away'. And then we forgot all about it.*

We decided that the next thing we wanted to look at was ischaemic heart disease. Being sceptics, does it really relate to saturated fat intake and all the other things that people look at? We were using the same 18 countries and ischaemic heart disease in various age groups, but we also managed to get hold of alcohol consumption and this is where Archie was particularly good with his contacts again. He managed to get the data broken down by beer, wine and spirits, in terms of ethanol equivalents. We had a fantastic time with this, we put it into our regression and looked at it every which way, and every which way I looked at it, I found a strong association with total alcohol and an equally strong association with wine consumption and very little with beer or spirits. After looking at various combinations of our data and bearing confounding in mind, we could not make this go away. So we were delighted by this news. We didn't believe it was a cause–effect relationship, although we wished it were true, because Archie in particular was a great wine drinker in those days and I have been ever since. And so we wrote this up. In fact I remember I actually did the drafting of both those papers. I think Archie wanted me to get the experience of writing publications, but also I had done the analysis, so it was in my mind just how it was structured. But I remember what he did in the second paper,[204] *I remember sitting one afternoon just writing it up, it was in more or less the final form. Archie added one thing that would almost be a sacrilege if anybody found out what was causing the beneficial effects, because basically the wine's all very well packaged as it is. And then he added, 'We are sorry we cannot advise our friends whether or not it is best to have red, white, or rosé'. That went off to the* Lancet *and caused quite a bit of interest. In fact I got invited, shortly after, to do an editorial based on that, and on the basis of that I wrote a whole string of editorials during the time of – was it Ian Munro's editorship? – which was very enjoyable, and of course they were all anonymous in those days. We didn't take it any further. We had a bit of speculation round the table. And remember Peter was teetotal. To be fair to Peter he never shoved his views on others, in terms of what it means in terms of a research question. At this stage we were seriously discussing with Peter and others, whether we should do some sort of clinical trial, or something, of alcohol. I think Michael Burr suggested that we did something with monks and nuns. We came to the conclusion that really it was just far too tenuous. This was just an example of a correlation analysis that crops up something. Of course that's how history proves you did it wrong. When I last checked on that paper, I think we got about 250-odd citations. It has gone throughout the medical literature – it's in the general stuff, it's in the biochemical stuff – it's always the paper that is cited as the foundation of what we thought of as a red herring.*

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[202] Cochrane A L, St Leger A S, Moore F. (1997) Health service 'input' and mortality 'output' in developed countries. *Journal of Epidemiology and Community Health* **32**: 200–205. Reproduced as a historical article in ibid. **51**: 344–348; (discussion) 349.

[203] St Leger A S, Cochrane A L, Moore F. (1979) Factors associated with cardiac mortality in developed countries with particular reference to the consumption of wine. *Lancet* **i**: 1017–1020. See also St Leger S. (2001) The anomaly that finally went away. J*ournal of Epidemiology and Community Health* **55**: 79.

[204] See notes 180, 202 and 203.

1976–78 School milk supplementation study

Peter Elwood

We also set up a study in seven year-old children to look at the effect of school milk and we selected schools in a deprived area, and we did this by standard criteria, which were indices of deprivation. We went to areas in south Wales with high indices of deprivation. We selected from all the schools in the defined areas, we selected children from families of four or more children, and social class 3 manual or lower, so that we were getting a group of deprived children. We supplied half of them with school milk for two years and we monitored that and paid surprise visits to the school to check who was actually getting the milk. The teachers were all intrigued by this study and cooperation was really very high indeed. And then we analysed growth over that two-year period and produced a very nice gradient where the children in social class 3 showed virtually no change in growth, they grew, but there was no difference between the ones given the milk and those not given the milk, and when we went down the social class to the unemployed, the nonclassifiable, then we found quite a difference, still just a few millimetres, but a sizeable difference in growth. If we multiplied that up by the number of years that the children might have received school milk, it was a worthwhile increment. We showed that school milk did have an appreciable and, we felt, worthwhile effect on the growth of the most vulnerable children; the Department of Health paid no attention to it and school milk was not reinstated.[205]

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[205] See discussion on page 86.

1976–82 Environmental lead studies

Peter Elwood

Lead in petrol was a very, very hot issue. A group was set up and led by a politician and doctor from Wales, an extraordinary, exceedingly forceful character, who dedicated himself to the Campaign for Lead-free Air (CLEAR). I became more and more angry at the bad epidemiological methods that were being used in journals and articles. I wrote one or two letters to him, pointing out that the data he was quoting and the comparisons that he was making were totally invalid. I wrote to him a number of times. But I felt this was an area in which we should make a contribution, so I set up one or two studies to look at lead.

Figure 74: Transport on traffic-less Tory Island, off the north coast of Ireland, *c.* 1970s.

The Welsh Office was interested and asked us to look at water lead. Some of the areas in Wales have a very acid surface water and old lead pipes. One or two studies had shown that the lead levels in the water were really quite high, higher than the WHO recommendation. We went to north Wales and did a number of surveys of water lead and blood lead and estimated that the contribution that water was making to blood lead levels was quite substantial. Whereas with air lead, no matter where we went we couldn't get estimates of the contribution to blood lead from air higher than about 10 per cent. Now there were uncertainties in this. Food lead was obviously a very important source and food handling wasn't nearly as careful as it is now. I suspect that a damaged conveyor belt might be repaired with lead solder, whereas now they wouldn't dare have lead solder anywhere near food handling. I suspect that the fall in lead levels which has been shown quite conclusively in many studies over the years[206] *has been largely due to a reduction in water lead and in food lead. We certainly showed that the lowering of water lead was important and was effective. On two occasions we were alerted to the fact that the Welsh water authority was going to change the pipes to an estate or to a village, and so we went and got blood lead levels and then we followed the blood lead levels following the change, the removal of the lead pipes and the putting in of copper pipes, and we showed very nicely the fall in blood levels and we showed the sort of half life of blood lead from those studies.*[207] *We also selected a town in East Anglia that had a lot of lead pipes, but had hard water, and we showed that there was a very substantial difference in both water lead levels in the hard-water area and the soft-water area and very substantial difference in blood lead levels. The relationship between lead in the water and blood was the same, but one was higher up the curve than the other in soft water.*[208]

The other study which got the headlines for a short period of time was comparing areas with heavy traffic and areas with very little traffic and estimating water lead, blood lead, and lead in the dust. We also did children in those days and dust lead was a very important source. We used to swab the children's hands and measure the amount of lead and

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[206] Elwood P C. (1983) Changes in blood lead concentrations in women in Wales 1972–82. *British Medical Journal* **286**: 1553–1555. Elwood P C, Toothill C. (1986) Further evidence of a fall in blood lead levels in Wales. *Journal of Epidemiology and Community Health* **40**: 178–180. Eight surveys were conducted between 1972 and 1982 showed a 30 per cent fall in blood lead concentrations in adult women in Wales over the period.

