



## Origins of Neonatal Intensive Care

Christie, DA; Tansey, EM

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Wellcome Witnesses  
to Twentieth Century Medicine

ORIGINS OF NEONATAL INTENSIVE CARE  
IN THE UK

A Witness Seminar held at the  
Wellcome Institute for the History of Medicine,  
London, on 27 April 1999

Witness Seminar Transcript edited  
by D A Christie and E M Tansey

Introduction by Professor Peter Dunn

Volume 9 – April 2001

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#### Key

##### Front cover photographs, L to R from the top:

Dr Herbert Barrie  
Professor David Edwards, Dr Jean Smellie, Professor Osmund Reynolds  
Professor Sir David Hull, Sir Christopher Booth  
Professor Malcolm Levene, Dr Lilly Dubowitz  
Professor Osmund Reynolds, Professor Robert Boyd (chair)  
Dr Rodney Rivers, Dr Pamela Davies (1924–2009)  
Professor Harold Gamsu (1931–2004), Professor Jonathan Wigglesworth  
Professor John Davis, Professor David Harvey

##### Back cover photographs, L to R from the top:

Dr Lilly Dubowitz, Professor David Delpy  
Professor Maureen Young, Dr Pamela Davies (1924–2009)  
Professor Neil McIntosh, Professor Denys Fairweather, Professor Sir David Hull  
Dr Beryl Comer (1910–2007), Professor Eva Alberman  
Professor Victor Dubowitz, Professor Malcolm Levene  
Professor Tom Oppé (1925–2007)

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## INTRODUCTION

The Wellcome Trust Centre History of Twentieth Century Medicine Group, assisted by Professor Osmund Reynolds, are to be warmly congratulated on gathering together such a group of 'golden oldies' while they are still around, in order to reminisce on the origins of neonatal intensive care. I was sad not to be able to get to the seminar and was thus all the happier to be invited to prepare this introduction to the transcript of the afternoon's proceedings. It makes interesting reading. The development of newborn care in this country since 1950 has been well covered under the able chairmanship of Professor Robert Boyd. Inevitably though, in the time available, some aspects received little attention, among which one could list the impact that hexachlorophane and nystatin had in the 1960s on those ubiquitous staphylococcal and monilial infections, the significance and management of polycythaemia, the advent of necrotizing enterocolitis and the importance of the transitional fetal circulation during adaptation to extrauterine life in the prevention of respiratory distress syndrome (RDS). More surprising was the lack of discussion of continuous positive airway pressure (CPAP) in the management of RDS.

If rhesus haemolytic disease and exchange transfusion triggered a surge in paediatric interest in the newborn in the 1950s, it was the introduction of the Usher regime and the use of positive pressure ventilation in the management of RDS that provided the main impulse to create special care baby units in major maternity units throughout the country during the 1960s. However, by the end of the decade, as Osmund Reynolds himself points out (page 17), the results had proved most disappointing and it was at this juncture that CPAP proved to be such a godsend, at any rate in our unit in Bristol. We introduced our modification of Gregory's technique in October 1971 with dramatic success (pages 24–25). Within three years the neonatal mortality of babies weighing over 1kg at birth (after excluding infants with lethal malformations) had fallen by 74 per cent – the RDS mortality fell by more than 80 per cent – at a time when the national mortality statistics were showing little change. This gave a great boost to the morale and efforts of those attempting to introduce a neonatal intensive care service with the slenderest of resources. During the next 11 years (1974–1985) the neonatal mortality statistic for our unit fell a further 18 per cent giving a total 92 per cent fall from the 1970 level.

In 1971 the Sheldon Report recommended the provision of one intensive care cot per 1000 births a year and in 1972 the British Paediatric Association (BPA) recognized the need for ten consultant perinatal/neonatal posts throughout the country to supervise an intensive care service. However, the BPA also decreed that neonatal care would remain in the hands of general paediatricians. But general paediatrics itself was very under-staffed and under-funded, and furthermore was largely based in children's hospitals rather than in the maternity units where most babies were born. Neonatal intensive care and, to a lesser extent, special care implies the need for continuous

observation and management. At that time, in the early 1970s, there were approximately 700 000 births each year in the UK, some 70 000 (10 per cent) of whom required special or intensive care. How could ten specialists possibly hope to provide an adequate service even with general paediatric assistance, especially as the availability of junior staff was desperately inadequate? The allocation of nurses for neonatal intensive care was also seriously insufficient, while the funding for essential equipment was virtually nonexistent. In our unit in Bristol, for example, with 32 special/intensive care cots, the annual budget for equipment was £500 at a time when it cost approximately £15 000 to set up a single intensive care cot with a 'life' of eight to ten years. Fortunately, charities like BLISS and public generosity helped to bridge the gap. But it could not supply the staffing. In 1980 the DHSS admitted that there were still only 12 neonatal consultant posts throughout the country. These factors seriously retarded the development of a neonatal intensive care service for more than a decade (page 4).

Against this background, in 1976, some 20 perinatal/neonatal paediatricians in the UK and the Republic of Ireland founded a pressure group that was soon to evolve into the multidisciplinary British Association of Perinatal Medicine (BAPM). Its aim was to improve the standard of perinatal care and, in particular, that of neonatal intensive care. The achievements of the Association include: agreement on a training programme for the subspecialty; guidelines for the recognition of suitable hospital training posts; definition of the categories of babies receiving neonatal care, and requirements in medical and nurse staffing and facilities at each level of care; national and regional surveys of the staffing and facilities available for care, and for the transfer of babies between units; production of a data set to facilitate standardized annual reports; organization of multicentre trials and of postgraduate education. Now, 25 years after its foundation, the BAPM has more than 600 members.

Meanwhile, during the 1970s, following a leader in the *Lancet* on the price of perinatal neglect (1974), a number of reports including the Oppé Report (1975), the Court Report (1976), and, later the Walker Report (1980) catalogued the serious deficiencies in the neonatal services in this country. In 1978 the BPA/Royal College of Obstetricians and Gynaecologists (RCOG) Liaison Committee produced detailed recommendations for the improvement of infant care during the perinatal period (page 61) and the parent bodies forwarded this document to the House of Commons Social Services Committee chaired by Mrs René Short, MP. The report of this Committee on Perinatal Mortality in 1980 detailed the extraordinary neglect of our perinatal services and, though largely ignored by Government, helped to speed up the provision of a countrywide neonatal intensive care service during the 1980s. But as staffing and facilities improved, the demands on the service also steadily increased because of the need to provide intensive care for the extremely premature infants previously considered pre-viable. Their numbers were at the same time being augmented by iatrogenic multiple pregnancies induced by treatment for subfertility. Throughout my years in practice there was never a time when the neonatal service was

adequately resourced or when the medical and nursing staff didn't have to work very unreasonable long hours. Frequently the service was near breaking point. My still-active colleagues assure me that the position has not changed, in spite of remarks to the contrary in the transcript. In our tertiary care neonatal unit in Bristol, 40 per cent of the intensive care cots have been closed down during the past year because of a lack of trained nursing staff and the need to refuse admission or make transfers to other units has increased enormously.

Three further points should be made. In the transcript I noted certain critical remarks concerning a lack of obstetric collaboration (pages 12 and 27). No doubt this was so in the early days. All I can say is that from 1958 when I started to work with the newborn in maternity units, I received nothing but support and help from my obstetric colleagues, and I remain most grateful to them.

Credit was rightly given during the seminar to our North American and Scandinavian colleagues for the advances in technique and equipment that they pioneered over the last half-century. Acknowledgement should also be given to Germany for producing that invaluable tool the transcutaneous oxygen monitor, and to The Netherlands and France for helping to lay the foundations of infant developmental assessment.

My last point concerns the neonatal nurses who have for many years borne the brunt of the neonatal intensive care workload. In 1977, the late Jean Boxhall, Paula Hale and others, including Anthea Blake, Mary Colbeck, Patricia Townsend and Sandra Reynolds, founded the Neonatal Nurses Association (page 67). Along with the *Journal of Neonatal Nursing* (edited for many years by Barbara Weller), the Association has done much to organize, educate and support nurses in their demanding and essential work. The neonatal service and the public owe them a great debt.

I am sure that readers will enjoy the anecdotes in these transcripts as much as I myself have. We should all be most grateful to the contributors and especially to Professor Osmund Reynolds.

**Professor Peter Dunn**  
**Bristol**



## WITNESS SEMINARS: MEETINGS AND PUBLICATIONS<sup>1</sup>

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 potentials 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 support 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 25 such meetings, most of which have been published, as listed in the table below.

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, whilst 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 copyright assignment forms. Copies of all additional correspondence received during the editorial process are deposited with the records of the meeting in Archives and Manuscripts, Wellcome Library, London.

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<sup>1</sup> The following text also appears in the 'Introduction' to recent volumes of *Wellcome Witnesses to Twentieth Century Medicine* 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 for historians new insights, fresh material for study and prompt fresh 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.

### Members of the Programme Committee of the History of Twentieth Century Medicine Group

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The Group's activities are overseen by the Programme Committee, which includes professional historians of medicine, practising scientists and clinicians. The Programme Committee during 2000–2001 comprised:

**Dr Tilli Tansey** – Historian of Modern Medical Science, Academic Unit (now Wellcome Trust Centre), and Convenor;

**Sir Christopher Booth** – Academic Unit (now Wellcome Trust Centre), former Director, Clinical Research Centre;

**Dr Robert Bud** – Head of Life and Environmental Sciences, Science Museum;

**Dr Daphne Christie** – Senior Research Assistant, Academic Unit (now Wellcome Trust Centre), and Organizing Secretary;

**Dr Gordon Cook** – Academic Unit (now Wellcome Trust Centre), former consultant, St Pancras Hospital for Tropical Diseases;

**Dr Chris O'Callaghan** – Consultant paediatrician, Leicester;

**Professor Roy Porter** – Historian of the Social History of Medicine, Academic Unit (now Wellcome Trust Centre).

## HISTORY OF TWENTIETH CENTURY MEDICINE WITNESS SEMINARS, 1993–2001

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- 1993**     **Monoclonal antibodies<sup>1</sup>**  
Organizers: Dr E M Tansey and Dr Peter Catterall
- 1994**     **The early history of renal transplantation**  
Organizer: Dr Stephen Lock
- Pneumoconiosis of coal workers<sup>2</sup>**  
Organizer: Dr E M Tansey
- 1995**     **Self and non-self: a history of autoimmunity<sup>1</sup>**  
Organizers: Sir Christopher Booth and Dr E M Tansey
- Ashes to ashes: the history of smoking and health<sup>3</sup>**  
Organizers: Dr Stephen Lock and Dr E M Tansey
- Oral contraceptives**  
Organizers: Dr Lara Marks and Dr E M Tansey
- Endogenous opiates<sup>1</sup>**  
Organizer: Dr E M Tansey
- 1996**     **Committee on Safety of Drugs<sup>1</sup>**  
Organizers: Dr Stephen Lock and Dr E M Tansey
- Making the body more transparent: the impact of nuclear magnetic resonance and magnetic resonance imaging<sup>4</sup>**  
Organizer: Sir Christopher Booth
- 1997**     **Research in General Practice<sup>4</sup>**  
Organizers: Dr Ian Tait and Dr E M Tansey
- Drugs in psychiatric practice<sup>4</sup>**  
Organizers: Dr David Healy and Dr E M Tansey
- The MRC Common Cold Unit<sup>4</sup>**  
Organizers: Dr David Tyrrell and Dr E M Tansey
- The first heart transplant in the UK<sup>5</sup>**  
Organizer: Professor Tom Treasure
- 1998**     **Haemophilia: recent history of clinical management<sup>6</sup>**  
Organizers: Professor Christine Lee and Dr E M Tansey

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

<sup>2</sup> 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.

<sup>3</sup> Lock S P, Reynolds L A, Tansey E M. (eds) (1998) *Ashes to Ashes – The history of smoking and health*. Amsterdam: Rodopi B V, 228pp.

<sup>4</sup> Tansey E M, Christie D A, Reynolds L A. (eds) (1998) *Wellcome Witnesses to Twentieth Century Medicine*, vol. 2. London: The Wellcome Trust, 282pp.

<sup>5</sup> Tansey E M, Reynolds L A. (eds) (1999) Early heart transplant surgery in the UK. *Wellcome Witnesses to Twentieth Century Medicine*, vol. 3. London: The Wellcome Trust, 72pp.

<sup>6</sup> 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.

- Obstetric ultrasound: historical perspectives**<sup>7</sup>  
Organizers: Dr Malcolm Nicolson, Mr John Fleming and Dr E M Tansey
- Post penicillin antibiotics**<sup>8</sup>  
Organizers: Dr Robert Bud and Dr E M Tansey
- Clinical research in Britain, 1950–1980**<sup>9</sup>  
Organizers: Dr David Gordon and Dr E M Tansey
- 1999 Intestinal absorption**<sup>10</sup>  
Organizers: Sir Christopher Booth and Dr E M Tansey
- The MRC Epidemiology Unit (South Wales)**  
Organizers: Dr Andy Ness and Dr E M Tansey
- Neonatal intensive care**<sup>11</sup>  
Organizers: Professor Osmund Reynolds and Dr E M Tansey
- British contributions to medicine in Africa after the Second World War**<sup>12</sup>  
Organizers: Dr Mary Dobson, Dr Maureen Malowany,  
Dr Gordon Cook and Dr E M Tansey
- 2000 Childhood asthma, and beyond**<sup>13</sup>  
Organizers: Dr Chris O'Callaghan and Dr Daphne Christie
- Peptic ulcer: rise and fall**  
Organizers: Sir Christopher Booth, Professor Roy Pounder and Dr E M Tansey
- Maternal care**<sup>14</sup>  
Organizers: Dr Irvine Loudon and Dr Daphne Christie
- 2001 Leukaemia**  
Organizers: Professor Sir David Weatherall, Professor John Goldman,  
Sir Christopher Booth and Dr Daphne Christie
- The MRC Applied Psychology Unit**  
Organizers: Dr Geoff Bunn and Dr Daphne Christie
- Genetic screening**  
Organizers: Professor Doris Zallen and Dr Daphne Christie

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<sup>7</sup> 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.

<sup>8</sup> Tansey E M, Reynolds L A. (eds) (2000) Post penicillin antibiotics: From acceptance to resistance? *Wellcome Witnesses to Twentieth Century Medicine*, vol. 6. London: The Wellcome Trust, 71pp.

<sup>9</sup> 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, 74pp.

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

<sup>11</sup> 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.

<sup>12</sup> 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.

<sup>13</sup> 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, in press.

<sup>14</sup> 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, in press.

## ACKNOWLEDGEMENTS

'Neonatal Intensive Care' was suggested as a suitable topic for a Witness Seminar by Professor Osmund Reynolds. He and Professor Robert Boyd provided many of the names of individuals to be invited, assisted us in planning the meeting and deciding the topics to be discussed. We are grateful to them for their input. We also thank Professor Peter Dunn for writing a useful introduction to these published proceedings and Professor Robert Boyd for his excellent chairing of the occasion. Our particular thanks also go to Dr Irvine Loudon, who read through an earlier draft of the transcript, and to Professor Herbert Barrie, Professor Harold Gamsu and Professor Osmund Reynolds for additional help. Professor Victor Dubowitz very kindly took the photographs and has provided the many prints used for this volume's cover.

As with all our meetings, we depend a great deal on our colleagues at the Wellcome Trust to ensure their smooth running: the Audiovisual Department and the Medical Photographic Library, Julie Wood, who has supervised the design and production of this volume, our indexer, Nina Boyd, and our readers, Lucy Moore and Andy Oppenheimer. Mrs Jaqui Carter is our transcriber, and Mrs Wendy Kutner and Mrs Lois Reynolds assist us in running the meetings. Finally, we thank the Wellcome Trust for supporting this programme.