[207] Thomas H F, Elwood P C, Welsby E, St Leger A S. (1979) Relationship of blood lead in women and children to domestic water lead. *Nature* **282**: 712–713.

[208] Elwood P C, Phillips K M, Lowe N, Phillips J K, Toothill C. (1983) Hardness of domestic water and blood lead levels. *Human Toxicology* **2**: 645–648.

relate that to blood lead. But the most delightful studies were the traffic-less islands. We chose three areas in Wales with different levels of traffic, from a rural area to a very heavily polluted area. The heavily polluted area was Port Talbot, where there's a motorway which is elevated above houses. Along this motorway we chose houses on the main road and houses with the motorway over above and we did lead sampling, lead air sampling and confirmed that the lead levels were very, very high, and air lead levels were very high. So we took blood from those women, from Beaufort at the top of one of the valleys, where there's quite high traffic, from Porth where there's a one-way system and very heavy traffic. But then we went to three islands. I got a colleague in Ireland and another colleague to do the surveys on Tory Island off the north coast of Ireland, a rather isolated community, and this we were told had no petrol traffic at all, never had and there was never likely to be any petrol traffic. My colleague was appalled to see a petrol driven van sitting some little distance from the harbour and made enquiries about it. Now remember it was an Irish island, an Irish community, and about two years previously the local authority had given a petrol-driven van to the islanders because there were two communities on the island and, the school was at one end of the island and, on wet days, the van would collect the children from the other community. The islanders had been told that petrol was put in at the back of the vehicle, and water in at the front, but they had forgotten to tell them that you also put in oil from time to time to lubricate the engine. So the van ran very happily for some time and then it seized up, and they just left it where it had ceased and never bothered with it again. With that background we felt we could call it a traffic-less island. We took blood from every adult, swept every house to get lead in dust, and measured air lead, we had one or two air samplers on the island. We then went to Arran Island off the west coast of Ireland, and again my colleague was appalled to see a petrol-driven Hillman car on the island and he made enquiries. And he found that the district nurse on the island had brought a car over, sometime previously, and every time she went to the mainland, at most once a month, but probably not even that often, she took her petrol can and collected two gallons of petrol, put it into the car, drove the car until the petrol ran out, and then just left it wherever it was, until she next went to the mainland. So again we felt that we could call it a traffic-less island. The third island was truly traffic-less, and that was Sark in the Channel Islands. We asked the doctor living on the island if he would take blood for us and he got permission from the Monsignor. There used to be a Dame of Sark, and one of the laws of the island of Sark is that only the Dame or the Monsignor is allowed to have a bitch, others can have dogs, and no one is allowed any mechanically driven vehicle of any kind, lawnmower included. So we truly did have a traffic-less, vehicle-less island, and we got blood from them. Well it was delightful that study, but we found that the lead levels were almost identical to the areas in Wales. There was very little difference between them. Tory had a terrible problem of alcoholism there and it may be that alcoholics do raise their blood lead for whatever reason, because they used to seal wine with lead in some way, but really there was very little difference.[209] *But I reckon that all the work that we did on lead was good epidemiology. I think that instead of doing all those studies, we should have done one really big study. There was one much bigger study, a survey of health in Wales in connection with health promotion. The Welsh Office had funded a group to do a study right across Wales, with about 2000 people examined in relation to heart disease, one of the heart prevention projects. Well we asked the team for a sample of blood from every person, so I got 2000 or 3000 samples of blood and we looked at that, and the one paper that we published was on blood lead and blood pressure. That was quite an issue and we entered into that debate as to whether or not lead is related to blood pressure.*[210] *The most curious publication of all that we got out of that was blood lead and platelet function. Blood lead is negatively related to platelet function, so we published a paper,*[211] *tongue in cheek, and I think it actually asks the question*

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[209] Elwood P C, Blaney R, Robb R C, Essex-Cater A J, Davies B E, Toothill C. (1985) Lead levels on traffic-less islands. *Journal of Epidemiology and Community Health* 39: 256–258.

[210] Elwood P C, Davey Smith G, Oldham P D, Toothill C. (1988) Two Welsh surveys of blood lead and blood pressure. *Environmental Health Perspectives* **78**: 119–121. Elwood P C, Yarnell J W G, Oldham P D, Catford J C, Nutbeam D, Davey Smith G, Toothill C. (1988) Blood pressure and blood lead surveys in Wales. *American Journal of Epidemiology* **127**: 942–945.

[211] Sharp D S, Beswick A, Renaud S, Toothill C, Elwood P C. (1991) Blood lead and platelet aggregation – evidence for a causal association. *Thrombosis and Haemostasis* **66**: 604–608.

at the end 'Does this mean that people exposed to lead have a lower risk of ischaemic heart disease?'

The studies on lead I think were good epidemiology, they weren't very big, I think we lost out in that way, but they achieved virtually nothing. I think CLEAR was scientifically scandalous in the way they distorted data.

Janie Hughes

It was lovely working in north Wales, because you just explained to the parents that there was a little worry about lead in the air and they were more than anxious to cooperate, even though it was to take a venous blood sample from a tiny infant. I took my daughter's little dancing doll, the music was from Dr Zhivago, *and it went round and round and round, and the kids were mesmerized by this doll, and I would try and distract them while the parents usually held the arm and Dr Elwood took the blood. So the parent was fully aware of what was going on.*

1979–ongoing Caerphilly cohort study

John Yarnell

The Caerphilly Prospective Study really started out of my work in women in that we went back to these women to ask them for blood and we had this fairly elaborate theoretical structure looking for the determinants of HDL cholesterol, both dietary and physical determinants. We thought that it would be a good idea to do this in men as well. I knew and Peter Elwood knew that probably we should concentrate on ischaemic heart disease. We had the example of Speedwell as being set up by David Bainton as a prospective study.[212] *We knew that it was not possible to do everything within that, so I think it was a strategy formulated in the unit itself to develop the Caerphilly study, which was genuine team work with the Director, Peter Elwood, and Peter Sweetnam insisting that we concentrate on 45 to 59 year olds to try to maximize the cost-effectiveness of the exercise. I suppose I was prepared to do a lot of the donkey work as well – two evening clinics a week, which we used to do out of normal working hours, because in the 45 to 59 years olds there was still a fairly high level of employment, although a proportion of men had retired or been forced to retire early. We also did a single morning clinic to which we invited everybody to have their fasting blood sample taken in the middle of the week. Peter Elwood and others helped on a very practical level with the morning clinics. I think a lot of the staffing arrangements were geared towards the Caerphilly study and as it went on Peter Elwood became even more enthusiastic. He was still doing some aspirin work then. Towards the end of the baseline examination it became fairly obvious that we ought to carry on with the cycle of work and we did make an unsuccessful bid the second time round to get funding from the British Heart Foundation. One of the things, however, that we had got funding for, or unofficial funding for, because he was very keen to do it, was for tests of platelet aggregation. I met Serge Renaud the first time on the same platform as Tom Meade talking about platelet studies. He had done a lot of cross-sectional work and was very convinced that his methods would be convertible to large-scale epidemiological studies. So he invited me over to his unit in Lyon and had this mobile laboratory which he wasn't using at the time, and he really jumped at the chance of bringing it to Caerphilly to use in our study. After some discussions with Peter, the two Peters if you like, we decided to do a pilot phase in the grounds of the Caerphilly Miners' Hospital and we got a group of volunteers plus the reproducibility group, we called back about 200 people from the first phase of the study to see whether these tests would be reproducible in terms of single measurements for an epidemiological study over a period of time. Serge brought one technician with him. She worked for about four or five months in parallel with our two technicians to get the thing up and running. In the pilot phase we found that these tests did seem robust enough or precise enough to characterize individuals with a single measurement. So that was the cornerstone of phase 2. We did have some interest from Stan Hepsinsall in Nottingham, in doing additional tests on the platelet active markers etc., but unfortunately we weren't able to get the funding for all of that. We were able to do some more platelet function tests in phase 3 of the study, but during phase 2 we went to some trouble to reconstruct the cohort by inviting people who had moved into the area, or somehow we had missed the first time, and this provided us with a new baseline of the second phase of the study and so it carried on with fresh tests being added at various stages. I think in phase 2 and perhaps more particularly at phase 3 we realized that this might go on for some time and we began being interested in looking at stroke as an outcome, and we persuaded David Bainton and Ian Baker to put stroke into the Speedwell study at that stage, which was working on its own regular three-year cycle.*

Peter Elwood

John Yarnell made the first contact with Serge Renaud, who had taken a similar path to me, had an interest in platelets, an interest in aspirin and so on, but he had determined to do platelet aggregation studies and so he had persuaded INSERM, the counterpart of the MRC in France, to give him money to equip a caravan with platelet equipment which he towed around France and the south of England, doing platelet tests.[213] *He had two platelet aggregometers (that were slightly modified O'Brien models). He had two of everything – two centrifuges, two platelet counters,*

[212] See note 130.

[213] See note 92. See photo on page 54.

including two coffee-making machines – in this caravan. It was delightful the way it was laid out, extremely efficient, in that the subject came into the caravan, a bed was lowered across the door (it was the only way he could do it), the man lay on the bench, gave his blood, was then thanked and let go, and immediately the platelet work started, so it was done while the blood was absolutely fresh. Renaud, bless him, agreed to lend us his caravan for however long it took to do all the men in Caerphilly.

I was terribly apprehensive. I thought that if we parked this outside men's houses that it would be vandalized in no time, but we compromised, we set it up in Caerphilly Miners' Hospital, who were marvellous. They put in hard-standing and steps for us, a cable into it for current, and Andrew Beswick, who has been an absolute brick in the unit, spent four years of his life doing nothing but platelet aggregation. We asked the men to come early in the morning and give a sample of fasting blood, and Andrew found that he could only do six in a morning. It's quite a complicated test. We did aggregation of three agonists. We had to wait then for cases of MI [myocardial infarction] to occur, and we waited, I think, five years and then worked on an analysis, and we found no evidence of prediction at all. We really went to town on this, the standard measures of aggregation, pen records, I think it was about 12 different measurements on these traces and then as a final attempt, I gave them to one of the girls, and I said, 'Look, treat these as wallpaper, sort them into different patterns, tell me at the end how you describe these patterns'. I think she had about ten patterns from no effect at all, to a crazy curve. We played around with this, but still there was absolutely no prediction. We published a paper in Heart,[214] *and I can tell you with amusement that in recent days, two people have quoted that paper as showing platelet function is predictive of ischaemic heart disease. There was one very, very scrappy prediction which I was uneasy about, but if we took the very early heart attacks, there was a vague suggestion that one of the tests might predict. So that was phase 1. We then heard about two new tests of platelet function, so five years later in the next phase, we put in those two tests. One was a method of looking at aggregation in whole blood, the original test requires platelet-rich plasma, and you have to spin the blood, remove the red and white cells, and then count the platelets. There's quite a lot of manipulation of the sample and its plasma, and we felt that that was not very realistic. So when this test, devised by Rod Flower,[215] came along on whole blood, we thought, 'This will be it'. So we did that test on every man and that again took Andrew Beswick another four years of his life and John O'Brien meanwhile had devised a very, very simple test.[216] The background physiology of platelets is that if platelets are damaged or exposed to ADP [adenosine diphosphate], then they are activated. But if you block that response with aspirin, you can still get them to aggregate if you expose them to high shear and in atheroma some of the platelets are exposed to high shear forces in the blood vessels and so that might be a separate method of activation. John O'Brien took a whole-blood sample, just the residue in the syringe, stuck it in a little filter holder, sucked the blood through at a pressure which meant that they were going through the filter at high shear and then he did a platelet count on the whole blood and on the blood that came through. There was a second measure which made the test very, very attractive, you simply sucked the blood through and counted the number of drops, which gives an indication of platelet activity. Again it took, I think, ten years after those two tests, and just within the last few weeks, I have analysed the data and the whole-blood test shows no trend, but when we divided the men into fifths by their whole-blood platelet test, there was a suggestive trend with stroke, but not significant. But the fifth of men with the most active platelets on the whole-blood test, have a significantly*

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[214] Elwood P C, Renaud S, Beswick A D, O'Brien J R, Sweetnam P M. (1998) Platelet aggregation and incident ischaemic heart disease in the Caerphilly cohort. *Heart* **80**: 578–582.

[215] Cardinal D C, Flower R J. (1980) The electronic aggregometer: a novel device for assessing platelet behavior in blood. *Journal of Pharmacological Methods* **3**: 135–158. *idem* (1979) The study of platelet aggregation in whole blood. [proceedings] *British Journal of Pharmacology* **66**: 94P–95P. Blackwell G J, Flower R J, Russell-Smith N, Salmon J A, Thorogood P B, Vane J R. (1978) Prostacyclin is produced in whole blood. [proceedings] ibid. **64**: 436P.

[216] Beswick A D, O'Brien J R, Limb E S, Yarnell J W G, Elwood P C. (1994) Shear induced filter blockage. A population-based appraisal of a method for the assessment of platelet, white cell and von Willebrand factor interactions. *Platelets* **5**: 186–192.

reduced risk of stroke. It's only one subgroup, but the risk we showed is about 0.5 and is statistically significant. So that has thrown us, the association's with stroke, and it's the wrong way round, and I am just writing it up at the moment for publication.[217]

Figure 75: Speedwell team, *c.* 1989. From left, seated: Roma Worner, Eileen Coleman, Janet Lloyd. Standing: Ian Baker, Peter Elwood, David Bainton.