Tilli Tansey

Daphne Christie

Wellcome Trust Centre for the History of Medicine at UCL

# ORIGINS OF NEONATAL INTENSIVE CARE IN THE UK

The transcript of a Witness Seminar held at the  
Wellcome Institute for the History of Medicine,  
London, on 27 April 1999

**Edited by D A Christie and E M Tansey**

## PARTICIPANTS

Professor Eva Alberman	Dr Patricia Hamilton
Dr Herbert Barrie	Professor David Harvey
Professor Roland Blackwell	Professor Sir David Hull
Miss Anthea Blake	Professor Neil McIntosh
Sir Christopher Booth	Professor Ross Mitchell
Professor Robert Boyd (Chair)	Professor Colin Normand
Professor Richard Cooke	Professor Tom Oppé
Dr Beryl Corner	Professor Osmund Reynolds
Dr Pamela Davies	Dr Rodney Rivers
Professor John Davis	Dr Jean Smellie
Professor David Delpy	Dr Ann Stewart
Dr Lilly Dubowitz	Dr Tilli Tansey
Professor Victor Dubowitz	Professor Jonathan Wigglesworth
Miss Caroline Dux	Professor John Wyatt
Professor Denys Fairweather	Professor Maureen Young
Professor Harold Gamsu	

**Others attending the meeting included:** Dr Simon Bignall, Dr Geoffrey Durbin, Professor David Edwards, Dr Jonathan Grant, Dr Jenny Hazelgrove, Dr Peter Hope, Professor Malcolm Levene, Dr Ben Lloyd, Dr Diana Manuel, Professor Anthony Milner, Miss Mae Nugent, Dr Chris O'Callaghan, Dr Jenny Stanton, Dr David Tyrrell, Professor Andrew Wilkinson, Dr David Zuck

**Apologies:** Professor David Baum, Professor Malcolm Chiswick, Professor Forrester Cockburn, Professor Peter Dunn, Dr Edmund Hey, Dr Anthony Lipscomb, Dr Clifford Robertson, Dr Jonathan Shaw

**Dr Tilli Tansey:**<sup>1</sup> The History of the Twentieth Century Medicine Group was established by the Wellcome Trust in 1990, to bring together historians, clinicians, and scientists who were interested in the recent history of medicine and medical science. We devised a number of strategies to try to meet that end, one of which is these Witness Seminars, where we get together people who have been involved in particular debates, or particular developments, to meet, to talk, to discuss, to debate, amongst themselves. The whole of this meeting will be recorded and we hope will be published in due course.

Neonatal intensive care is a subject that has had a lot of Wellcome Trust interest for many years, and indeed is now currently receiving interest from our Policy Unit.<sup>2</sup> Neonatal intensive care has also been covered in *Wellcome News*, a copy of which I hope you all have.<sup>3</sup> It begins, ‘Premature babies now stand a good chance of living to be healthy children. Thirty years ago, the position was very different’. That is precisely why we are having a Witness Seminar on the subject, to discuss what the changes were, why and how they came about. We are delighted that we have been able to persuade Robert Boyd to chair this meeting. I am sure he needs little introduction to this audience. He is a distinguished paediatrician, formerly Professor of Paediatrics in Manchester, and now Principal of St George’s Hospital Medical School, who has written widely on perinatal medicine, the function of the placenta, and the fetal lung. We are absolutely delighted that we have lured him away from St George’s to Euston Road, so I will hand over to Robert now.

**Professor Robert Boyd:**<sup>4</sup> Thank you very much, Tilli. Those of you who know me, will know that I am probably, with the exception of a few historians, the least well-qualified person in this room to chair a session about neonatology. Perhaps, Beryl, you could begin and talk about your involvement in the 1940s.

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<sup>1</sup> Dr Tilli Tansey is Convenor of the History of Twentieth Century Medicine Group and Historian of Modern Medical Science at the Wellcome Trust Centre for the History of Medicine at University College London.

<sup>2</sup> After the meeting several participants were asked by the Policy Unit of the Wellcome Trust to take part in a study examining the scientific basis of neonatal intensive care. A copy of the report will be available from the Wellcome Trust’s Policy Unit in spring 2001.

<sup>3</sup> Ferry G. (1999) Saving babies: Historical advances in neonatal intensive care. *Wellcome News* 18: 10–12.

<sup>4</sup> Professor Robert Boyd FRCP FRCPC FMedSci FFPHM (b. 1938) was Research Fellow and Senior Lecturer at University College Hospital, London, from 1967 to 1980, Professor of Child Health and Paediatrics in the Faculty of Medicine, University of Manchester, from 1981 to 1996, and has been Principal and Professor of Child Health, St George’s Hospital Medical School, London, since 1996. His published works are on child health, general practice, and fetal and placental physiology.



**Dr Beryl Corner:**<sup>5</sup> My involvement in neonatology began in 1942, when I was requested by the Medical Officer of Health for Bristol to provide total medical care, both preventative and curative, to all babies in a large new obstetric unit at Southmead Hospital, which covered all the teaching in that subject for the University of Bristol and for the training of midwives for the Central Midwives Board (140 beds altogether). The central part of my brief was to develop a service for premature babies which would cover the whole catchment area – a population of approximately one million people – and, of course, would also provide emergency cover for the whole South-West region (between four and five million people) as requested.<sup>6</sup>

In January 1946, the first premature baby unit was opened with eight cots, in accommodation made available from the labour ward suite. There were separate rooms for food preparation and for storage of equipment. The essential features were those that had been laid down in the principles of premature baby care by Hess in Chicago<sup>7</sup> and subsequently by Mary Crosse at the Sorrento Maternity Hospital in Birmingham.<sup>8</sup> There were considerable problems because, in the immediate postwar years, there were no plastic or disposable materials, no incubators were available, there was no piped oxygen, no micromethods for biochemistry, no electronic monitoring, and, with the immediate postwar problems, there was no designated medical or nursing staff apart from the normal staffing of the department. The only antibiotics available at that time were penicillin, sulphonamides and tetracycline.<sup>9</sup> More importantly, there was no foreign exchange by which equipment or drugs could be purchased from the USA or elsewhere.

The basic principles applied were meticulous aseptic nursing techniques and great attention to every detail in the care of these babies. Perhaps most important was the training of nurses and midwives in frequent, meticulous, *recorded* observations of the appearance and behaviour of these babies, in addition to the normal information of recording vital signs and feeds. This was *a new development* in the training of nurses

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<sup>5</sup> Dr Beryl Corner FRCP HonFRCPCH HonDSc (b. 1910) set up the Premature Baby Unit at Southmead Hospital, Bristol, in 1946. She was Clinical Lecturer in Child Health, University of Bristol, from 1942 to 1976 and has been Emeritus Consultant Paediatrician, Avon Health Authority, since 1976.

<sup>6</sup> For a history of the care of premature babies in the Bristol area, from 1946 to 1952, see Meeting at Southmead Hospital, Bristol. (1949) Demonstration of Neonatal Department, Southmead Hospital. [Summary]. *Proceedings of the Royal Society of Medicine XLII*: 909–922. See also The Southmead General Hospital Management Committee. (1952) *The Care of the Premature Baby in the Bristol Area*. A Symposium. Bristol: Southmead Hospital.

<sup>7</sup> Dr Julian Hess was Medical Director at the Michael Reese Hospital, Chicago, from 1922 to 1956. See Hess J H. (1922) Premature infants, in Abt A. (ed.) *Pediatrics*, vol. 2. Philadelphia: W B Saunders. Hess J H, Lundeen E C. (1949) *The Premature Infant*. Philadelphia: J B Lippincott. See also Butterfield L J. (1993) Historical perspectives of neonatal transport. *Pediatric Clinics of North America* 40: 221–239.

<sup>8</sup> Dr Victoria Mary Crosse (1901–1972) was appointed in 1931 by the Public Health Department in Birmingham to set up and run a unit at the Sorrento Hospital for the care of premature babies. See Crosse V M. (1945) *The Premature Baby*. London: Churchill Livingstone. Dunn P M. (1998) The development of newborn care in the UK since 1930. American Academy of Pediatrics Thomas E Cone, Jr Lecture on Perinatal History. *Journal of Perinatology* 18: 471–476. See also page 70.

<sup>9</sup> The introduction of penicillin, and other antibiotics has been the subject of a recent Witness Seminar. See Tansey E M, Reynolds L A. (eds) (2000) Post penicillin antibiotics: From acceptance to resistance? *Wellcome Witnesses to Twentieth Century Medicine*, vol. 6. London: The Wellcome Trust.

and midwives because the details observed and recorded were far more than in the normal care of newborn babies – the forerunner of ‘intensive care’.<sup>10</sup> Further special features of the service were methods for keeping the babies warm during transport, so that all babies were fetched into hospital or moved between different departments of the obstetric unit utilizing special transport arrangements, and were always accompanied by a premature unit trained staff member.

It was soon found that post mortems became an essential part of the service; a pathologist was appointed who developed expertise in neonatal post mortems, and more than 90 per cent of post mortems were obtained on stillbirths and neonatal deaths. As a result of the detailed clinical observations and special post mortem arrangements, identification and description of clinical problems of premature babies became possible. The principal problems that were described were those of neonatal jaundice leading to kernicterus, respiratory distress syndrome and other respiratory problems.<sup>11</sup> This led to the definition of respiratory distress syndrome in 1959 at the Montreal Paediatric Conference.<sup>12</sup> Various neurological syndromes were described in detail and, in due course, other biochemical aberrations such as hypoglycaemia and hypocalcaemia.<sup>13</sup>

Very soon it became obvious that there were large gaps in the knowledge and physiology of the newborn infant. Consequently, during the 1950s, the need for intensive research became evident, and this was developed principally in Boston, USA, by Clement Smith, in Oxford by Geoffrey Dawes, in Cambridge by Robert McCance and in London by Kenneth Cross.<sup>14</sup> Stimulated by McCance in 1959, the Neonatal

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<sup>10</sup> Professor Osmund Reynolds wrote: ‘A definition of neonatal intensive care that was discussed during the setting up of this meeting was “The use of relatively sophisticated techniques to care for ill or vulnerable newborn infants, such as mechanical ventilation, total parenteral nutrition and continuous monitoring of vital signs”.’ Note on draft transcript, 30 November 2000.

<sup>11</sup> See, for example, Aidin R, Corner B, Tovey G. (1950) Kernicterus and prematurity. *Lancet* ii: 1153–1156. Corner B, Berry E, Neale A V. (1960) Hyperbilirubinaemia in premature infants and the effect of synthetic vitamin K. *Lancet* i: 715–717. See also page 74.

<sup>12</sup> Rudolph A J, Smith C A. (1960) Idiopathic respiratory distress syndrome of the newborn. An international exploration. *Journal of Pediatrics* 57: 905–921.

<sup>13</sup> Professor Harold Gamsu wrote: ‘I would have liked to mention the role of Marvin Cornblath in defining the importance of symptomatic neonatal hypoglycaemia [Cornblath M, Odell G B, Levin E Y. (1959) Symptomatic neonatal hypoglycemia associated with toxemia of pregnancy. *Journal of Pediatrics* 55: 545–562]. Also the role of Gerald Neligan (see pages 26 and 32) in Newcastle [Neligan G A, Robson E, Watson J. (1963) Hypoglycaemia in the newborn. A sequel of intrauterine malnutrition. *Lancet* i: 1282–1284]. Subsequently, Cornblath collaborated closely with Robert Schwartz in Cleveland, USA, and I was fortunate in being able to spend a year working in his laboratory.’ Letter to Dr Daphne Christie, 17 December 2000. See also page 74.

<sup>14</sup> Professor Geoffrey Dawes CBE FRS (1918–1996) was a Fellow of Worcester College, Oxford, from 1946 to 1985, Emeritus Fellow from 1985, and Director of the Nuffield Institute for Medical Research, from 1948 to 1985. He was Director of the Charing Cross Medical Research Centre, from 1984 to 1989. See Liggins G. (1998) Geoffrey Sharman Dawes. *Biographical Memoirs of Fellows of the Royal Society* 44: 111–125. Professor Osmund Reynolds wrote: ‘His book, *Foetal and Neonatal Physiology* (1968), was a landmark in the field.’ Note on draft transcript, 30 November 2000. Professor Robert McCance CBE FRCP FRS (1898–1993) was Professor of Experimental Medicine at the University of Cambridge from 1945 to 1966, later Emeritus. He was Director of the Medical Research Council Infantile Malnutrition Research Unit, Mulago Hospital, Kampala, Uganda, from 1966 to 1968. See Widdowson E M. (1995) Robert Alexander McCance. *Biographical Memoirs of Fellows of the Royal Society* 41: 263–280. Professor Kenneth Cross FRCP (1916–1990) qualified in medicine at St Mary’s

Society, of which I was a founder member, was established so that physiologists and neonatologists could get together to look at their problems. I think one or two others here were at that first meeting at Scarborough, where we all met in the basement after dinner one night to establish the Neonatal Society.<sup>15</sup>

The last important thing that I want to mention is that in 1959 the Ministry of Health set up a Committee on Prematurity. The consultants on that were Wilfrid Sheldon, Norman Capon from Liverpool and myself. Norman Capon had had a premature baby unit in Liverpool, and during the 1950s the service for premature babies had been expanded to many of the teaching centres, for example, Freddy Miller and Gerald Neligan up in Newcastle. But in 1959, when we discussed what were the needs to set up premature baby units all round the country, the most important thing was, and I drew the attention of the committee to this, that there were a large number of babies who were not classified as premature but who were in need of special care, and the same care that we gave to premature babies should be extended to those babies. When the Committee Report came out in 1961, the recommendation was made that we should call them 'special care infant units' and not 'premature baby units' any more, because we had switched to cover all the problems of neonatology that we then knew about.<sup>16</sup>

**Boyd:** Thank you very much, that's a marvellous start. Before we move on to the 1960s and 1970s – those who were in at the creation, are there things you would like to add to or subtract from Beryl's view? Who else was in the cellar at Scarborough?

**Professor Tom Oppé:**<sup>17</sup> I was not in the cellar but was a founder member of the Neonatal Society and early on I became Honorary Clinical Secretary when Tom Stapleton departed for Australia. I had learnt some neonatal physiology from Kenneth Cross and from Clement Smith, and Beryl had taught me about the clinical care of the newborn. I am thus contemporary with the older participants this afternoon.

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Hospital Medical School, London, in 1940 and was Professor of Physiology at the London Hospital Medical School from 1960 to 1981, later Emeritus. See Davis J A. (1994) Kenneth William Cross. *Munk's Roll* 9: 107–109. Dr Beryl Corner wrote: 'Clement Smith was Associate Professor of Pediatrics, Boston Lying-in Hospital, Harvard Medical School, USA.' Note on draft transcript, 5 December 2000.

<sup>15</sup> The Neonatal Society was founded in 1959. Dr Beryl Corner wrote: 'The founder members of the British Paediatric Association at the original meeting that the decision was made to form the Neonatal Society were Tom Stapleton, Wilfrid Payne, Robert McCance, A Holzel, Peter Tizard, J O Forfar, Hugh Jolly, Beryl Corner, Ronald Illingworth, Victoria Mary Crosse, Otto Wolff and Geoffrey Dawes. Professors Douglas Hubble and James Hutchison were also there but did not become active members of a neonatal group. Once the Society was founded, a number of other people immediately joined and, as far as I can make out from the history of the Neonatal Society, the total initial number of members in 1959 was 37, including the names we have already mentioned.' Note on draft transcript, 5 December 2000. The inaugural meeting of the Neonatal Society was held on 5 November 1959. See McCance R A. (1974) The foundation and early years of the Neonatal Society, in *The Neonatal Society Annual Report, 1974*. 1–11.