Peter Elwood

In those days a sample of 2500 wasn't particularly small. We would have liked it to be bigger, but I was so insistent that the Caerphilly study should be intensive, that we should collaborate with as large a number of collaborators as possible and add in as many variables as possible. For instance, at a later stage we added in lead, we added in arthritis with Silman, and we added other things, such as homocysteine with Dr Job Ubbink and antioxidants with Strain and Thurnham.[218] *It was a very intensive study, so rather than recruit large numbers, we were prepared to go on for a long time. You see it was a very stable area. Some of the cohort studies in London and places like that got into trouble trying to follow up people. Initially we had thought of ten years, but I don't think we had thought of that as an absolute end to the study. Now with regard to women, we were aware of the opportunity that we were missing, not looking at men and women, and so towards the end of the study we added in 250 women, and sadly nothing to my knowledge has ever been published about those women. When we started to analyse them, and I took a personal interest in those 250 women and looked at a number of things in them, but Peter Sweetnam pointed out that the drift by the laboratory estimations, there was always a drift over time and the women came in at the end, so we would either have to compare the women with the last 250 men in Caerphilly or we would have to indulge in some rather dubious standardization process, with the drift and the changes in the laboratories. So sadly we found it difficult.*

Figure 76: Speedwell team, *c.* 1989. From left: Janet Lloyd, Roma Worner, Ian Baker, David Bainton, Eileen Coleman.

[217] Elwood P C, Beswick A, Pickering J, McCarron P, O'Brien J R, Renaud S R, Flower R J. (2001) Platelet tests in the prediction of myocardial infarction and stroke: evidence from the Caerphilly study. *British Journal of Haematology* **113**: 514–520.

[218] Mulholland C W, Elwood P C, Davis A, Thurnham D I, Kennedy O, Coulter J, Fehily A, Strain J J. (1999) Antioxidant enzymes, inflammatory indices and lifestyle factors in older men: a cohort analysis. *Quarterly Journal of Medicine* **92**: 579–85. Strain J J, Elwood P C, Davis A, Kennedy O, Coulter J, Fehily A, Mulholland C W, Robson P J, Thurnham D I. (2000) Frequency of fruit and vegetable consumption and blood antioxidants in the Caerphilly cohort of older men. *European Journal of Clinical Nutrition* **54**: 828–833. See Appendix.

BIOGRAPHICAL NOTES

Professor Sir William Asscher

Kt FRCP (b. 1931) was Professor of Medicine at the University of Cardiff from 1976 to 1987 and Director of the Institute of Nephrology in Cardiff from 1970 to 1987. In 1988 he became Dean (later Principal) of St George's Hospital Medical School, London, until his retirement in 1996. He was Chairman of the Committee on the Review of Medicines of the Department of Health from 1985 to 1987 and Chairman of the Committee on Safety of Medicines from 1987 to 1993.

Dr David Bainton

MRCP (1941–2002) was a member of the scientific staff of the MRC Epidemiological Research Unit (South Wales) from 1970 to 1973, leaving to take an MSc at the London School of Hygiene and Tropical Medicine, moving to the Avon Area Health Authority and later the Gwent Health Authority. He was Senior Lecturer at the Centre for Applied Public Health Medicine, Cardiff, at the University of Wales College of Medicine from 1989 to 2001 and Honorary Consultant in Public Health Medicine at Gwent Health Authority from 1994 until his retirement in 2001.

Anthony Barber

(Lord Barber of Wentbridge from 1974) PC TD DL (b. 1920) was Minister of Health and member of the Cabinet from 1963 to 1964, later Chairman of Standard Chartered Bank plc from 1974 to 1987.

Professor David Barker

FRCP FRCOG FRS has been Director of the Medical Research Council Environmental Epidemiology Unit at the University of Southampton since 1984.

Dr Evan Bedford

CBE FRCP (1898–1978) joined the Middlesex Hospital in 1926, where he later became Consultant Physician, later also at the National Heart and Connaught Hospitals. He was Chairman of the Council of the British Heart Foundation and editor of the *British Heart Journal*. See Somerville W. (1984) Davis Evan Bedford. *Munk's Roll* 7: 28–30.

Dr Bill Berry

Was Chief Chief Medical Officer (Nutrition) in the Department of Health from about 1960 to perhaps 1980. Information from Dr Peter Elwood.

Sir Christopher Booth

Kt FRCP (b. 1924) trained as a gastroenterologist and was Professor of Medicine at the Royal Postgraduate Medical School, Hammersmith Hospital, London, from 1966 to 1977 and Director of the Medical Research Council's Clinical Research Centre, Northwick Park Hospital, Harrow, from 1978 to 1988, and Harveian Librarian at the Royal College of Physicians from 1989 to 1997. He was the first Convenor of the Wellcome Trust's History of Twentieth Century Medicine Group from 1990 to 1996.

Professor Gustav Born

FRCP FRS was Vandervell Professor Emeritus of Pharmacology at King's College, London, from 1978 to 1986, later Emeritus.

Dr Michael Burr

FFPHM (b. 1937) was in general practice from 1962 to 1966 and in public health until he was appointed a member of scientific staff at the Epidemiology Unit in 1970. He was Consultant Epidemiologist to the unit from 1979 and honorary consultant to the health authority until he joined the University of Wales College of Medicine in Cardiff in 1993.

Dr Jeffrey Chapman

(1923–2000) was a medical member of the scientific staff at the Pneumoconiosis Research Unit, leaving to become a medical officer of a whaling ship, the leader of one of the National Coal Board medical teams working on pneumoconiosis and a member of the Medical Research Council headquarters staff dealing with occupational medicine from 1959 to 1980. See Cochrane A L with Max Blythe. (1989) *One Man's Medicine: An autobiography of Archie Cochrane.* London: British Medical Journal for the Memoir Club, 160.

Professor Eric Cheeseman

(1912–1987) was Professor of Medical Statistics, Queen's University of Belfast, from 1961to 1977, later Emeritus. He had been a staff member of the Statistical Committee of the MRC from 1929 to 1939, and Research Statistician with the Statistical Research Unit of the MRC from 1946 to 1948.

Professor Archie Cochrane

CBE MBE FRCP FFCM (1909–1988), medical scientist and epidemiologist, whose independent wealth supported his studies in interwar Berlin, Vienna and The Hague, and a year in a field ambulance unit supporting the International Brigade in the Spanish Civil War before returning to complete his medical studies at University College Hospital, London. He qualified in 1938 before joining the Royal Army Medical Corps, was captured in 1941 and a prisoner of war in Salonica, where he conducted his first clinical trial. Following the war his work for a Diploma in Public Health at the London School of Hygiene and Tropical Medicine was supported by a Rockefeller fellowship. He was appointed to the Medical Research Council's Pneumoconiosis Research Unit in 1948. In 1960 he was appointed David Davies Professor of Tuberculosis and Diseases of the Chest at the Welsh National School of Medicine, Cardiff, becoming Director of the Epidemiological Research Unit in Cardiff in 1961 until his retirement in 1974. See also Cochrane A L. (1976) The development of epidemiology in MRC Units in Wales (1945–1975): a personal view. *Journal of the Royal College of Physicians* **10:** 316–320. (1988) Obituary: A L Cochrane. *British Medical Journal* **297:** 63 (signed ALC), 355, 419, 614, 1704. His papers are available for study at the Cochrane Archive, Llandough Hospital, Penarth, Cardiff.

Dr R H L (Dick) Cohen

CB MRCS (1907–1998) was on the staff of the MRC from 1948, serving as Deputy Chief Medical Officer from 1957 to 1962, when he was seconded to the Ministry of Health as Principal Medical Officer from 1962, Deputy Chief Medical Officer to Sir George Godber from 1967, and finally as the first Chief Scientist to the Department from 1972 until his retirement in 1973. See Wilson J M G. (1998) Richard Cohen: First Chief Scientist at the DHSS. *Journal of the Royal Society of Medicine* **91:** 222–224.

Professor Sir Richard Doll

Kt CH OBE FRCP FRS (b. 1912) was Director of the MRC Statistical Research Unit from 1961 to 1969 and subsequently Regius Professor of Medicine at the University of Oxford from 1969 to 1979, later Emeritus. He was Chairman of the Adverse Reaction Subcommittee, Committee on Safety of Medicines, from 1970 to 1977 and has been Honorary Consultant, MRC/Cancer Research UK/BHF Clinical Trial Service Unit and Epidemiology Studies Unit, Radcliffe Infirmary, Oxford, since 1983.

Dr Peter Elwood

FRCP (b. 1930) was a member of the scientific staff of the Epidemiological Research Unit (South Wales) from 1963 and its Director from 1974 until its closure in 1995. He qualified in medicine at Queen's University, Belfast, in 1954 and worked with John Pemberton from 1958 to 1963. He was to retire in 1995 but has ignored the advice and still works almost full time, supported by Janie Hughes and Janet Pickering, a statistician in the unit from 1977 to 1982. He holds Honorary Professorships in the Department of Epidemiology, Statistics and Public Health Medicine in the University of Wales College of Medicine and the Department of Social Medicine in the Univeristy of Bristol, and is a Visiting Professor in the Department of Science at the University of Ulster.

Dai Dan Evans

was General Secretary of the South Wales area National Union of Mineworkers in the 1950s and 1960s. Information from Dr Julian Tudor Hart, 18 April 2002.

Dr Joan Faulkner (Lady Doll)

(1914–2001) qualified in 1937, took the Diploma in Public Health in 1942, and joined the MRC staff in 1943 as research assistant to Dr Philip D'Arcy Hart. She joined headquarters staff in 1945 and retired as Senior Principal Medical Officer in 1979.

Professor Charles Fletcher

CBE FRCP (1911–1995) directed the MRC Pneumoconiosis Research Unit from 1945 to 1952 and was Secretary of the MRC Committee on Bronchial Research from 1954 to 1976. He was Professor of Clinical Epidemiology at the Royal Postgraduate Medical School, Hammersmith Hospital, London, from 1973 to 1976, later Emeritus, and Physician to

Hammersmith Hospital from 1952 to 1976. See also a videotape interview with Professor Charles Fletcher by Max Blythe, held at the Royal College of Physicians of London. See note 9.

Dr Harold 'Bill' Foreman

FRCP (1898–1980) was physician-superintendent of Sully Hospital, a sanitorium that became a centre for cardiothoracic medicine in south Wales. He had been a prisoner of war with Archie Cochrane and was instrumental in the relocation of Archie's epidemiology and medical statistics course to Sully Hospital from Richmond Road, Cardiff in 1962. See Robson K. (1984) Harold Mason Foreman. *Munk's Roll* **7:** 189–190. See also See note 20, 176–178.

Dr John Gallacher

AfBPsS, CPsychol (b. 1956) was a member of the MRC Epidemiology Unit from 1977 until 1997 when he became a lecturer in epidemiology in the University of Wales College of Medicine, Cardiff. He introduced psychosocial questionnaires, audiometry and noise exposure into Phase II of the Caerphilly study and a series of tests of cognitive function into Phase III and IV. He continues to work with Peter Elwood on these data and is organizing the cognitive tests for Phase V.

Dr John Gilson

CBE FRCP (1912–1989) served at the RAF Physiological Laboratory in Farnborough during the Second World War because of his interest in respiratory physiology, where he developed oxygen masks that improved air flow. He joined the MRC Pneumoconiosis Research Unit in 1946, becoming Director in 1952 until his retirement in 1976. See Kilpatrick G S. (1994) John Carey Gilson. *Munk's Roll* **9:** 197.

Dr Philip D'Arcy Hart

CBE FRCP (b. 1900) trained in medicine at University College Hospital, London, where he became a Consultant Physician. Interested in developing a career in medical research, and encouraged by Sir Thomas Lewis, he became a member of the MRC's staff, and in 1937 undertook the survey he here describes (see page 3). In 1948 he became the Director of the MRC Tuberculosis Research Unit until his retirement in 1965, to become a grant-holder of the MRC in the laboratories of the National Institute for Medical Research, London.

Dr Julian Tudor Hart

(b. 1927) was first an epidemiologist working in the Epidemiology Research Unit in 1961, before moving to general practice in 1961 until 1988. See Mullan F. (1995) Interview with Julian Tudor Hart, February 1995. Primary Care Oral History Project, 1995–98. Modern Manuscripts Collection, National Library of Medicine, Bethesda, MD, USA. Dr Tudor Hart's practice records from 1965 to 1992 are held as CMAC/GP/13 in Archives and Manuscripts, Wellcome Library, London.

Mr Nick Henderson

MRCVS FIPR (b. 1926) was a veterinary surgeon and is Executive Director of the European Aspirin Foundation. He is a Liveryman of the Society of Apothecaries.

Professor Ian Higgins

Was one of the three original scientific staff appointed to the Epidemiological Research Unit in 1961.

Sir Austin Bradford Hill

Kt FRS (1897–1991) was Professor of Medical Statistics at the London School of Hygiene and Tropical Medicine from 1945 until his retirement in 1961. His series of 17 articles in the *Lancet* in 1937 introduced the medical researcher to the use of statistics (reprinted as *Principles of Medical Statistics.* London: *The Lancet,* 1937). He was made an Honorary Fellow of the Royal College of Physicians in 1963. See Doll R. (1994) Austin Bradford Hill. *Biographical Memoirs of Fellows of the Royal Society* **40:** 129–140.

Sir Harold Himsworth

KCB FRCP FRS (1905–1993), a distinguished clinical scientist, was Professor of Medicine and Director of the Medical Unit at University College Hospital, London, from 1939 to 1949 and Secretary of the MRC from 1949 until his retirement in 1968. See Black D A K, Gray J. (1995) Sir Harold Percival Himsworth KCB. *Biographical Memoirs of Fellows of the Royal Society* **41:** 201–218. Gray J, Booth C. (1994) Sir Harold Himsworth. *Munk's Roll* **9:** 238–241.