<sup>16</sup> Ministry of Health. (1961) Prevention of prematurity and the care of premature infants. *Report of the Sub-Committee of the Central Health Services Council*. London: HMSO.

<sup>17</sup> Professor Tom Oppé CBE FRCP (b. 1925) was Professor of Paediatrics at the University of London, St Mary's Hospital Medical School, from 1969 to 1990, later Emeritus. His many positions included Chair of the Committee on Paediatrics, Royal College of Physicians, from 1970 to 1974, Consultant Adviser in Paediatrics for the Department of Health and Social Security, from 1971 to 1986, and Dean of the Faculty of Medicine, University of London, from 1984 to 1986.

I want to underline the importance of the Neonatal Society in the establishment of neonatal care. Membership was restricted to the few physiologists and their coworkers who were interested in applying fetal and neonatal research to clinical practice, and to clinicians who actively engaged in relevant research. Meetings were run rather like those of the Physiological Society, with short presentations of original work that had to demonstrate hard evidence to justify conclusions and be subject to penetrating, but not unfriendly, criticism. The development of neonatal intensive care in the 1960s and 1970s was underpinned by the scientific standard exemplified by the Neonatal Society.

**Boyd:** Jean, did you want to add anything about precreationism?

**Dr Jean Smellie:**<sup>18</sup> I wasn't actually in the cellar in Scarborough, but I was at the first meeting when we initiated the Neonatal Society. I think that what Beryl said is so important, that virtually all the advances that emerged at that time were based on very careful clinical observations. Out of these came, for example, Bound, Butler and Spector's 'Classification and causes of neonatal deaths', which highlighted the importance of the preterm baby, of respiratory difficulty and the respiratory distress syndrome.<sup>19</sup>

**Boyd:** I think the last word on this section to Chris Booth then.

**Sir Christopher Booth:**<sup>20</sup> I wanted to pay tribute to McCance and his contribution, because I think the work he did, particularly on electrolyte detection in the newborn, brought into neonatal research something that nobody else was paying any attention to at the time.<sup>21</sup> I recall him reading papers at the Medical Research Society, back in the 1950s, and on one occasion he gave this paper, and a rather noisy gentleman in the audience, who was interested in calcium metabolism, got up and said, 'Now, Professor McCance, how do you imagine blah, blah, blah?', to which McCance replied coldly, 'Sir, we do not imagine, we measure'.

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<sup>18</sup> Dr Jean Smellie FRCP HonFRCPC (b. 1927) qualified at Oxford and then University College Hospital, London, in 1950. She trained in paediatrics at the Royal Manchester Children's Hospital, Great Ormond Street, University College Hospital and Oxford, between 1952 and 1961. She was Honorary Consultant Paediatrician and Senior Lecturer, University College Hospital, London, from 1970 to 1993, later Emeritus, and Honorary Consultant Paediatric Nephrologist at Guy's and Great Ormond Street Hospitals, Honorary Senior Lecturer Community Child Health, Southampton, from 1984 to 1992. Some of her own experiences of the early development of neonatal care, mainly at University College Hospital, are written in a letter to Dr Daphne Christie, 1 April 2000, and will be deposited with the records of this meeting in Archives and Manuscripts, Wellcome Library, London.

<sup>19</sup> Bound J P, Butler N R, Spector W G. (1956) Classification and causes of perinatal mortality. *British Medical Journal* 22: 1191–1196. See also Smellie J M. (1958) Neonatal deaths. *Proceedings of the Royal Society of Medicine* 51: 856–858. *idem* (1963) Respiratory difficulty in the newborn, in Perry K M, Sellors R H. (eds) *Chest Diseases*. London: Butterworths, 1–17.

<sup>20</sup> Sir Christopher Booth Kt FRCP (b. 1924) trained as a gastroenterologist and was the first Convenor of the Wellcome Trust's History of Twentieth Century Medicine Group, from 1990 to 1996, and Harveian Librarian at the Royal College of Physicians from 1989 to 1997. He was Professor of Medicine, 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.

<sup>21</sup> See note 14 and Ashwell M. (ed.) (1993) *op. cit.* note 34.

**Boyd:** Which brings us on comfortably, I think, to the next section. John, I think you have kindly agreed to open the batting there.

**Professor John Davis:**<sup>22</sup> I had just better give a brief biography about how I came into this. I was working at St Mary's Hospital at the time when Kenneth Cross<sup>23</sup> got interested in the physiology of the newborn with a series of research assistants, including June Wilkie;<sup>24</sup> and as we are going to be a bit short on contributions about temperature control, it might be appropriate to say that this was Kenneth's interest at the time when there was considerable dispute about whether babies raised their metabolic rate in order to keep warm, or simply lowered it because they were cold.<sup>25</sup> I think the person who drew attention to this problem was Moore, who reported that infusions of noradrenaline caused a considerable rise in the body temperature of newborn animals.<sup>26</sup> This ultimately resulted in the demonstration by David Hull, who is here, and Michael Dawkins,<sup>27</sup> who sadly is not, that what newborn rabbits, if not newborn human infants, do in response to a cold environment is to switch on their brown fat organ. I remember that it was I who pointed out the existence of this organ, not having the remotest idea what it was for, to Michael Dawkins, asking, 'Why do newborn rabbits have a kind of stole of fat cells round their shoulder blades?' It was, of course, David Hull who showed that this was brown fat, which burns as fuel to keep babies warm.<sup>28</sup> This was followed not long afterwards by the demonstration, I think it was by Hugh Jolly, that babies who were kept warm did much better than babies who were kept cold.<sup>29</sup> This didn't seem to be a matter

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<sup>22</sup> Professor John Davis FRCP (b. 1923) was first Nuffield Fellow in neonatal physiology in the Nuffield Institute (1957–1959), after which he joined Professor Tizard's neonatal research unit based at the Hammersmith Hospital, London, as Senior Lecturer and then Reader before taking up the Chair of Paediatrics at Manchester in 1967. He was Professor of Paediatrics, and Fellow of Peterhouse, University of Cambridge, from 1979 to 1988, Professor Emeritus and Fellow Emeritus since 1988.

<sup>23</sup> See note 14.

<sup>24</sup> See note 30.

<sup>25</sup> Cross K W, Stothers J K, Stratton D. (1975) An indirect estimate of total brain energy metabolism in the newborn infant. *Journal of Physiology* 250: 15P–16P. Cross K W, Stothers J K, Warner R M, Woodrough R W. (1975) The application of thermography to the detection of energy metabolism of the brain of the new-born infant. *ibid.* 252: 44P–45P.

<sup>26</sup> Professor John Davis wrote: 'My recollection is that Dr (later Professor) Roland Edward Moore FRSM worked at Charing Cross in the Department of Physiology in the late 1950s.' Letter to Dr Daphne Christie, 6 December 2000. Moore later worked as Senior Lecturer in Physiology at the Royal Free Hospital, London, and afterwards as Professor of Physiology, Trinity College, Dublin. See Thompson G E, Moore R E. (1968) A study of newborn rats exposed to the cold. *Canadian Journal of Physiology and Pharmacology* 46: 865–871. Komaromi I, Moore R E, Sinanan K. (1969) Central effects of noradrenaline and GABA on thermogenesis in the neonatal rabbit. *Journal of Physiology* 202: 118P.

<sup>27</sup> Michael Dawkins was Consultant Pathologist at Hammersmith Hospital's Neonatal Research Unit, London, and was succeeded by Professor Jonathan Wigglesworth (see note 92).

<sup>28</sup> Hull D, Segall M M. (1965) The contribution of brown adipose tissue to heat production in the new-born rabbit. *Journal of Physiology* 181: 449–457. Aherne W, Hull D. (1966) Brown adipose tissue and heat production in the newborn infant. *Journal of Pathology and Bacteriology* 91: 223–234.

<sup>29</sup> Hugh Reginald Jolly FRCP (1918–1986) was house physician to Sir Wilfrid Sheldon at the Hospital for Sick Children, Great Ormond Street, London, and in 1951 was appointed Consultant in Plymouth, and then Paediatrician in Charge at Charing Cross Hospital, London (1965–1983). See Laurance B M. (1989) Hugh Reginald Jolly. *Munk's Roll* 8: 246–250. His many published works include *Diseases of Children* (1964), *Book of Child Care* (1975), *Common Sense about Babies and Children* (1983) and *The First Five Years* (1985).

of how warm or how cold they were kept, but of how much effort they had to put in into trying to keep warm, because a very large part of the total cardiac output tends to go through the brown fat organ, at any rate, in the rabbit, if it is trying to keep warm, and which is then not available for other purposes. At any rate, their work tidied up that particular aspect of neonatal physiology very neatly.

And it is worth saying that one of the reasons why Kenneth Cross came to slightly incorrect conclusions at one point, about whether babies in low oxygen concentrations raised or lowered their metabolic rate, was because he was taking the air from the cold street in Paddington General Hospital and comparing it with warmer oxygen, resulting in conclusions which were later invalidated by, I think, June Hill.<sup>30</sup> Tom [Oppé] might have more to say about that. So very early on, I think, we arrived at the situation where the incubator became relevant, having been up to that time a kind of toy that nobody knew quite what to do with.

The next thing that I am going to say is that while other people have mentioned the roots of neonatal care, some in university departments of physiology, and some in the perinatal mortality survey, I would like to draw attention to the great influence of technical advances. I think one of the most useful was the invention of the plastic feeding tube, and from there we can go all the way to nuclear magnetic resonance (NMR) imaging.<sup>31</sup> The new technology was very rapidly taken up and enabled the subject to advance very much faster than it would have done otherwise. That's all I am going to say at the moment.

**Boyd:** Thank you very much indeed, John. Maureen, I am very conscious of the St Thomas' angle on all this.

**Professor Maureen Young:**<sup>32</sup> I want first of all to pay tribute to Joseph Barcroft who is my guru and who gave the whole subject of fetal and neonatal physiology a great

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<sup>30</sup> June Wilkie (née Hill) (1925–1996) was Kenneth Cross's research assistant (see page 8) and researched in the late 1950s and early 1960s into the relationship between environmental temperature, oxygen consumption and metabolic rate in newborn mammals and children. She married Professor Douglas Wilkie (see note 215) in 1949. See Wilkie J. (1959) The oxygen consumption of new-born and adult mammals. Its dependence on the oxygen tension in the inspired air and on the environmental temperature. *Journal of Physiology* 149: 346–373.

<sup>31</sup> For the story of how infant nuclear magnetic resonance (NMR) studies began, see Christie D A, Tansey E M. (eds) (1998) Making the human body transparent: The impact of nuclear magnetic resonance and magnetic resonance imaging, in Tansey E M, Christie D A, Reynolds L A. (eds) *Wellcome Witnesses to Twentieth Century Medicine*, vol. 2. London: The Wellcome Trust, 25–26.

<sup>32</sup> Professor Maureen Young (b. 1915) graduated in physiology from Bedford College for Women, where she worked from 1933 to 1938. She spent two years at a London Blood Transfusion Unit at the beginning of the Second World War and returned to teach at Bedford. Later she was one of the first women to join the staff of the Physiology Department at St Thomas' Hospital Medical School, London, after the war. She worked at the hospital for 36 years. She was one of the founder members of the Neonatal Society and was President from 1984 to 1987. A copy of her letter to Dr David Gordon, Professor Osmund Reynolds and Dr Tilli Tansey, dated 26 April 1999, which describes the changes in physiology and clinical practice in St Thomas' Hospital and University College London during the 1960s and 1970s, will be deposited with the records of this meeting in Archives and Manuscripts, Wellcome Library, London.

boost before the war.<sup>33</sup> He started these studies when he was already 60 years of age, and he had a tremendous influence on McCance and Widdowson<sup>34</sup> and on the American, Don Barron, who went back to Yale and started to spread news of the subject over there. I went to St Thomas' Hospital in 1947, as a demonstrator in physiology, and found a lot of very enthusiastic doctors who had returned from the Second World War. The first thing I did with Arthur Buller<sup>35</sup> was to see if curare passed across the rabbit placenta,<sup>36</sup> because it had just been introduced into anaesthesia and used at Caesarean section. The paediatricians were very keen to know a lot of things. The activity of the cardiovascular reflexes in the newborn for instance, and with Walter Holland and Dennis Cottom<sup>37</sup> we tried to provide some of the answers. They also wanted to know how they could measure the oxygen in the newborn blood and how to help the babies whose oxygenation was poor. At that time we measured oxygen in the blood using the 'Van Slyke apparatus', it had a mighty reservoir of mercury and guzzled blood and was, therefore, very unsuited for measurement on the small volumes of blood obtained from the newborn.<sup>38</sup>

But there was an American called Scholander, who was developing micromethods for measuring oxygen in blood and respiratory gases, and at St Thomas' we decided to start a BSc course in respiratory physiology and teach the students about these methods.<sup>39</sup> It

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<sup>33</sup> Sir Joseph Barcroft Kt CBE HonFRSE HonFRCOG FRS (1872–1947) was Reader (1919) and Professor of Physiology (1926–1937) in Cambridge, and was appointed Director of the Unit of Animal Physiology, Agricultural Research Council, in 1941. His research interests included studies of the properties of blood, especially blood gases and the oxygen-carrying function of haemoglobin, and studies on the physiology of the fetus. See, for example, *The Respiratory Function of the Blood* (1914) and *Researches on Prenatal Life* (1946). See also Roughton F J W. (1948–1949) Joseph Barcroft. *Biographical Memoirs of Fellows of the Royal Society* 6: 315–345.

<sup>34</sup> Dr Elsie Widdowson CH CBE HonFRCP FRS (1906–2000) studied in the Department of Experimental Medicine, University of Cambridge (1938–1966), and then in the Infant Nutrition Research Division (1966–1972). She was President of the Nutrition Society (1977–1980), the Neonatal Society (1978–1981) and the British Nutrition Society (1986–1996). See Anon. (2000) Elsie Widdowson. *The Daily Telegraph*, 22 June 2000, page 12. Ashwell M. (ed.) (1993) *McCance and Widdowson: A scientific partnership of 60 years, 1933 to 1993*. London: British Nutrition Foundation. See also note 14.

<sup>35</sup> Professor Osmund Reynolds wrote: 'He became Chief Scientist, among other things.' Note on draft transcript, 30 November 2000. See Reynolds L A, Tansey E M. (eds) (2000) *Clinical research in Britain, 1950–1980*, in *Wellcome Witnesses to Twentieth Century Medicine*, vol. 7. London: The Wellcome Trust, 56–58.

<sup>36</sup> Buller A J, Young I M. (1949) The action of D-tubocurarine chloride on the fetal neuromuscular transmission and the placental transfer of this drug in the rabbit. *Journal of Physiology* 109: 412–420.

<sup>37</sup> Dr Dennis Cottom FRCP (1924–1971) was Consultant Physician at St Thomas' Hospital, London, in 1958, and Consultant Physician at the Hospital for Sick Children, Great Ormond Street, London, in 1963. See Wilson B D R. (1982) Dennis George Cottom. *Munk's Roll* 6: 122–123.

<sup>38</sup> See Cottom D, Young I M. (1965) Venous pressure measurement in exchange transfusion. *Archives of Disease in Childhood* 40: 323–325. *idem* (1966) Arterial and venous blood pressure responses during a reduction in blood volume and hypoxia and hypercapnia in infants during the first two days of life. *Pediatrics* 37: 733–742. Holland W W, Young I M. (1956) Neonatal blood pressure in relation to maturity, mode of delivery and condition at birth. *British Medical Journal* ii: 1331–1333. *idem* (1958) Some physiological responses of neonatal arterial blood pressure and pulse rate. *ibid.* ii: 276–278.

<sup>39</sup> Professor Per Fredrik Scholander (b. 1905) was Professor of Physiology and Director of the Institute of Zoophysiology, University of Oslo, Norway, from 1955 to 1958, and Professor of Physiology, Scripps Institute of Oceanography, University of California, USA, from 1958 to 1974. See Scholander P F, Fleminster S C, Irving L. (1947) Microgasometric estimation of blood gases; combined CO<sub>2</sub> and O<sub>2</sub>. *Journal of Biological Chemistry* 169: 173–181. Scholander P F, Irving L. (1947) Micro-blood gas analysis in fractions of cubic millimeter of blood. *ibid.* 169: 561–569. See also page 14.

was a very, very good time indeed, because the physicians were interested and they, believe it or not, came to help us demonstrate in the physiology department. This was when I met Os Reynolds and it has been great to know him since and it was very exciting when he became an FRS.<sup>40</sup>

**Boyd:** He did the BSc?<sup>41</sup>

**Young:** He did the BSc, yes. Shall I tell them about the fencing, Os? Just that he [Os] was hardly ever there in fact, he was always fencing. The next opportunity came from the obstetricians. Ian Donald<sup>42</sup> was very keen to help those babies whose respiration was not up to scratch. We had a very exciting time with Ian because he wanted to improve on the ventilators that were already in use. These had many disadvantages and he had the very bright idea that he would record the respiration of the newborn infant, using a plethysmograph, to observe the rate and volume which was then amplified. These preliminary experiments were incredibly crude and I must say nobody took us very seriously. For one thing, Ian used a valve that was operated by a solenoid which made a tremendous clanging noise, he had to seal the baby into the plethysmograph and the alginate sealing material sometimes solidified and sometimes it did not! As I said, we weren't taken too seriously, but we were able to do a demonstration at the Physiological Society.<sup>43</sup> The RAF and Fleet Air Arm gave us advice and the apparatus was further developed at the Hammersmith Hospital. As a result of the tremendous interest at St Thomas' in perinatal medicine generally, in 1964 the university started an academic department of obstetrics and gynaecology. The idea came from Peter Sharpey-Schafer,<sup>44</sup> Professor of Medicine, and was supported strongly by one of the consultant obstetricians, Joseph Wrigley. Philip Rhodes became the professor and I was a new departure, becoming a lecturer in physiology in a clinical department of obstetrics. I think two important things can be said about this department. One was that we started a BSc course in perinatal physiology and again we had the most tremendous help from paediatricians; many of them are here, and they used to come and lecture to the preclinical students during this course. My own group took on the study of placental transfer of amino acids and later the protein

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<sup>40</sup> See note 56.

<sup>41</sup> Professor Osmund Reynolds wrote: 'Scholander was not at St Thomas', he published the method [see note 39]. The BSc course was set up by Maureen and colleagues in Henry Barcroft's [Son of Sir Joseph Barcroft (see notes 33 and 47)] Physiology Department at St Thomas.' Note on draft transcript, 30 November 2000.

<sup>42</sup> Professor Ian Donald CBE FRCOG FRCP (1910–1987) trained in obstetrics and gynaecology in London. He was appointed Reader at St Thomas' Hospital, London, and then at the Hammersmith Hospital, London, where his main research interest was respiratory problems of the newborn. In 1954 he was appointed to the Regius Chair of Midwifery at the University of Glasgow. His initial work on ultrasound was at the Royal Maternity Hospital and the Western Infirmary in Glasgow; he moved to the new Queen Mother's Hospital at Yorkhill in 1964. He received many honours, including the Blair Gold Medal, the Eardley Holland Gold Medal, the Victor Bonney Prize and the Maternité Prize of the European Association of Perinatal Medicine. See Wolstenholme G, Luniewska V. (1989) Ian Donald. *Munk's Roll* 8: 136–138. See also note 85.

<sup>43</sup> Donald I, Young I M. (1952) An automatic respiratory amplifier. *Journal of Physiology* 116: 4P.

<sup>44</sup> Professor Peter Sharpey-Schafer FRCP (1908–1963) was Senior Lecturer, Department of Medicine, Postgraduate Medical School, Hammersmith Hospital, London, from 1936 to 1948, then Professor of Medicine, London University, Director of the Medical Unit, St Thomas' Hospital Medical School, London, from 1948.



turnover rate in developing tissues; this was possible because of the recent technical developments in amino-acid analysis.<sup>45</sup> We worked on perfused placentas of small animals and on sheep. Finally, I am quite sure Joseph Barcroft would have been very proud of all the distinguished people in this room who have worked in perinatal medicine.<sup>46</sup>

**Boyd:** Thank you, Maureen. I am not sure whether it is the right moment to say that I am probably the only person here who sat on Joseph Barcroft's knee, but that is another story.<sup>47</sup> The other area where things were going on was north of the border and, Ross, I think you kindly said you'd kick off a little bit of thought about Scotland.

**Professor Ross Mitchell:**<sup>48</sup> I rather feared that there would be solid ranks of aged Scotsmen in the front row, challenging every word I say, but I am glad to see I am amongst friends, so I can be as biased as I want! I have tried to think what was different in Scotland from the rest of the United Kingdom, in terms of intensive neonatal care. One of the things that was different, at least in degree if not in kind, was that the clinical practice of Scottish teaching hospitals, up until the 1970s, was very much dominated by the university academic departments run by the professors of child health and obstetrics. And in the early 1950s in no centre in Scotland did the professor of obstetrics and the professor of paediatrics share a primary interest in the newborn. In some centres the obstetricians were still objecting to paediatricians coming in, in other centres the obstetricians were keen to go ahead, but the paediatricians had other interests. The change began in 1956 when James Walker came from the MRC Obstetric Medicine Research Unit in Aberdeen to the Chair of Obstetrics in Dundee, and there he worked with the Professor of Child Health, John Henderson, who had a long history of neonatal interest.<sup>49</sup> The first thing that Walker did was to institute a new large special care baby unit of some 20 cots, which was equipped with all the things

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<sup>45</sup> Professor Maureen Young wrote: 'My own group was interested in fetal growth and fetal nutrition, because of the growing interest in the "small" baby. With the recent development of automatic analysers we were able to take on a study of the placental transfer of amino acids, little studied before. Later, we extended the work to the measurement of protein turnover rate in developing tissues.' Letter to Dr Daphne Christie, 8 December 2000.

<sup>46</sup> Professor Osmund Reynolds wrote: 'Three volumes of the *British Medical Bulletin* give a good overview of perinatal research in the UK in the 1960s and 1970s. *Foetal and Neonatal Physiology* (1961), *The Foetus and the Newborn – Recent Research* (1966) and *Perinatal Research* (1975).' Note on draft transcript, 30 November 2000.

<sup>47</sup> Professor Robert Boyd wrote: 'Sir Joseph Barcroft's son, Henry, was Professor of Physiology at St Thomas', London. Henry's wife, Dr Bridget (Biddy) Barcroft, was a close friend of my mother, Dr Amelie Boyd (we shared a household during the war). My father, J Dixon Boyd, an embryologist and subsequently Professor of Anatomy at Cambridge, was close to Sir Joseph and is one of four supportive colleagues thanked in the preface to *Researches on Prenatal Life* [see note 33].' Note on draft transcript, 13 December 2000.

<sup>48</sup> Professor Ross Mitchell FRCPE FRCPCH DCH (b. 1920) graduated in Edinburgh and, after war service in the Royal Navy, trained in paediatrics in Liverpool, Edinburgh, London and the Mayo Clinic, USA. He was appointed Consultant Paediatrician in Dundee in 1955 and Neonatal Paediatrician in 1960, and held Chairs of Child Health in Aberdeen from 1963 to 1972, and in Dundee from 1973 to 1985.

<sup>49</sup> Professor James Walker CBE FRCPGlas FRCOG (1916–1995) was Professor of Obstetrics and Gynaecology in the University of St Andrews, from 1956 to 1967, and University of Dundee, from 1967 to 1981. Professor Ross Mitchell wrote: 'Professor John Henderson FRCPE (1907–1985) was the first Professor of Child Health in the University of St Andrews from 1951 to 1967 and in the University of Dundee from 1967 to 1972. He was President of the British Paediatric Association from 1971 to 1972.' Letter to Dr Daphne Christie, 2 December 2000.

that were current, the Astrup machines and all the rest that we'd been using at that time, and the new Oxygenaire round incubators,<sup>50</sup> which many of you will remember, and which represented an advance until superseded by more highly developed models.<sup>51</sup>

**Booth:** This is just a factual point, here, which I think is important, and that is that James Walker didn't go from Aberdeen to Dundee, he went from the Hammersmith.<sup>52</sup>

**Mitchell:** I see what you mean, I believe he stopped at the Hammersmith briefly on the way. Yes [much laughter]. So then I moved a few years later to Aberdeen and this was the start of a period of very fruitful collaboration with my obstetric colleague, Sir Dugald Baird,<sup>53</sup> in which I used the experience gained in Dundee to plan a much larger 30-cot unit in the Aberdeen Maternity Hospital. I think these two units were the first purpose-built large intensive care units for the newborn in Scotland and certainly amongst the first in the UK. They represented a major advance because for the first time they provided the space, which many premature baby units didn't have in the past, for all the new equipment that had to be gathered round the incubators. They provided dedicated medical and nursing staff who were trained in that particular field and, being identifiable hospital units, they commanded their own resources, which I think was a considerable advantage.

At that time we were all beginning to be more active in resuscitation, and the work of Dawes and Cross and others has been mentioned.<sup>54</sup> We realized the dangers of asphyxia and we started endotracheal intubation early in Aberdeen because we were fortunate in having in the MRC Obstetric Unit a physiologist, Frank Hytten, and an outstanding young anaesthetist, Mike Tunstall. Tunstall took on the training of the paediatric staff in endotracheal intubation very successfully, and it was just a short step from that to starting intermittent positive pressure ventilation, first for recurrent apnoea and then later for a whole range of respiratory problems.<sup>55</sup> I believe it was

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<sup>50</sup> Professor Ross Mitchell wrote: 'The Astrup apparatus allowed the assessment of acid-base status using very small samples of blood. The Oxygenaire Company made medical equipment and, in the late 1950s, their representatives regularly attended neonatal meetings to ascertain paediatricians' requirements, incorporating them into an improved resuscitation trolley and a new round incubator.' Letter to Dr Daphne Christie, 2 December 2000.

<sup>51</sup> Baker J P. (1996) *The Machine in the Nursery. Incubator technology and the origins of newborn intensive care*. Baltimore, London: The Johns Hopkins University Press. Professor Harold Gamsu wrote: 'They had a double Perspex wall which would have conferred more efficient thermal control. Unfortunately, condensation between the two layers made the baby nigh invisible, and they were withdrawn. Soon after this, Oxygenaire was bought by Vickers Medical.' Note on draft transcript, 17 December 2000.

<sup>52</sup> See note 49.

<sup>53</sup> Sir Dugald Baird Kt FRCOG HonFRCPGlas (1899–1986) was Regius Professor of Midwifery in the University of Aberdeen, from 1937 to 1965, formerly Obstetrician-in-Chief at the Aberdeen Maternity Hospital and Visiting Gynaecologist at the Aberdeen Royal Infirmary, and Honorary Director of the Obstetric Medicine Research Unit, Medical Research Council.

<sup>54</sup> See note 14.

<sup>55</sup> Reid D H, Tunstall M E. (1966) The respiratory distress syndrome of the newborn. A method of treatment using prolonged nasotracheal intubation and intermittent positive pressure respiration. *Anaesthesia* 21: 72–80. Tunstall M E, Cater J I, Thomson J S, Mitchell R G. (1968) Ventilating the lungs of newborn infants for prolonged periods. *Archives of Disease in Childhood* 43: 486–497. See also Dinwiddie R, Mellor D H, Donaldson H C, Tunstall M E, Russell G. (1974) Quality of survival after artificial ventilation of the newborn. *ibid.* 49: 703–110.

largely because Tunstall himself trained all the paediatric staff in the techniques that we never encountered the difficulties that many other centres reported. By 1967 we had ventilated more than 100 infants with no appreciable complications and with a very great reduction in mortality, at a time when in many centres it was being said that ventilation was too dangerous and should only be adopted as a last resort. So that takes us down to the beginning of the 1970s, by which time every Scottish teaching centre had a professor of paediatrics with a major interest in the care of the newborn and every centre had at least one full-time consultant in neonatal paediatrics, so there was a general improvement in care in the early 1970s.

I am not going to talk further about the 1970s at this point, but I would just like to make two points. One is that those special care infant units that we started in 1959 in Dundee and in 1963 in Aberdeen, which seemed to be the last word at the time and more than adequate, and which many people felt were over-lavish, by the late 1970s had proved quite inadequate for their task, because of the increase in multiple births, because of the survival of very low birthweight infants and because of the lack of storage for the various bits of equipment that were accumulating, so that there were continually changing needs between 1960 and 1980.

And the last point I should like to make is that I believe the most rapid and most effective advances in intensive care of the newborn are made when obstetricians, paediatricians, anaesthetists, biochemists and physiologists, collaborate together to achieve the same ends.

**Boyd:** Thank you very much, Ross. That's extremely helpful. Who would like to come in at this point? What about you, Os?

**Professor Osmund Reynolds:**<sup>56</sup> I wanted to start by thanking Maureen [Young] for not disclosing what an undistinguished BSc in physiology I had achieved under her tutelage, but that was where I got fired up by perinatal medicine. One particular spin-off was that Maureen taught me to measure blood gases using the Roughton–Scholander syringe, which was a glass piece of apparatus<sup>57</sup> and with

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<sup>56</sup> Professor Osmund Reynolds CBE FRCP FRCOG FRCPCH FMedSci FRS (b. 1933) joined Professor Leonard Strang's (see note 66) Department of Paediatrics at University College Hospital, London, in 1964, after posts at St Thomas' Hospital (where he qualified in 1958), and at Harvard and Yale Universities where he worked with Dr Dav Cook (see note 65). He held a personal Chair in Neonatal Paediatrics in the University of London (1976–1996), Emeritus since 1996, and was Head of the Department of Paediatrics at University College and Middlesex School of Medicine, London (1987–1992). He has been President of the Neonatal Society and has received the James Spence Medal of the Royal College of Paediatrics and Child Health, the Dawson–Williams Memorial Prize of the British Medical Association, the Harding Award of Action Research, and the Maternité Prize of the European Association of Perinatal Medicine. He was Specialist Adviser to the House of Commons Health Select Committee and its predecessor committees (1978–1992) during the production of four reports on perinatal and related topics [Short Report. House of Commons Social Services Committee, Session 1979–1980. (1980) *Perinatal and Neonatal Mortality*. London: HMSO. House of Commons Social Services Committee, Session 1983–1984. (1984) *Perinatal and Neonatal Mortality: Follow-up*. London: HMSO. House of Commons Social Services Committee, Session 1988–1989. (1989) *Perinatal, Neonatal and Infant Mortality*. London: HMSO. House of Commons Social Services Committee, Session 1991–1992. (1992) *Maternity Services*. London: HMSO].