Dr Sheila Howarth (Lady McMichael)

FRCP (1920–2000) joined the staff of the headquarters office of the MRC in 1964. She retired as Principal Medical Officer in 1980, having held responsibilities at office level for much of the MRC clinical research programme, including the Clinical Research Centre. She had previously (1943–1945) been engaged in research, mainly on the cardiovascular system, at the British Postgraduate Medical Federation, University College London, and the Institute of Cardiology.

Mrs Janie Hughes

(b. 1944) joined the MRC Epidemiological Research Unit in April 1964 and has worked under the directorship of both Archie Cochrane and Peter Elwood. She has been involved in most of the major studies mentioned in the transcript and still assists Professor Peter Elwood as he continues to work well into retirement.

Dr Philip Hugh-Jones

(b. 1917) was Consulting Physician and Director of the Chest Unit at King's College Hospital, London, and Consulting Physician and part-time Director of the MRC Clinical Pulmonary Physiology Research Unit at Hammersmith Hospital, London, from 1964 to 1967 when it was taken over by the University of London. He had been on the scientific staff of the MRC Pneumoconiosis Unit from 1945 to 1955.

Professor Edward H Kass

(1917–90), physician, medical researcher and a world expert in infectious diseases. He was William Ellery Channing Professor of Medicine at Harvard Medical School, Founder and Director of the Channing Laboratory. His interest in bacteriuria led to questions about its possible relationship to hypertension and he collaborated with Bill Miall and Ken Stuart and his son Steven, from Barbados first in Jamaica and later in the Rhondda Valley, south Wales, which he described as 'twelve years preceptorship in epidemiologic methods and approaches to the study of chronic diseases'. See Kass A M. (1996) 'A Brief History of the Channing Laboratory,' talk given on 31 October 1996. (www.channing.harvard.edu/kass.htm, visited 4 February 2002).

Professor Stewart Kilpatrick

OBE FRCP (b. 1925) was Registrar at the Pneumoconiosis Research Unit in south Wales from 1952 to 1955. He followed Archie Cochrane as David Davies Professor of Tuberculosis and Chest Diseases at the University of Wales College of Medicine, Cardiff, from 1971 and was Dean of Clinical Studies and later Vice-Provost from 1987 until his retirement in 1990 and Consultant Physician for the South Glamorgan Area Health Authority from 1963 to 1990 .

Sir Thomas Lewis

CBE FRCP FRS (1881–1945), Welsh cardiologist and clinical scientist, directed the first of the MRC's research units, the Department of Clinical Research, established at University College Hospital Medical School, London, from 1919 until his retirement in 1945. He was awarded one of the first Beit Fellowships in 1910. See Drury A N, Grant R T. (1945–48) Sir Thomas Lewis. *Obituary Notices of Fellows of the Royal Society* **5:** 179–202. A collection of his papers, CMAC/PP/LEW, is held in Manuscripts and Archives, Wellcome Library.

Professor Thomas Meade

FRCP FRS (b. 1936) has been Director of the MRC Epidemiology and Medical Care Unit since 1970, first at Northwick Park Hospital then at the Wolfson Institute of Preventive Medicine in 1992. He is also Honorary Consultant in Epidemiology at St Bartholomew's Hospital, London, and Northwick Park Hospital, Harrow.

Sir Edward Mellanby

FRS (1884–1955) was Secretary of the Medical Research Council (MRC) from 1933 to 1949.

Dr William Miall

(b. 1917) was a member of the scientific staff of the MRC's Pneumoconiosis Research Unit from 1951 to 1961, when he joined the MRC's Epidemiological Research Unit until appointed Director of the MRC Epidemiology Unit in Jamaica from 1962 to 1970; a consultant in epidemiology and member of the scientific staff in the Epidemiology and Medical Care Unit at Northwick Park Hospital, Harrow, from 1971 to 1983.

Mr Fred Moore

(b. 1915) was a member from 1950 to 1985 of the Pneumoconiosis Research Unit, moving to the Empidemiological Research Unit, later the Epidemiology Unit.

Dr Ian Munro

FRCP (1923–1997) was editor of the *Lancet* from 1976 to 1988. He had joined the staff of the *Lancet* in 1951 and was deputy editor from 1965.

Dr Shaun Murphy

(b. 1951) has been Departmental Manager of the Department of Social Medicine at the University of Bristol since 1993 and writes on the history of social medicine.

The Rt Hon Sir Patrick Nairne

GCB MC (b. 1921) had a Civil Service career from 1947 to 1981 serving in the Admiralty, the Ministry of Defence and the Cabinet Office. He was Permanent Secretary of the Department of Health and Social Security from 1975 until 1981.

Dr Andy Ness

(b. 1962) has been a Senior Lecturer in Epidemiology at the University of Bristol since 1997. From 1993 to 1997 he held a Wellcome Training Fellowship in Epidemiology at the University of Cambridge, and was senior registrar in public health medicine at Cambridge in 1997.

Dr Peter Oldham

Was a statistician at the Epidemiological Research Unit, trained by Sir Austin Bradford Hill. See Oldham P D. (1968) *Measurement in Medicine: The interpretation of numerical data.* London: English Universities Press.

Professor Linus Pauling

(1901–1994) advocated the use of large doses of vitamin C to cure cancer and other diseases. He received the Nobel Prize for Chemistry in 1954 for his work on the chemical bond and its application to the structure of complex substances, such as proteins and antibodies, and was awarded the 1962 Nobel Peace Prize for his campaign against nuclear weapons.

Professor Anthony Seaton

CBE FRCP FRCPE FMedSci (b. 1938) has been Professor of Environmental and Occupational Medicine at Aberdeen University since 1988. He was Director of the Institute of Occupational Medicine, Edinburgh, from 1978 to 1990; Editor of *Thorax* from 1977 to 1982; Chairman of the Department of Environment Expert Panel on Air Quality Standards from 1991 to 2002; President of the British Thoracic Society in 1999; and a member of the Department of Health Committee on Medical Aspects of Air Pollution.

Professor Sir Stanley Peart

FRS FRCP (b. 1922) was Professor of Medicine, University of London, at St Mary's Hospital Medical School, from 1957 to 1987, later Emeritus. He was a Trustee of the Wellcome Trust from 1975, and Deputy Chairman from 1991 until 1994.

Professor John Pemberton

FRCP (b. 1912) was Professor of Social and Preventive Medicine at Queen's University, Belfast, from 1958 to 1976, later Emeritus, and Consultant in Social and Preventive Medicine at the Royal Victoria Hospital, Belfast. He was a founder member and first treasurer of the Society for Social Medicine in 1957 and co-founder of the International Epidemiological Association in the same year. He confirmed the existence of byssinosis in flax workers in Northern Ireland in 1963. See also Pemberton J. (1998) Social medicine comes on the scene in the United Kingdom, 1936–1960. *Journal of Public Health Medicine* **20:** 149–153. *idem* (2002) Origins and early history of the Society for Social Medicine in the UK and Ireland. *Journal of Epidemiology and Community Health* **56:** 342–346, photograph on page 345. McPherson K, Dunnell K. (2002) Society for Social Medicine 1977–1992. *Journal of Epidemiology and Community Health* **56:** 347–348.