<sup>57</sup> This is the piece of apparatus that Professor Maureen Young mentions on page 10.

which it took about three-quarters of an hour to do duplicate samples. So I learnt to do blood gases, got interested in perinatal things which Maureen was up to and then wound up as Peter Sharpey-Schafer's house physician. I was then forced to go and do a paediatric job, because the guy who was the paediatric houseman (Dr Pat Bennett) got mumps, so I was drafted, and that's how I got into paediatrics. By chance I ran into an epidemic of bronchiolitis, so having learnt to use the Roughton–Scholander syringe and having been taught by Steve Semple<sup>58</sup> to get arterial samples from adults (and also ventilate adults with chronic bronchitis incidentally), it was an obvious next step to try and do blood gases by arterial sampling in infants. So I did that.<sup>59</sup>

Around that time, I remember Herbert Barrie, who is here, using (I didn't know anything about it at the time) Ian Donald's puffer ventilator. I recently had occasion to reread Ian Donald's papers and I think he has been tremendously underrated. There are two absolutely wonderful papers in the *Lancet*, following on from the paper in the *Journal of Physiology* which Maureen referred to earlier.<sup>60</sup> The first was a big one in the *Lancet* on negative pressure,<sup>61</sup> but he had got all the same problems that one seemed to keep hearing about later with the neck seal and pulling the baby up and down. So he developed a 'positive pressure' machine (the 'puffer').<sup>62</sup> I think most of the original work was done at St Thomas', but he then moved to the Hammersmith. Anyway, Herbert was using one, I remember, at some stage, probably in the early 1960s at St Thomas'. Then the ventilator action went mainly to South Africa,<sup>63</sup> and the other developments we have heard about in Scotland.<sup>64</sup>

I went to Boston, to work with Dav Cook<sup>65</sup> on a model of hyaline membrane disease

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<sup>58</sup> Professor Steve Semple FRCP (b. 1926) was Lecturer (1959), Senior Lecturer (1961), Reader (1965) and then Professor of Medicine (1969) at St Thomas' Hospital Medical School, London. He was Professor of Medicine at the Middlesex Hospital Medical School, London, from 1970 to 1987, and Professor of Medicine and Head of the Department of Medicine at University College London, from 1987 to 1991, Emeritus since 1991.

<sup>59</sup> Reynolds E O R. (1963) Arterial blood gas tensions in acute disease of lower respiratory tract in infancy. *British Medical Journal* i: 646–648. *idem* (1963) The effect of breathing 40% oxygen on the arterial blood gas tensions of babies with bronchiolitis. *Journal of Pediatrics* 63: 1135–1139.

<sup>60</sup> *op. cit.* note 43.

<sup>61</sup> Donald I, Lord J. (1953) Augmented respiration: studies in atelectasis neonatorum. *Lancet* i: 9–17.

<sup>62</sup> Donald I. (1954) Augmented respiration: emergency positive-pressure patient-cycled respirator. *Lancet* i: 895–899.

<sup>63</sup> Professor Harold Gamsu wrote: 'Where they were first used in children, and subsequently in neonates with tetanus [Smythe P M, Bull A. (1959) Treatment of tetanus neonatorum with intermittent positive pressure respiration. *British Medical Journal* ii: 107–113]. Later by Heese, Harrison, Malan, Klein and others, in newborns with respiratory distress [Heese H de V, Harrison V C, Klein M, Malan A F. (1970) Intermittent positive pressure ventilation in hyaline membrane disease. *Journal of Pediatrics* 76: 183–193].' Note on draft transcript, 25 July 2000.

<sup>64</sup> See page 12.

<sup>65</sup> Dr Herbert Barrie wrote: 'Dr Charles Davenport (Dav) Cook, was Head of the Outpatient Services at the Children's Medical Center in Boston, Massachusetts, USA, and subsequently Professor and Chairman at Yale University Hospital in Newhaven, Connecticut, then Chief of Pediatrics at Kings County Hospital in Brooklyn, New York, and later on Professor of Pediatrics at the University of Rochester School of Medicine, New York.' Note on draft transcript, 28 November 2000.

in lambs. I had followed, incidentally, Leonard Strang<sup>66</sup> who was out there and Herbert Barrie, who had been there just before Leonard, so there was a sort of tradition of us guys going over there. While working on the model of hyaline membrane disease,<sup>67</sup> I got the opportunity to fool around seeing if it was possible to get some notion about how you might ventilate surfactant-deficient lungs in the lamb. And perhaps I will say this now, but all the way along the line in perinatal medicine, there's been this to-ing and fro-ing between animal work, based on the physiology which we have heard something about, and then defining the questions in the babies, and seeing if we could solve them in the animals, and feeding the results back into the babies.

I went back to London in 1964 where Sharpey-Schafer had intended that I should go back and start an academic paediatric unit at St Thomas', but he unfortunately died while I was in the States. I was without the membership (MRCP), so I had a real problem. But fortunately Leonard [Strang] wanted somebody who could operate on sheep, so I went back and joined him, and had a great time for several years, helping him doing his super work on lung physiology in the lamb, mechanisms of secretion of lung liquid, and permeability of the alveolar and capillary membranes.<sup>68</sup> But bit by bit I began to infiltrate the neonatal unit at University College Hospital, where Jean [Smellie] and Colin [Normand] were working together, of course,<sup>69</sup> with Leonard. By the beginning of 1966 we had got a programme going where we could ventilate any

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<sup>66</sup> Professor Robert Boyd wrote: 'Reflecting on the balance as a whole (and speaking from the perspective of one who worked on the margins of the field through the 1960s and 1970s), I feel the role of Leonard Strang is under-emphasized. Through those years there were two Schools of Clinical Paediatrics which overwhelmingly dominated clinical neonatology. One was Tizard's School first at the Hammersmith in London and subsequently at Oxford, which is pretty well covered in the symposium. The other is Strang's School at University College Hospital, London. In clinical neonatology Tizard had Jon Scopes (see note 182) as a lieutenant and Leonard Strang had Osmund Reynolds (see note 56). Strang's group had an enormous impact on the physiological basis of neonatology. This was especially in the area of the physiology of the developing lung [summed up in Strang's book *Neonatal Respiration* (1977)], and establishing the careers of individuals such as Olver and Walters in addition to Reynolds both of whom have continued to work on perinatal pulmonary physiology. He also fostered or developed the careers of those working in adjacent fields such as Shaw (perinatal nutrition), Rivers (haematology) and myself and others (placental physiology). Bernadette Modell was another of his protégés who (together with the additional support and later support of Fairweather) did critical early work in prenatal molecular diagnosis of thalassaemia. Strang's hallmark was scientific rigour, vigour and enthusiasm.' Edited from a letter to Dr Daphne Christie, 25 January 2000. Professor Osmund Reynolds wrote: 'Professor Leonard Birnie Strang FRCP (1925–1997) trained in Newcastle and was much influenced by Sir James Spence. He held an MRC Research Fellowship at the Royal Postgraduate Medical School, Hammersmith Hospital, London, went to Harvard to work with Dr Dav Cook (see note 65) in 1961–1962, and set up the new Academic Department of Paediatrics at University College Hospital, London, in 1963. This became one of the most successful departments in the UK, with a major international reputation. His main research interest was in the adaptation of the fetal lung to air breathing. He was President of the Neonatal Society and received the James Spence Medal of the Royal College of Paediatrics and Child Health.' Note on draft transcript, 30 November 2000. See Boyd R. (2000) Leonard Birnie Strang. *Munk's Roll* 10: 472–474.

<sup>67</sup> Reynolds E O R, Jacobson H N, Motoyama E K, Kikkawa Y, Craig J, Orzalesi M M, Cook C D. (1965) The effect of immaturity and prenatal asphyxia on the lungs and pulmonary function of newborn lambs. The experimental production of respiratory distress. *Pediatrics* 35: 382–392. See also page 74.

<sup>68</sup> Boyd R D H, Hill J R, Humphreys P W, Normand I C S, Reynolds E O R, Strang L B. (1969) Permeability of lung capillaries to macromolecules in foetal and newborn lambs and sheep. *Journal of Physiology* 201: 567–588. Olver R E, Reynolds E O R, Strang L B. (1973) Foetal lung liquid, in *Foetal and Neonatal Physiology. Proceedings of the Sir Joseph Barcroft Centenary Symposium*. Cambridge: Cambridge University Press, 186–207.

<sup>69</sup> Dr Jean Smellie married Professor Colin Normand in 1961.

baby who was unwilling to breathe, using Bennett ventilators initially, but also trying to prevent anything which the physiology and pathology had thrown up that might be life threatening or potentially damaging to the brain, like hypoglycaemia and hyperbilirubinaemia, as well as keeping the PO<sub>2</sub>, PCO<sub>2</sub> and pH normal, and feeding them early, keeping them warm and so on. At the same time we'd no idea whether this kind of intervention in the very small would be beneficial or not – although we thought it would. It was generally believed at the time that it would probably be disastrous, because they would all end up damaged, because of the work done by Drillien – it's very sad that she's not here today – which had suggested that there would be a very high, unacceptably high, rate of disability among the survivors.<sup>70</sup> So from 1 January 1966, we followed them all up, and Ann Stewart has been responsible for that and no doubt we will hear from her later.<sup>71</sup>

At that time, there were very few mechanical ventilator survivors anywhere in the world. Paul Swyer, for example, published his first paper in 1964 from Toronto; he got one survivor out of 18 babies with hyaline membrane disease, or as it became known, respiratory distress syndrome.<sup>72</sup> The trouble was surfactant deficiency.<sup>73</sup> We published our first paper in the *Lancet* in 1968.<sup>74</sup> Of course the throughput was quite small in those days, but we got 30 per cent survival over a period of 18 months. We found that the apnoeas did well and Ross had shown that too. But the real problem were the babies with hyaline membrane disease who wouldn't breathe during the first day of life. They virtually all died but if they breathed on their own and then needed ventilating they usually survived, as did the infants with less severe respiratory problems. And that was the stimulus to see if one couldn't learn to ventilate bad hyaline membrane disease in a better way. It became plain after a while that you could alter the arterial PO<sub>2</sub> and PCO<sub>2</sub> independently of one another by suitable manipulations of the ventilator settings and that (at a slow rate) indices of blood oxygenation were proportional to mean airway pressure (whether altered by length of inspiration or end-expiratory pressure).<sup>75</sup> We

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<sup>70</sup> See Drillien C M. (1964) *The Growth and Development of the Prematurely Born Infant*. Edinburgh, London: E & S Livingstone Ltd.

<sup>71</sup> See page 38 and notes 161 and 164.

<sup>72</sup> Delivoria-Papadopoulos M, Swyer P R. (1964) Assisted ventilation in terminal hyaline membrane disease. *Archives of Disease in Childhood* 34: 481–484.

<sup>73</sup> See page 75.

<sup>74</sup> Professor Osmund Reynolds wrote: 'Dr Paul Swyer MD FRCP set up the neonatal unit at the Hospital for Sick Children in Toronto [Ontario, Canada] in the 1950s–1960s, which became one of the most prominent in North America. He was a pioneer of many aspects of neonatal intensive care, including mechanical ventilation, transport and regionalization.' Note on draft transcript, 30 November 2000. A copy of a letter from Dr Paul Swyer to Professor Osmund Reynolds, dated 29 March 1994, which gives an account of his work in neonatal intensive care from the 1950s will be deposited with the records of this meeting in Archives and Manuscripts, Wellcome Library, London. See Adamson T M, Collins L M, Dehan M, Hawker J M, Reynolds E O, Strang L B. (1968) Mechanical ventilation in newborn infants with respiratory failure. *Lancet* ii: 227–231.

<sup>75</sup> Reynolds E O R. (1971) Effect of alterations in mechanical ventilator settings on pulmonary gas exchange in hyaline membrane disease. *Archives of Disease in Childhood* 46: 152–159. Herman S, Reynolds E O R. (1973) Methods for improving arterial oxygen tension in infants mechanically ventilated for severe hyaline membrane disease. *ibid.* 48: 612–617.

introduced the results of all this in a big rush at the beginning of 1970, because it was mostly found out at the end of 1969, and we got an immediate four-fold increase in the survival rate for ventilated babies with bad hyaline membrane disease, which persisted. It went up from 11 per cent to between 40 and 50 per cent,<sup>76</sup> and then improved further. Of course all this got superseded later for good reason by, in particular, surfactant replacement and ultra-high-frequency ventilation. And we also at that time got going transporting babies from other hospitals,<sup>77</sup> while mechanically ventilated during the journey. This developed in a very major way. So, for example, in 1975, we published our experiences over three years: 222 babies were transported from other hospitals with 109 of them ventilated in transit, of whom 50 per cent survived.<sup>78</sup> And that really, I think, underpinned the development of regionalization, because it showed that it was practical to transport extremely ill babies. So that's how the ventilator work got going in our neck of the woods.

**Boyd:** Herbert, do you want to add or subtract anything?

**Dr Herbert Barrie:**<sup>79</sup> Yes. When I was a student at University College Hospital and a House Officer in 1950, the Premature Baby Unit didn't exist,<sup>80</sup> only a linen cupboard kept by a sister with green fingers. If she thought a baby needed special care, that is where the baby went.

**Boyd:** Was that Linda Collins?

**Barrie:** No, Sister Edwards. Nobody else was allowed to go near it, which was probably a good thing. For me, neonatology began after I came back from America, where I worked in the same research laboratory, before Leonard Strang who in turn was followed by Osmund Reynolds. Incidentally, he may not have been a great physiology student but he was a very distinguished fencer of Olympic

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<sup>76</sup> Reynolds E O R, Taghizadeh A. (1974) Improved prognosis of infants mechanically ventilated for hyaline membrane disease. *Archives of Disease in Childhood* 49: 505–515.

<sup>77</sup> Blake A N, Collins L M, Langham J, Reynolds E O R. (1970) Portable ventilator-incubator for newborn infants. *Lancet* ii: 25–26.

<sup>78</sup> Blake A N, McIntosh N, Reynolds E O R, St Andrew D. (1975) Transport of newborn infants for intensive care. *British Medical Journal* iv: 13–17. Professor Osmund Reynolds wrote: 'We went on to show that survival rates were higher if the mother was transported prior to delivery [Blake A M, Pollizer M J, Reynolds E O R. (1979) Referral of mothers and infants for intensive care. *British Medical Journal* i: 414–416].' Note on draft transcript, 30 November 2000. Dr Pamela Davies wrote: 'I do think credit might be given to Storrs and Taylor who had earlier reported experience of transporting 122 babies born elsewhere in 1969 to the Hammersmith Neonatal Unit [Storrs C N, Taylor M R H. (1970) Transport of sick newborn babies. *British Medical Journal* iii: 328–332].' Letter to Dr Daphne Christie, 11 December 2000.

<sup>79</sup> Dr Herbert Barrie FRCP FRCPC (b. 1927) qualified at University College Hospital, London, in 1950 and was Harvard Research Fellow at the Children's Medical Center, Boston, Massachusetts, in 1958–1959, Senior Registrar at St Thomas' Hospital, London, from 1959 to 1965, and Consultant Paediatrician at Charing Cross Hospital, London, from 1966 to 1986. His special interests include neonatal resuscitation, intensive care and transport of sick infants. Copies of his reports on the special care baby unit at Charing Cross Hospital, from 1966 to 1984, will be deposited with the records of this meeting in Archives and Manuscripts, Wellcome Library, London.

<sup>80</sup> The Premature Baby Unit at University College Hospital, London, opened in 1954. See page 23.

standard.<sup>81</sup> He was also a very distinguished Paediatric Senior House Officer at St Thomas' where I was Senior Registrar, but that's another story.