Professor Sir Richard Peto

FRS (b. 1943) has been Professor of Medical Statistics and Epidemiology at the University of Oxford since 1992. He was an MRC Research Officer from 1967 to 1969 before moving to the University of Oxford in 1969, as Lecturer from 1972 and Reader in Cancer Studies from 1975.

Sir George Pickering

FRS (1904–1980) was Regius Professor of Medicine in Oxford in the Department of Clinical Research from 1956 until his retirement in 1969. He was a member of the MRC and its Clinical Research Board from 1954 to 1958. A collection of his papers, CMAC/PP/GWP, is held by Archives and Manuscripts, Wellcome Library.

Sir Robert Platt

(Lord Platt of Grindleford from 1967) Bt FRCP (1900–1978) was Professor of Medicine at the University of Manchester from 1945 to 1965 and President of the Royal College of Physicians from 1957 to 1962. See his autobiography, *Private and Controversial.* London: Cassell, 1972.

Dr John Fraser Roberts

CBE FRCP FRCPsych FRS (1899–1987), a pioneer in medical genetics, studied animal breeding at Edinburgh, and later qualified in medicine in 1936. He was Director of the MRC Clinical Genetics Research Unit at the Institute of Child Health, London, and Honorary Consultant in Medical Genetics at the Hospital for Sick Children, Great Ormond Street, London, from 1957 until his retirement in 1964. He had been Director of the Burden Mental Research Department at the Stoke Park Colony, Bristol, from 1933 to 1957 and Consultant in Medical Genetics at the Royal Eastern Counties Hospital, Colchester, from 1946 to 1980 and was associated with the Eugenics Society for 37 years. See Polani P E. (1989) John Alexander Fraser Roberts. *Munk's Roll* **8:** 416–420.

Professor Richard Selwyn Francis Schilling

CBE FRCP (1911–1997) was Professor of Occupational Health at the London School of Hygiene and Tropical Medicine from 1960 until his retirement in 1976, later Emeritus, and Director of the Rockefeller Unit of Occupational Health (later Institute) from 1956. He had been Secretary of the Industrial Health Research Board of the MRC from 1942 to 1946 at the time of Charles Fletcher's appointment. See his autobiography, Schilling R. (1998) *A Challenging Life: Sixty years in occupational health.* London: Canning. See also Schilling R. (1997) Obituary: Richard Selwyn Francis Schilling. *British Medical Journal* **315**: 1546.

Professor Gerry Shaper

FRCP FRCPath (b. 1927) qualified in Cape Town, South Africa, joining the Department of Medicine at Makerere University Medical School, Kampala, Uganda, in 1957, moving to the MRC Social Medicine Unit at the London School of Hygiene and Tropical Medicine in 1970 and in 1975 to the Department of Epidemiology and Public Health as Professor of Clinical Epidemiology at the Royal Free Hospital School of Medicine, London, until his retirement in 1992, later Emeritus.

Professor Michael Shepherd

CBE FRCP FRCPsych was Professor of Epidemiological Psychiatry at the Institute of Psychiatry, University of London, and Hon. Physician at the Bethlem Royal and Maudsley Hospitals, King's College Hospital, London, from 1965 to 1988, later Emeritus.

Professor George Davey Smith

FSPHM (b. 1959) has been Professor of Clinical Epidemiology in the Department of Social Medicine at the University of Bristol since 1994. He had a part-time attachment at the MRC Epidemiology Unit from 1986 to 1987 and has collaborated closely with them since.

Professor Stephen Stansfeld

MBBS PhD MRCP MRCPsych (b. 1951) has been Professor of Psychiatry at St Bartholomew's and the Royal London School of Medicine and Dentistry, Queen Mary and Westfield College, since 1999. He was a Wellcome Trust Research Training Fellow at the Institute of Psychiatry, London, at the time of his first involvement with the Caerphilly study. More recently, he has been Senior Lecturer in Social and Community Psychiatry, Reader and Co-Director of the Whitehall II study at University College London. See Marmot M G, Davey Smith G, Stansfeld S A, Patel C, North F, Head J, White I, Brunner E, Feeney A. (1991) Health inequalities among British Civil Servants: The Whitehall II study. *Lancet* **337:** 1387–1393.

Dr Antony Selwyn St Leger

FFCM (b. 1948) has been a consultant and senior lecturer in public health medicine at the University of Manchester since 1980. He was at the MRC Epidemiology Unit (South Wales) from 1974 to 1980.

Dr Alice Stewart

FRCP (1906–2002) worked on MRC-funded projects for Dr Leslie Witts during the war, including a study of pneumoconiosis, 1945–46, became a lecturer in the Nuffied Department of Social Medicine at the University of Oxford in 1946, a reader in 1949 and head of the Social Medicine Unit until her retirement in 1974. Her work on radiation risks and childhood cancer put her at odds with the medical establishment. With the statistician, George Kneale, she established in 1953 what became the Oxford Survey of Childhood Cancer, one result was that pregnant women were no longer sent for X-rays. In 1974 she started her collaboration with Thomas Mancuso on the health of nuclear workers in the USA, which led to congressional investigations in 1978–79. She was awarded the Livelihood Award, the alternative Nobel, in 1986 and the Ramazzini Prize for epidemiology in 1992, and was one of the founders of the *British Journal of Industrial Medicine*. See Anonymous. (2002) Obituaries: Dr Alice Stewart. *The Times* (27 June 2002). See also note 40.

Professor David Strachan

FRCP FMedSci (b. 1957) has been Professor of Epidemiology at St George's Hospital Medical School, London, since 1997. Although he never worked at the MRC Epidemiology Unit he recently collaborated closely with the unit on studies of the relationship between several chronic infections and coronary heart disease in the Caerphilly cohort. He also has major research interests in the epidemiology of asthma and allergy. He was a Wellcome Research Training Fellow in Clinical Epidemiology at the Department of Community Medicine at the University of Edinburgh from 1985 to 1987.

Mr Peter Sweetnam

(b. 1941) was a statistician at the Epidemiological Research Unit (South Wales) from 1966 until the final cessation of MRC funding in 1999.

Dr Hugh F Thomas

(b. 1952) was a research officer at the MRC Epidemiology Unit, Cardiff, from 1976 to 1981 and after medical training from 1995 to 1999. He has been Honorary Archivist of the Cochrane Archive, Llandough Hospital, Penarth, South Glamorgan, since 1998. He is now in general practice in Eastbourne. See Thomas H F. (1999) Medical research in the Rhondda valleys. *Postgraduate Medical Journal* 75: 257–259.