In the States, I met Virginia Apgar at a small and select meeting with people like Stanley James, Bill Silverman, and Richard Day. I was immensely impressed by what she was doing as she was resuscitating babies with oxygen down a tube in the trachea.<sup>82</sup> This seemed so obvious that when I came back I thought the first priority was to put proper resuscitation on the map instead of the useless manoeuvres at the time. I very soon discovered that there were some babies who, after they had been resuscitated, stopped breathing again when you stopped ventilating. Most of them were all right and breathed on their own but there were always some, especially the very premature, who could not breathe on their own. The problem was how to go on ventilating them for hours if not days. Fortunately, we had an endless supply of immensely fit medical students at St Thomas' and we put them to work, which they did willingly. I am not quite sure what they got out of it, but they sat there for hours finger-ventilating<sup>83</sup> apnoeic babies, and before mechanical ventilators this worked well. However, after 24 hours and up to 36 hours, we began to run into problems. We didn't run out of medical students but into problems of humidification, which I didn't realize for a time. It was also obvious to me that this was not the best use of medical students.

My interest in resuscitation brought me in contact with Ian Donald<sup>84</sup> – a tremendous enthusiast, who, as an obstetrician, was doing more for babies than many paediatricians and getting little recognition. He said, 'I have built a ventilator, if you come to Glasgow, I'll give it to you, provided you fetch it as I can't send it through the post'. He showed me his unit in Glasgow and what he was doing on ultrasound – this would be about 1962 – and which has been such a great advance, not only in obstetrics, but the whole of medicine.<sup>85</sup> Ian Donald thought PhD research fellows

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<sup>81</sup> Professor Osmund Reynolds wrote: 'I didn't go to the Olympics although I was in the squad for 1952; I got a team bronze medal in the 1955 World Championships (the same year as not doing very well in the physiology BSc).' Note on draft transcript, 1 February 2000.

<sup>82</sup> Virginia Apgar (1909–1974) was appointed Director of Anesthesiology at Columbia Presbyterian Medical Center in 1938 and later granted full professorship. She is best known for introducing a series of measurements (the Apgar score) to evaluate the infant's heart rate, muscle tone, respiratory effort, colour and muscle irritability (see note 141 and page 73). See also Medical Society of the County of New York. (1956) Resuscitation of Newborn Infants. A Report by the Special Committee on Infant Mortality. *Obstetrics and Gynecology* 8: 336–361.

<sup>83</sup> A method whereby intermittent positive pressure puffs of oxygen are delivered to the baby by finger occlusion of an opening near the attachment of the endotracheal tube. The method is described in Barrie H. (1963) Resuscitation of the newborn. *Lancet* i: 650–655. Dr Herbert Barrie wrote: 'This paper generated an extraordinary amount of interest when it was published – perhaps because it was the first detailed description of the procedure.' Note on draft transcript, 28 November 2000. See Barrie H. (1963) *Resuscitation Problems of the Newborn*. A film from the labour wards and nurseries of St Thomas' Hospital and the Lambeth Hospital, London. Loughborough: Riker Laboratories. See also page 34.

<sup>84</sup> See note 42.

<sup>85</sup> Much of Ian Donald's work is described in 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. See also note 42 and Donald I. (1969) On launching a new diagnostic science. *American Journal of Obstetrics and Gynecology* 103: 609–628.



were often more productive than doctors. He produced a suitcase filled with a formidable array of electronics, much of it designed by himself and built by his PhD engineers, which was basically a kind of electronic finger. I got the suitcase back to St Thomas' and soon had a chance to use it on a very premature baby with severe respiratory distress syndrome whom I kept alive for about three days. Again, it was the problem of humidification just as I thought we had turned the corner. It took a while to sort this out but 1962 was the earliest I had a baby on a respirator for as long as three days. By 1963, I had moved on to the Bird respirator<sup>86</sup> and my first survivor from severe respiratory distress syndrome. The Bird respirator and the Astrup analyser<sup>87</sup> were unexpected bonuses of adult cardiac surgery which was growing faster and was better funded than neonatology. If you made friends with the cardiac surgeons you had access to a Bird respirator and the Astrup plus, in my case, keen and helpful anaesthetists, although we still lacked humidification. However, I am still in regular contact with someone who is now 35 and who, as a premature infant in 1964, was ventilated for some four or five days. The 1960s can best be summed up as the decade when effective resuscitation led to intensive care in special centres to which babies would have to be transported with all the new problems that this entailed.

**Boyd:** That's a very good note on which to end, at least a generation and a half follow up. Thank you, Herbert, very much.

**Professor Victor Dubowitz:**<sup>88</sup> I thought I might add just two brief negative notes about that period. I worked in Sheffield at the time and Harold Gamsu<sup>89</sup> in the audience will probably remember that period. As I recall there was only one infant ventilator available and that belonged to the anaesthetists and was kept at the Children's Hospital half a mile up the road. So in our special care unit, if we ever considered ventilating a baby, it was a question of either shipping the baby up to the children's ward or managing to convince the anaesthetists that they could do without

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<sup>86</sup> Dr Herbert Barrie wrote: 'The Bird respirator was designed and marketed by Dr Forest Bird in c. 1975, originally for use in adults. It is "pressure cycled", that is, the pressure builds up to a preset point at which the valve in the box moves across, shutting off the gas supply until breathing out is completed. However, the circuitry was fearfully complicated.' Note on draft transcript, 28 November 2000.

<sup>87</sup> Dr Herbert Barrie wrote: 'The Astrup apparatus was a blood gas analyser designed by Dr P Astrup in Denmark. It measured the pH, PCO<sub>2</sub> and PO<sub>2</sub> of very small blood samples so that these could be corrected if abnormal and kept as far as possible within physiological limits.' Note on draft transcript, 28 November 2000.

<sup>88</sup> Professor Victor Dubowitz MD FRCP FRCPCH (b. 1931) graduated from the University of Cape Town in 1954 and came to England in 1956 for some postgraduate experience before returning to general practice. He consolidated his commitment to paediatrics during his 11 years in Illingworth's department in Sheffield, where he was successively Lecturer, Senior Lecturer and Reader. He was also able to develop his special interests in muscle disorders and in the neurology of the newborn, and to establish a fruitful academic liaison with his wife, Lilly (see note 163), who moved over from endocrinology to neonatology. In 1972 he was appointed to the newly established Chair of Paediatrics and Neonatal Medicine at the Hammersmith Hospital, London, following Tizard's move to Oxford (see page 44), and became Emeritus in 1996. He is author or co-author of eight books (three with his wife) and founder of two journals, *Neuromuscular Disorders* (1991) and *European Journal of Paediatric Neurology* (1977). He has been President of the British Paediatric Neurology Association, The European Paediatric Neurology Society, the Medical Art Society and is Foundation President of the World Muscle Society.

<sup>89</sup> See note 123.

their ventilator for 24 hours. So I would have thought there probably weren't any successes at that time, but perhaps Harold might have a better recollection.<sup>90</sup>

The other thing is in the mid-1960s I spent a year in New York, mainly doing other things, but I did visit Bill Silverman's unit and, in fact, they had just done their fifth ventilator support with a Bourns<sup>91</sup> ventilator, as I recall, which they got from the military as a sop to their conscience. That was their fifth successive death and they were almost giving up at that time, and were very frustrated by the very poor results with ventilation. And that was a prime unit in the States.

**Professor Jonathan Wigglesworth:**<sup>92</sup> I, of course, as a perinatal pathologist, was actually a pupil of Walter Spector and Michael Dawkins, both of whom have been mentioned,<sup>93</sup> and I went to the Hammersmith from University College Hospital as a sort of quality control man, for all these terrible deaths from neonatal intensive care, after Michael's unfortunate death. So I arrived at the Hammersmith in November 1965 and because my memory is not brilliant back to that period, I actually looked up my post mortems from the end of 1965 to the end of 1967 yesterday, just to see what forms of clinical care had been given to babies who had ended up as being investigated by me in the autopsy room. In the first six months, from November 1965 to May 1966, I did 12 autopsies on babies who had been ventilated at the Hammersmith. In those days they were using a Hammersmith-made ventilator, made in our marvellous workshops, which worked like a sort of mechanical finger, driven, I believe, by the pressure from the oxygen cylinder that released the pressure at a

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<sup>90</sup> Professor Harold Gamsu wrote: 'We certainly did not have a ventilator at our disposal at that time (1959–1962). We supported babies with respiratory difficulty by administering oxygen into the incubator and after a visit by Robert Usher (see note 152), with glucose and bicarbonate given intravenously – though with imperfect biochemical control due to the large blood sample size that was needed in those days. At this time we felt obliged to maintain the inspired oxygen concentration in preterm babies at less than 40 per cent, believing that to exceed this would increase the risk of retrolental fibroplasia. It was only later that we came to realize that in some babies curtailing the oxygen they breathed added to the risk of death or brain damage if they survived [Patz A. (1957) The role of oxygen in retrolental fibroplasia. *Pediatrics* 19: 504–524. Avery M E, Oppenheimer E H. (1960) Recent increase in mortality from hyaline membrane disease. *Journal of Pediatrics* 57: 552–559]. When the determining factor was shown to be the arterial PO<sub>2</sub>, and we were able to measure PO<sub>2</sub> reliably in small samples of arterial blood, a more rational policy evolved but that came later [Cross K W. (1973) Cost of preventing retrolental fibroplasia? *Lancet* ii: 954–956].' Letter to Dr Daphne Christie, 17 December 2000.

<sup>91</sup> Dr Herbert Barrie wrote: 'This may be wrong. I am almost certain the Bourns infant respirator did not come on the scene until ten years later.' Note on draft transcript, 5 February 2000. Professor Osmund Reynolds wrote: 'Herbert is referring to the Bourns BP-200 infant ventilator which was designed around the work described in note 75 and was launched in 1974. Victor is probably referring to an earlier Bourns machine.' Note on draft transcript, 30 November 2000.

<sup>92</sup> Professor Jonathan Wigglesworth MD FRCPATH FRCPC (b. 1932) was appointed Senior Lecturer in Paediatric Pathology at the Hammersmith Hospital, London, in 1965, Professor of Perinatal Pathology from 1985 to 1998, Professor Emeritus since 1998. He has published more than 100 papers on various subjects including placental pathology, fetal growth retardation, fetal lung development and perinatal lung pathology, fetal brain development and perinatal brain damage as well as writing or editing a number of books on the subject. He is now retired.

<sup>93</sup> Professor Walter Spector FRCP FRCPATH (1924–1982) was Professor of Pathology in the University of London at St Bartholomew's Hospital Medical School and was appointed to the Chair in 1962. He was a member of the scientific board of the Foundation for the Study of Infant Death and a governor of St Bartholomew's Hospital. See Judah J D. (1984) Walter Graham Spector. *Munk's Roll* 7: 550–551. See also page 7 and notes 19 and 27.

particular pressure and frequency that you set. And again following on from Herbert Barrie, the problems that we met were very obvious: babies who died had massive inspissated secretions as a result of lack of humidification. Later I think it was solved at the Hammersmith, by having a continuous drip, or periodic drip, of saline down the endotracheal tube, until we went on to other types of mechanical ventilator.<sup>94</sup>

The other thing I should just mention by the way. The first baby I ever did an autopsy on in November 1965 had arrived in a hyperbaric oxygen chamber from Woking and, 'Only treated in two atmospheres', it says according to my notes.<sup>95</sup> The babies all had umbilical arterial and venous catheters, because micromethods were being used extensively already by that time at the Hammersmith, so a lot of biochemical work was going on.<sup>96</sup> They were being treated by trihydroxyaminomethane (THAM),<sup>97</sup> bicarbonate and many other drugs in addition to mechanical ventilation according to their biochemical status.

Another problem at that time, quite apart from arterial thrombi affecting major vessels in some of the cases with umbilical catheters, was that there was a lot of infection with *Pseudomonas pyocyanea* (which, of course, we never see these days), because we didn't know at that time about the fact that it was living in all the water that was hanging around the ventilators, in waste traps, and so on, in the intensive care unit. So these were the sort of problems we were getting.

The first baby to survive with respiratory distress syndrome long enough to get bronchopulmonary dysplasia, I see I did an autopsy on in December 1966. Of course we didn't call it bronchopulmonary dysplasia, because it wasn't described as such until the following year and we still called it organizing hyaline membrane disease at that time. So that is some of the background to what was going on at the Hammersmith in the second half of the 1960s.

**Smellie:** Can I come back very quickly following Herbert's reference to the 'prem unit' at University College Hospital. We were a little hampered in the early 1950s by an anaesthetist who liked resuscitating babies with gastric oxygen. This was not considered to be the province of the paediatrician. We were, however, enormously helped by the cooperation of Will Nixon,<sup>98</sup> who was then our Professor of Obstetrics

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<sup>94</sup> See page 31.

<sup>95</sup> Professor Osmund Reynolds wrote: 'There was a brief vogue in the 1960s for treating hyaline membrane disease with hyperbaric oxygen. This was led by James Hutchison in Scotland and it soon proved ineffective [Hutchison J H, Douglas T A, Smith G. (1962) Studies in the treatment of the pulmonary syndrome of the newborn. *Lancet* ii: 465–469. See also Nelson N M, Reynolds E O R. (1964) Hyperbaric oxygen in patients with veno-arterial shunts. *New England Journal of Medicine* 271: 497–499]. The premature son of President Kennedy died while being treated in this way in Boston in 1963.' Note on draft transcript, 30 November 2000.

<sup>96</sup> See page 10. See also Astrup P, Jørgensen K, Siggaard Andersen O, Engel K. (1960) The acid–base metabolism. A new approach. *Lancet* i: 1035–1039.

<sup>97</sup> op. cit. note 114. See also page 75.

<sup>98</sup> Professor William Nixon FRCS FRCOG (1903–1966) was Professor of Obstetrics and Gynaecology, University of London, and Director of the Obstetric Unit, University College Hospital, London, from 1946.

and who, with Dick Bonham-Carter, established a monthly perinatal meeting.<sup>99</sup>

The Premature Baby Unit at University College Hospital was opened in 1954 with 12 cots under Bernard Schlesinger and Dick Bonham-Carter.<sup>100</sup> During the late 1950s, a number of clinical experimental studies were carried out because of Dick's interest in cardiac physiology<sup>101</sup> and complemented by Mavis Gunther's observations on the placental transfer of blood in relation to timing and the position of the baby after birth.<sup>102</sup>

**Reynolds:** I was just recalling, following on from what Jonathan Wigglesworth said, that we, I think, had a particularly bad experience with rotten lung fibrosis or bronchopulmonary dysplasia in the mid-to-late 1960s, and this was all bound up with the fact that we couldn't seem to get any survivors from hyaline membrane disease if they needed ventilation within the first 24 hours, although the ones ventilated later did okay. Half of them died with intraventricular haemorrhages quickly, and the other half – which was much worse – died with rampant lung fibrosis, even big babies of two to two-and-a-half kilos, at about a fortnight of age.<sup>103</sup> So I analysed three years' work on this and published a paper in *Pediatrics* in 1970,<sup>104</sup> saying that these babies who were surfactant deficient and needed ventilating within 24 hours did so badly that maybe you just shouldn't do it, because it was hell for everybody, parents and everybody else. The question was: what was that all about? At that time we were ventilating them at rates of 60–80 breaths a minute, and using very high peak airway pressures (above 35cm water), because we had to in order to keep their arterial PO<sub>2</sub> up – PCO<sub>2</sub> was not a problem. We eventually did several years' worth of pathology with Taghizadeh, who did the histology,<sup>105</sup> relating the appearance of the lung inflated

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<sup>99</sup> Dr Jean Smellie wrote: 'One of the pioneers of special care for premature infants was Dr (later Professor) Elaine Field. The history of the University College Hospital Paediatric Department (unpublished) records that, "From 1939 to 1945 these infants were nursed in a warm darkened room in the basement of the obstetric hospital and their mortality was the lowest recorded in the UK". Dr Field also initiated two-monthly perinatal meetings of paediatricians and obstetricians which became a regular feature, with pathologist input, thereafter.' Letter to Dr Daphne Christie, 14 December 2000.