Ms Mary Thomas (Mrs Hart)

(b. 1940) was a fieldworker at the Medical Research Council Pneumoconiosis Research Unit from 1960 to 1962, and later for the MRC Medical Epidemiology and Medical Care Unit. Dr Julian Tudor Hart: 'When Mary was working for the MRC, which she did for most of our working lives, there was a time when she was the head of our research unit: she was running the team, organizing everything, a very responsible job, and doing it very well indeed. She had got a fearsome reputation in Tom Meade's unit. Her starting hourly rate of pay was less than the street crossing lady outside the school.' Interview with Julian Tudor Hart conducted by Andy Ness on 14 June 2000.

Dr David Tyrrell

CBE FRCP FRCPath FRS (b. 1925), physician and virologist, was previously Director of the MRC Common Cold Unit, Salisbury, from 1982 to 1990 and Deputy Director of the Clinical Research Centre, Harrow. He served as a Trustee of the Nuffield Foundation from 1977 to 1992 and on committees concerned with clinical research ethics, genetic manipulation, use of dangerous pathogens, AIDS and BSE.

Professor Martin Vessey

CBE FRCPE FRCGP FRCP FMedSci FRS (b. 1936) was Professor of Public Health, formerly Social and Community Medicine, at the University of Oxford from 1974 until his retirement in 2000, later Emeritus. He had been a Scientific Officer in the Department of Statistics at Rothamsted Experimental Station from 1960 to 1965, a member of the Scientific Staff at the MRC Statistical Research Unit from 1966 to 1969 and Lecturer in Epidemiology at the University of Oxford from 1969 to 1974.

Professor Owen Wade

CBE FRCP (b. 1921) was a clinical assistant at the Pneumoconiosis Research Unit from 1948 to 1951, when he moved to the University of Birmingham as Lecturer, later Senior Lecturer in Medicine until his appointment as Whitla Professor of Therapeutics and Pharmacology at Queen's University, Belfast, from 1957 to 1971, returning to Birmingham as Professor of Therapeutics and Clinical Pharmacology from 1971 to 1986. See his autobiography, *When I Dropped the Knife*. Bishop Auckland: Pentland Press, 1996.

Dr Christopher Wagner

(1923–2000), a pathologist educated in South Africa, was a member of the scientific staff of the Pneumoconiosis Unit, Llandough Hospital, Penarth, Cardiff, from 1962 to 1988. His 1960 paper on 'diffuse pleural mesothelioma and asbestos exposure in the North Western Cape province' implicated exposure to blue asbestos and the development of a particular type of cancer. See Anonymous. (2000) Christopher Wagner. *The Daily Telegraph* (12 July 2000), 27. McConnochie K. (2000) Chris Wagner. *The Guardian* (1 July 2000), 22.

Professor Estlin Waters

(b. 1934) born in Toronto, Canada, was Senior House Officer at the Pneumoconiosis Research Unit, Llandough Hospital, Penarth, Cardiff, from 1960, joining the Epidemiology Research Unit in 1965 until moving to the University of Southampton on his appointment as Senior Lecturer in 1970, Reader in 1975 and Professor of Community Medicine from 1976 to 1990. He was Professorial Fellow until his retirement in 1994, later Emeritus. He was on the Council of the International Epidemiological Association from 1971 to 1977 and 1981 to 1984, serving as Membership Secretary and General Secretary from 1974 to 1977.

Dr Jean Weddell

(b. 1928) qualified in 1953 and spent five years in South Korea and Jordan working on tuberculosis control. She had been a student on Archie Cochrane's tuberculosis and chest diseases course at Sully Hospital and became a member of the MRC scientific staff, joining of the Epidemiology Research Unit (South Wales) from 1966 to 1970. She took part in the development of computerized information systems for child health, cancer registration, perinatal care and a register of those with learning difficulties as well as the higher specialist training of registrars in public health medicine.

Dr Martin Wright

FRCP (1912–2001), the inventor of the peak flow meter, was a bioengineer who joined the Medical Research Council Pneumoconiosis Research Unit at Llandough Hospital, Penarth, South Glamorgan in 1949. He moved in 1957 to the National Institute for Medical Research, Mill Hill, London, to work solely on instrument development, then in 1969 to the MRC's Clinical Research Centre at Northwick Park Hospital, Harrow. He developed, among other equipment, the Wright respirometer, the continuous infusion pump now universally used in terminal and postoperative care, an infant apnoea monitor and the standard breath alcohol detector. The MRC holds the patents on all his inventions. See Anonymous. (2001) Martin Wright. *The Times* (23 March 2001), 25. Wright C M. (2001) Basil Martin Wright. *British Medical Journal* **322:** 1308.

Mrs Sheila Wright (neé Smith)

(b. 1919) was the Medical Research Council's Publications Officer from 1950 to 1952, when she edited one of the PRU's reports, and from 1970 to 1980 as a Grants Committee Secretary.

APPENDIX

Epidemiology Unit's collaborators during the Caerphilly Study, 1979–99

Diagnosis of ischaemic stroke
Tony Bayer, Llandough Hospital; Shah Ebrahim, University of Bristol.

Haemostatic factors
John O'Brien, Mike Etherington, St Mary's Hospital, Portsmouth; Gordon Lowe, University of Glasgow; Philip Whitehead, Ceridwen Spence, Frenchay Hospital; Serge Renaud, INSERM, Lyon, France; John Martin, Philip Bath, Wellcome Research Laboratories, Beckenham, Kent; John Giddings, Arthur Bloom, University Hospital Cardiff; David Hutton, Cardiff Royal Infirmary; Rod Flower, University of Bath; Professor Stan Heptinstall, University of Nottingham.

Lipids
Professor Tom Hayes, Keith Davies, University Hospital, Cardiff; Dolores Price, Caerphilly and District Miner's Hospital; Colin Bolton, Bristol; Norman Miller, St Thomas' Hospital, London; Paul Durrington, J Mackness, University of Manchester.

Hormones
Diane Riad-Fahmy, Tenovus Institute, Cardiff; Vincent Marks, University of Guildford.

Biochemistry
Job Ubbink, University of Pretoria, South Africa; Sean Strain and David Thurnham, University of Ulster; Neal Benewitz, USA; John Yudkin, Whittington Hospital, London.

Bacterial and other antibodies
David Strachan, St George's Hospital Medical School, London.

Trace elements
Hartmut Ising, Berlin; Colin Toothill, University of Leeds.

Psycho-social factors
Stephen Stansfeld, St Bartholomew's and the Royal London School of Medicine and Dentistry, Queen Mary and Westfield College; Teresa Yeung, University of Wisconsin, USA.

Hearing loss
Stuart Gatehouse, MRC Hearing Institute, Nottingham; Adrian Davies, University Hospital, Cardiff.

Cognitive function
Carole Brayne, Felicia Huppert, University of Cambridge; Professor Keith Wesnes, University of Reading; Brian Stollery, Pat Rabbitt, University of Manchester.

Dr Peter Elwood, note on draft manuscript, 27 March 2002.

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