<sup>100</sup> Dr Bernard Schlesinger OBE FRCP (1896–1984) started the unit for premature babies at University College Hospital, London. He was Consulting Physician to University College Hospital, the Hospital for Sick Children, Great Ormond Street, London, and the Royal Northern Hospital. See Bonham-Carter R E. (1989) Bernard Edward Schlesinger. *Munk's Roll* 8: 441–442. Dr Richard Bonham-Carter FRCP (1910–1994) was Physician to the Hospital for Sick Children, Great Ormond Street, London, from 1947 to 1975, and to University College Hospital, London, from 1948 to 1966. See Norman A P. (2000) Richard Bonham-Carter. *Munk's Roll* 10: 41–43. See notes 10 and 80.

<sup>101</sup> Dr Jean Smellie wrote: 'Dick's interest in cardiology led to a research study of the mean venous pressure in the first hours of life [Bonham-Carter R E, Bound J P, Smellie J M. (1956) Mean venous pressures in the first hours of life. *Lancet* i: 1320–1323] to establish whether respiratory distress syndrome was due to cardiac failure, only to find that it was the infants with low pressure who did least well.' Letter to Dr Daphne Christie, 1 April 2000.

<sup>102</sup> Gunther M. (1957) The transfer of blood between baby and placenta in the minutes after birth. *Lancet* i: 1277–1280.

<sup>103</sup> Professor Osmund Reynolds wrote: 'We were putting small amounts of saline down the endotracheal tube throughout.' Note on draft transcript, 30 November 2000. See note 135.

<sup>104</sup> Reynolds E O R. (1970) Indications for mechanical ventilation in infants with hyaline membrane disease. *Pediatrics* 46: 193–202.

<sup>105</sup> Taghizadeh A, Reynolds E O R. (1974) Pathogenesis of bronchopulmonary dysplasia following hyaline membrane disease. *American Journal of Pathology* 82: 241–264.

at autopsy to what ventilator settings we had used in life. We thought that this very particular experience, although nobody sees it any more, was due predominantly to damaging the lung by directing high pressures at a fast rate into a lung whose alveoli remained collapsed. We were grossly distending and tearing the terminal airways, which then fibrosed up. We did see lesions which correlated with the length of time they breathed high oxygen concentrations, but much more important were the awful terminal airway lesions. We first wrote this up in the *Lancet* in 1967, the same year as Northway, Rosan and Porter, having shown that when these babies died between five days and about a fortnight of age, surfactant had reappeared in their lungs.<sup>106</sup> So the main reason for the problem was mechanical trauma, not persisting lack of pulmonary surfactant, but with oxygen also involved.

And the main reason why we got our huge increase, our step change in survival, at the beginning of 1970, was because of what we learnt from the studies of ventilator settings, which enabled us to ventilate babies at much lower pressures and, to some extent, lower oxygen too. I think this is an experience which is quite different from the modern so-called bronchopulmonary dysplasia, which is obviously multifactorial and occurs particularly in the exceedingly small. This was a problem with big babies, and it was very nasty at the time.

**Corner:** I wanted to say two things. First, we never saw a case of necrotizing enterocolitis, which has not yet been mentioned by anybody, prior to 1967, and we knew it didn't exist, because of our very high post mortem rate and our very careful care of all our babies. So we know it didn't exist, and seemed to occur when we started fairly extensive catheterization, venous catheterization, for all sorts of different purposes.

The next thing I was going to say which I haven't heard anybody mention yet, and I know if Peter Dunn<sup>107</sup> had been here, he would have done, is about the use of continuous positive airway pressure (CPAP) for artificial ventilation. We used this quite extensively in the early 1970s with very good results, but it needed very careful

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<sup>106</sup> Hawker J M, Reynolds E O R, Taghizadeh A. (1967) Pulmonary surface tension and pathological changes in infants dying after respirator treatment for severe hyaline membrane disease. *Lancet* ii: 75–77. Northway W H, Rosan R C, Porter D Y. (1967) Pulmonary disease following respirator therapy of hyaline-membrane disease. Bronchopulmonary dysplasia. *New England Journal of Medicine* 276: 357–368.

<sup>107</sup> Professor Peter Dunn FRCP FRCOG FRCPC DCH (b. 1929) graduated from the University of Cambridge in 1953 and trained in perinatal medicine in Birmingham, San Francisco and then Bristol where he was responsible for the university neonatal service from 1969 to 1988. In 1971 he introduced in the UK continuous positive airway pressure using a Gregory box (op. cit. note 108). His research interests include congenital dislocation of the hip (British Orthopaedic Association Gold Medal) and fetal adaptation to extrauterine life (De Snoo-van't Hoogerhuigs Medal and Prize). In 1975 he founded the British Association of Perinatal Medicine and was Inaugural President from 1980 to 1984, and Consultant to the World Health Organization (WHO) from 1970 to 1990. He is currently Emeritus Professor of Perinatal Medicine and Senior Research Fellow, University of Bristol. He has recently been elected James Spence Medalist for 2001 by the Royal College of Paediatrics and Child Health. See Dunn P M. (1998) op. cit. note 8. *idem* (2000) Newborn care in the UK since 1928, in Valman B. (ed.) *The Royal College of Paediatrics and Child Health at the Millennium*. London: Royal College of Paediatrics and Child Health, 41–48.

working and we had to get the pressure right.<sup>108</sup> At that stage we had got the equipment that would give us the right pressure and the right flow rate and so on, and this became very important, but it was certainly quite effective at that stage.

**Davis:** Two things that have not been mentioned that I think ought to come up at this point. One, of course, is the discovery by Pattle at Porton Down, of the importance of pulmonary surfactant in the maintenance of a functional residual lung volume,<sup>109</sup> which led to the realization with Mary Ellen Avery<sup>110</sup> that the real problem in the respiratory distress syndrome is the lack of surfactant, partly, I believe, as a result of prematurity and partly, I suspect, because of a mechanism that Abrams reported, whereby if you mix fibrin with surfactant, it generates the hyaline membrane that led to respiratory distress syndrome being called hyaline membrane disease.<sup>111</sup> Thus, a fibrinous exudate forms in the premature lung as a result of the various insults to which it is subjected and inactivates surfactant.

But what I really want to say is that quite early on, when Leonard Strang was working at the Hammersmith, he pointed out that hypoxaemia in the face of very high oxygen tensions in the lung in babies with respiratory distress was due basically to shunting, that a great deal of the cardiac output was going *past* the lung instead of through it.<sup>112</sup> And this tied in, up to a point, with the Usher regime that nobody's mentioned, whereby babies were treated by infusions of bicarbonate and glucose.<sup>113</sup> This was followed by the introduction of THAM [trihydroxyaminomethane], which produced the most extraordinarily dramatic effects on blood oxygen tension; one dose suddenly raising it from near zero to well above toxic levels.<sup>114</sup> Later on, Clifford Robertson and

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<sup>108</sup> Professor Harold Gamsu wrote: 'First described by G Gregory and colleagues in 1971 who developed this technique after the serendipitous observation by Vincent Harrison and colleagues in Cape Town in 1968 of the significance of grunting in hyaline membrane disease.' Note on draft transcript, 17 December 2000. See Harrison V C, Heese H de V, Klein M. (1968) The significance of grunting in hyaline membrane disease. *Pediatrics* 41: 549–559. Gregory G A, Kitterman J A, Phibbs R H, Tooley W H, Hamilton W K. (1971) Treatment of idiopathic respiratory distress syndrome with continuous positive airway pressure. *New England Journal of Medicine* 284: 1333–1340. See also Dunn P M. (1974) Respiratory distress syndrome. Continuous positive airway pressure (CPAP) using the Gregory box. *Proceedings of the Royal Society of Medicine* 67: 245–247.

<sup>109</sup> Pattle R E. (1955) Properties, function and origin of the alveolar lining layer. *Nature* 175: 1125–1126. *idem* (1975) The lung surfactant: an introduction. *Journal of Reproduction and Fertility Supplement* 23: 645–650.

<sup>110</sup> Professor Mary Ellen Avery (b. 1927) was Professor of Paediatrics, Harvard Medical School and Physician-in-Chief, later Emeritus, Children's Hospital, Boston. *op. cit.* note 111.

<sup>111</sup> See Avery M E, Mead J. (1959) Surface properties in relation to atelectasis and hyaline membrane disease. *American Journal of Disease of Children* 41: 489–495. Pattle R E, Claireaux A, Davies P A, Cameron A G. (1962) Inability to form a lung-lining film as a cause of the respiratory distress syndrome in the newborn. *Lancet* ii: 469–475. Taylor F B, Abrams M D. (1966) Effect of surface active lipoprotein on clotting and fibrinolysis and of fibrinogen on surface tension of surface active lipoprotein. *American Journal of Medicine* 40: 346–350. Avery M E. (2000) Surfactant deficiency in hyaline membrane disease: the story of discovery. *American Journal of Respiratory Critical Care in Medicine* 161: 1074–1075.

<sup>112</sup> Strang L B, McLeish H M. (1961) Ventilatory failure and right-to-left shunt in newborn infants with respiratory distress. *Pediatrics* 28: 17–27. See also note 66.

<sup>113</sup> See notes 90 and 152.

<sup>114</sup> Gupta J M, Dahlenburg G W, Davis J A. (1969) Changes in blood gas tensions following administration of amine buffer THAM to infants with respiratory distress syndrome. *Archives of Disease in Childhood* 42: 416–427. Robertson C. (1969) Experience with use of THAM in the newborn. *ibid.* 44: 544. See also page 75.

I were able to show that some cases of hyaline membrane disease were caused purely by shunting, without major pulmonary problems, a condition that got labelled as persistent fetal circulation, as if you can have a persistent fetal circulation without a placenta. When I was working with Geoffrey Dawes<sup>115</sup> in Oxford, I found that I could produce this syndrome to order in rabbits. Stanley James did the same thing later in lambs by asphyxiating the mother while the fetus was still *in utero* and then letting her recover before being delivered of the baby, which almost invariably developed this syndrome, whereas the same degree of asphyxia at birth had no such effect.<sup>116</sup>

**Professor Denys Fairweather:**<sup>117</sup> I rather hesitate to put an obstetric oar into this discussion, but Ross Mitchell referred to some positive and some negative aspects of the interplay between obstetricians and paediatricians in the early days.<sup>118</sup> In the time you are talking about, between 1955 and 1959, I was in Aberdeen as a registrar with Dugald Baird<sup>119</sup> and his team. While Dugald Baird I don't think interacted a great deal with the Professor of Paediatrics there at that time, his introduction of people like Frank Hytten, Raymond Illsley, Angus Thomson and W Z Billewicz (Bill) into the unit and the development of his meticulous collection and analysis of obstetric case records and pathological data together with his organization of regular meetings – which included a paediatrician (Mark Frazer) and a pathologist to analyse and discuss perinatal mortality and develop a classification system – was an important milestone in this story for which Baird deserves credit.

One other thing concerning the interaction between obstetricians and paediatricians. After Aberdeen I moved to Newcastle when Freddy Miller, Donald Court, Gerald Neligan and Willie Walker were paediatric consultants there. I was able to develop a close relationship with them, in those early days, because of my involvement in the haemolytic disease of the newborn story. Changing obstetric practice in the management of rhesus isoimmunization (with regional referral centres) meant that obstetricians were intervening to deliver affected infants at earlier gestations (from 35 to 30 weeks) to prevent intrauterine death and stillbirth due to severe rhesus disease, resulting in increased numbers of neonates with problems of prematurity requiring intensive neonatal care as well as the need for exchange transfusion. This in the early

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<sup>115</sup> See note 14.

<sup>116</sup> Professor John Davis wrote: 'I did not publish my work in Dawes's laboratory on the induction of what is called persistent fetal circulation; Stanley James published his in the 1980s. See also Robertson N R, Hallidie-Smith K A, Davis J A. (1967) Severe respiratory distress syndrome mimicking cyanotic heart-disease in term babies. *Lancet* ii: 1108–1100.' Letter to Dr Daphne Christie, 6 December 2000.

<sup>117</sup> Professor Denys Fairweather FRCOG (b. 1927) became Registrar in Obstetrics and Gynaecology in Aberdeen in 1955, and then Senior Lecturer in Obstetrics and Gynaecology in Newcastle in 1959. In 1966 he was appointed Professor and Head of the Department of Obstetrics and Gynaecology at University College Hospital, London, retiring in 1992. He served the final three years as Pro Vice-Chancellor for Medicine of the University of London. He held senior offices in the International Planned Parenthood Federation (1988–1994), Family Planning Association (1985–1998) and the International Federation of Gynaecology and Obstetrics (1985–1994), and served also on numerous World Health Organization, Medical Research Council and General Medical Council committees.

<sup>118</sup> See page 12.

<sup>119</sup> See note 53.

1960s must have increased the pressure to have more neonatal paediatricians and to develop regional intensive neonatal care units.

**Mitchell:** Denys and I were working together about that time. I wasn't going to bring in personalities more than I needed to, but the fact was that Sir Dugald Baird was very keen to start neonatal work and to pursue it in Aberdeen long before this, but John Craig, the paediatrician, was an adult physician of the old order. He had been an adult physician in the Infirmary and he took over the paediatrics, as so many did at that time, and he and Baird were not on the same wavelength at all. Ian Donald has also been mentioned<sup>120</sup> and he wouldn't let a paediatrician near his research on newborn babies if he could help it. It was his field, he was outstanding, a most eminent man, but the Professors of Paediatrics, Stanley Graham, and after him Jim Hutchison,<sup>121</sup> found him uncooperative to put it bluntly, and that's what I mean when I say time and time again the opportunity was there for advances in care of the newborn, but either the obstetrician or in other cases the paediatricians, wouldn't work closely as a team, and I think this is quite a cogent factor.

**Boyd:** I see quite a lot of resonance about that.

**Professor Colin Normand:**<sup>122</sup> I would like to follow up the previous remarks about paediatricians and obstetricians. From about 1955 the paediatricians conducted a regular weekly round of the antenatal wards at University College Hospital for the very reasons that we have just heard about. It was tremendously contributory.

In those days, the principal serious condition that paediatricians felt they could treat successfully was haemolytic disease of the newborn and this treatment could take up a great deal of their time. I suspect that consultant neonatologists may get appointed nowadays having carried out scarcely a single exchange transfusion. During six months at Queen Charlotte's Hospital in 1960 I had to perform well over 100 exchange transfusions on about 50 babies.

Haemolytic disease of the newborn demonstrated that paediatricians could quickly learn its somewhat complex clinical and technical management. But this was in marked contrast to the reluctance with which, in general, they felt willing or able to acquire the skills and experience of ventilating the lungs of the newborn infants with severe respiratory difficulty.

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<sup>120</sup> See note 42.

<sup>121</sup> See notes 15 and 95.

<sup>122</sup> Professor Colin Normand FRCP HonFRCPCH (b. 1928) trained in paediatrics at the Hospital for Sick Children, Great Ormond Street, London, Johns Hopkins Hospital, Baltimore, and University College Hospital, London, between 1959 and 1971. He was Professor of Child Health, University of Southampton (1971–1993) and Dean of Medicine (1990–1993). His many publications in the neonatal field have mainly related to the absorption of lung liquid in the neonatal lung and to the biochemistry of pulmonary surfactant. See, for example, Normand I C S, Reynolds E O R, Strang L B. (1970) Passage of macromolecules between alveolar and interstitial spaces in foetal and newly ventilated lungs of the lamb. *Journal of Physiology* 210: 151–164. Caesar P A, McElroy M C, Kelly F J, Normand I C S, Postle A D. (1991) Mechanisms of phosphatidyl choline acyl remodelling by human fetal lung. *Journal of Respiratory Cell and Molecular Biology* 5: 363–370.



**Professor Harold Gamsu:**<sup>123</sup> I would like to contribute to what has been said about the relationships between paediatricians and obstetricians, because there has been a tremendous sea change. Looking back on my own career, I can remember distinctly some very uncomfortable moments which emanated from the lack of conversation and interchange between us. You talk about the induction of preterm delivery in babies affected by rhesus incompatibility. One terrifying predicament that I can recall was being faced with three babies one weekend, all of whom were premature, and all of whom had very severe rhesus incompatibility and haemolytic disease. I spent all weekend doing exchange transfusions, while the obstetrician who had induced the deliveries went off for a long weekend. He had not consulted with me before making the decision to induce.

What produced a tremendous change was the demonstration to our obstetric colleagues that we could, in fact, do something about babies that weren't breathing at birth. Prior to that time, I can remember being involved in all those ridiculous manoeuvres like intragastric oxygen and putting babies on to some sort of tilting tray to get them to breathe. But in the late 1950s, when we had the facility to give positive pressure ventilation, initially via a face mask, and were able to convert a previously apnoeic limp baby into one that was lusty and crying, was the first time we demonstrated our *bona fides* to our obstetric colleagues and we were no longer *persona non grata* in the labour ward. That was a really important change and the most recalcitrant obstetricians, whom I certainly won't name, had to admit that we paediatricians might be of some use, and relinquished their responsibility for the newborn.<sup>124</sup>

**Professor Neil McIntosh:**<sup>125</sup> I think one of the critical elements for the improvement of neonatal care at University College Hospital was Os's ability to understand that medical staff came and went, but nurses were there more or less continuously. I remember, as a pre-registration locum houseman (that is a student locum), that at night I had to cover casualty, and all the paediatric admissions, the paediatric ward,

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<sup>123</sup> Professor Harold Gamsu FRCP FRCPCH (b. 1931) graduated in Johannesburg in 1954. His training in paediatrics commenced there, and continued subsequently in Sheffield and in Cleveland, Ohio. He was appointed as Wates Fellow at King's College Hospital, London, in 1965, then Senior Lecturer, Reader in Paediatrics and Director of the Neonatal Unit, 1979, and in 1994 Professor of Neonatology, later Emeritus. He established the London Perinatal Group in the 1970s, later known as the Thames Regional Perinatal Group.

<sup>124</sup> Professor Harold Gamsu wrote: 'At about this time, perinatal collaboration began between the hitherto separated specialties of obstetrics and neonatal paediatrics. The benefits of this are exemplified by what has happened in maternal diabetes and the health and survival of her offspring. In the 1950s and 1960s, the outlook for the baby of a diabetic mother was poor. The perinatal mortality was about 25 per cent. Respiratory distress syndrome accounted for ±30 per cent of deaths. This contrasts markedly with the situation at present where the perinatal mortality has dropped to about 1 per cent and respiratory distress accounts for few, if any, of these. Neonatal care undoubtedly contributed to these improved results, but the meticulous management of the mother's diabetes, and of the pregnancy and labour, is predominantly responsible.' Letter to Dr Daphne Christie, 17 December 2000.

<sup>125</sup> Professor Neil McIntosh FRCP (b. 1942) was Senior Registrar in Paediatrics at University College Hospital, London, from 1972 to 1977, Paediatrician and Neonatologist at St George's Hospital, London, from 1978 to 1987, when the Regional Perinatal Intensive Care Centre was then established. He has been Professor of Neonatology and Child Life and Health, University of Edinburgh, since 1987.

and the neonatal unit, which at that stage was ventilating babies, as a single person with Os being my superior. If a baby collapsed on the neonatal unit, I might be in casualty resuscitating a child. But the good thing was that by the time that I actually got to the neonatal unit, Anthea [Blake] or one of the other sisters would already have intubated the baby and got it on the ventilator. This was due to two things. First, Os's ability to let nurses intubate, and secondly the use of oral intubation. At that stage the Hammersmith used nasal intubation, which was much more fiddly. There was also a real mystique behind it, so that nurses weren't allowed to do it. The reliance placed on nurses at that time was reflected in the procedure book at University College Hospital. The first page just said, 'Sister knows it all'.

**Boyd:** Well, funnily enough I was going to ask Anthea to come in, but I didn't set Neil McIntosh up to that lead in. How did the things we've been talking about feel from the nursing side?

**Miss Anthea Blake:**<sup>126</sup> I think many of the nurses of my era came into neonatal care through midwifery, because at that time it was customary to spend at least three months in a neonatal unit as part of your midwifery training,<sup>127</sup> so I think quite a lot of people who perhaps hadn't thought much about neonatal care, began to get hooked on it during that time. I certainly found it very fascinating and stayed in neonatal care after midwifery training. I think it is right to say that the nursing care around the clock, I think, must have had a lot to do with the quality of care that the baby had. Beryl Corner has mentioned earlier that careful observation is very important and that's what nurses particularly train at and are good at, this meticulous observation and recording of what they see and passing that information on to people who can work in teams with them. I think it has been particularly exciting to have lived through that time; when I first went into neonatal care, it was very, very rare for a ventilated baby to survive and now it's just routine. I can remember struggling with Bennett ventilators that were not designed to give the type of respiratory ratio and pressures that we were then using following Os's work. I am sure they would not have passed all the CE markings<sup>128</sup> and the quality control they are required to do now and it horrifies me to think of some of the equipment that we used then. Basically, it wasn't particularly safe, or at least it turned out not to be terribly safe in use sometimes. But everything has to start somewhere and it has been very interesting for me to be in at the beginning.

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<sup>126</sup> Miss Anthea Blake RSCN SCM (b. 1942) joined the neonatal nursing team of University College Hospital, London, in 1968 as a postregistration student on UCH's six-month 'Prem Baby Course' and has continued on the staff there ever since as staff nurse, sister, neonatal nursing course teacher and now senior nurse. She was one of the six founder members of the Neonatal Nurses Association (see note 258) and has a particular interest in parent support and bereavement care.

<sup>127</sup> See Christie D A, Tansey E M. (eds) (2001) Maternal care. *Wellcome Witnesses to Twentieth Century Medicine*, vol. 12. London: The Wellcome Trust (in press).

<sup>128</sup> New devices coming onto the European Union market carry a CE (Conformity European) marking which allows patients, clinicians and other users to be confident that the manufacturer is demonstrating that its products perform as the manufacturer intends and are safe when used as instructed.

**Reynolds:** I should have said this earlier when I was talking about the programme of care that we got going by the beginning of 1966. The most important part of it was having nurses doing the intubations, because there were no house staff around very much, and there was no way of resuscitating any baby who collapsed in a heap. So that's absolutely right.

I wanted also to follow on very briefly from what John Davis said. I think it was Milly Stahlman who showed that if you stifled pregnant sheep their lambs developed hyaline membrane disease.<sup>129</sup> I am reminded of this because the project I did when I was in Boston, involved delivering very immature lambs without asphyxiating them. They all developed the problem if they were surfactant deficient, so that showed that the very immature delivered early got the illness spontaneously, the slightly older ones you had to stifle as well, and in the term ones you couldn't do it.<sup>130</sup> This seemed very like the situation in the human infant.

The other thing was, yes, it was very important work that Leonard [Strang] did at the Hammersmith about right to left shunts, showing that the hypoxaemia at the beginning of the illness was almost exclusively due to right to left shunts.<sup>131</sup> We followed this up in the late 1960s and Jonathan Shaw was very much involved in this. I was doing brachial artery punctures and he was doing radial artery punctures<sup>132</sup> because you needed to get upper body samples. We showed that after the first two or three days, the right to left shunts had become very much less, and the hypoxaemia was largely due to ventilation–perfusion (V/Q) imbalance because of uneven airways obstruction.<sup>133</sup> And this is a major reason why we all realized we needed to have continuous blood gas analysis. The arterial PO<sub>2</sub> swung all over the place with very small changes in inspired oxygen concentration, just like in chronic bronchitis. And that was the stimulus, together with the need for better ventilator control, for getting involved with David Delpy and his colleagues over in medical physics, to see if we could get methods going for the continuous measurement of blood gases, because of the huge swings of PO<sub>2</sub> – you couldn't possibly control the baby with intermittent samples.

**Boyd:** Thanks very much. If I can just press on, Beryl, I think we will come back to the physics in evaluating the brain, but I have got just three questions I wonder if we can consider. One question is did Sweden have an influence? I am conscious we have talked a lot about the States, but no mention of Sweden. Secondly, the Nuffield

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<sup>129</sup> Stahlman M T, LeQuire V S, Young W C, Merrill R E, Birmingham R T, Payne G A, Gray J. (1964) Pathophysiology of respiratory distress in newborn lambs. *American Journal of Disease of Children* **108**: 375–393. Stahlman M T. (1984) The history of the hyaline membrane disease and the development of its concepts, in Stein L. (ed.) *Hyaline Membrane Disease*. Orlando: Grune and Stratton, 1–16.

<sup>130</sup> op. cit. note 67.

<sup>131</sup> op. cit. note 112.

<sup>132</sup> op. cit. note 59. Shaw J C L. (1968) Arterial sampling from the radial artery in premature and full-term infants. *Lancet* **ii**: 389–390.

<sup>133</sup> Adamson T M, Hawker J M, Reynolds E O R, Shaw J C L. (1969) Hypoxaemia during recovery from severe hyaline membrane disease. *Pediatrics* **44**: 168–178.

Institute, and thirdly a rather different question: I am still not quite clear from our discussions what made the difference between ventilators doing lousily, with the babies inspissated or dead, to ventilators doing well. What were the real antecedents? Can we just have a minute or two on those three points?

**Professor Sir David Hull:**<sup>134</sup> Just for information, it was Eoin Aberdeen, a cardiac surgeon at Great Ormond Street, who realized that putting 1cc of saline down into the nasoendotracheal or the tracheotomy tube made all the difference to survival of children after cardiac surgery.<sup>135</sup>

**Professor John Wyatt:**<sup>136</sup> Could I ask a question for those who were there at the time? I understand that Bjorn Westin in Stockholm was cooling babies with asphyxia pallida and not resuscitating them with positive pressure ventilation,<sup>137</sup> and because of recent interest in hypothermia, I would be interested to know to what extent this work aroused interest at the time. How much interest was there in hypothermia treatment?

**Hull:** Yes. I remember some of that debate long ago. Westin was cooling babies and hoping that they would survive. At the same time in this country there was a lot of concern about hypothermia. Unrecognized hypothermia had distorted the results of many of the studies that had been done on newborn animals. There was also the appreciation that hypothermia for any length of time, increased the metabolic load and therefore the risks of dying. There were also quite a few reports of hypothermic injuries in infants.<sup>138</sup>

It is difficult, very difficult indeed, to cool a baby quickly. The number of babies who might benefit from hypothermia are few because most babies asphyxiated at birth recovered with intubation and proper ventilation within minutes and before they could be cooled. Thus to dip them *all* into ice-cool water would have led to more harm than good even if hypothermia were beneficial. I think one or two people tentatively tried it in this country, but alternative methods came along and displaced the necessity for it.

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<sup>134</sup> Professor Sir David Hull FRCP FRCPC (b. 1932) was Lecturer in Paediatrics, Oxford (1963–1966), Consultant Paediatrician, Hospital for Sick Children, Great Ormond Street, London (1966–1972), Foundation Professor of Child Health at the University of Nottingham (1972–1996), President of the Neonatal Society (1987–1991), and President of the British Paediatric Association (1991–1994).

<sup>135</sup> Aberdeen E. (1965) Mechanical pulmonary ventilation in infants. Tracheostomy and tracheostomy care in infants. *Proceedings of the Royal Society of Medicine* 58: 900–902. Professor Sir David Hull wrote: 'Adding saline kept the secretion moist and loose.' Note on draft transcript, 20 December 2000.

<sup>136</sup> Professor John Wyatt FRCP (b. 1952) worked as a clinical research fellow at University College Hospital Neonatal Unit, London, from 1984. He became Consultant Neonatologist at University College Hospital in 1988 and is currently Professor of Neonatal Paediatrics at University College London.

<sup>137</sup> Westin B, Miller J A, Nyberg R, Wedenberg E. (1959) Neonatal asphyxia pallida treated with hypothermia alone or with hypothermia and transfusion of oxygenated blood. *Surgery* 45: 868–879. *idem* (1962) Hypothermia and transfusion with oxygenated blood in the treatment of asphyxia neonatorum. *Acta Paediatrica Scandinavica* 139: 1–80.

<sup>138</sup> Silverman W A, Sinclair J C. (1966) Temperature regulation in the newborn infant. *New England Journal of Medicine* 274: 146–148. Hutchison J H. (1969) Hypothermia in infancy. *Medicine, Science and the Law* 9: 224–227. Dunn J M, Miller Jr J A. (1969) Hypothermia combined with positive pressure ventilation in resuscitation of the asphyxiated neonate. Clinical observations in 28 infants. *American Journal of Obstetrics and Gynecology* 104: 58–67.

**Mitchell:** In Sweden, John Lind and Petter Karlberg were very instrumental in advancing this general field<sup>139</sup> and perhaps we are touching on the kinds of baby that you would treat, the different kinds, because in about 1960 Gerald Neligan in Newcastle, Petter Karlberg in Gothenburg and I in Dundee studied maturity and the measurement of maturation and helped to differentiate the different kinds of baby that would be treated in different ways.<sup>140</sup> When I see Lilly and Victor Dubowitz sitting over there, I think it is something we ought perhaps to mention, because their work, our work and that of many others on maturity did have quite a profound effect on determining methods of management.

**Corner:** Two historical events which I feel I must mention in this meeting. We treated the first baby with rhesus haemolytic disease in 1943, because we had the Army Blood Transfusion Service in the grounds of our hospital and they were then experimenting on the detection of rhesus blood group types. In 1945, our Professor of Obstetrics said to me, 'Beryl, what's all this rhesus business about?'. We had been diagnosing the cases since 1943 when the blood from all the mothers had been tested antenatally for rhesus factors. This was a recognition really by the obstetrician that there was a paediatrician doing something there!

The next important thing occurred in June 1948 when, for the first time, I was phoned by the Professor of Obstetrics to say that he was going to deliver quadruplets at two o'clock in the afternoon by Caesarean section and would I please be in the theatre to assist with the care of these quadruplets and be ready to receive them in the premature care unit. The first three babies were delivered easily, but the fourth quadruplet was very difficult to deliver. They couldn't rupture the sac and when the baby came out she was limp and pale. It would then have been around a three Apgar score (but this was before Apgar scores were used).<sup>141</sup> We had no resuscitation equipment nor intubation; we had nothing except a human mouth and a rubber catheter and a large oxygen cylinder, so with those things we got the baby going and

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<sup>139</sup> Professor Ross Mitchell wrote: 'Professor John Lind (1909–1983) was Professor of Paediatrics in Stockholm. He made major contributions to the knowledge of the fetal circulation and of neonatal cardiovascular physiology. His associate, Petter Karlberg, studied the metabolism of newborn infants and in 1963 became Professor of Child Health in Gothenburg. In the 1960s Aberdeen, Dundee, Gothenburg, Newcastle and Stockholm collaborated closely in perinatal research.' Letter to Dr Daphne Christie, 2 December 2000. Dr Jean Smellie wrote: 'Professor John Lind was particularly interested in the pulmonary circulation and in the closure of the ductus arteriosus after birth. Like our group, he was interested in transient postnatal systolic murmurs [Adams F H, Lind J. (1957) Physiologic studies on the cardiovascular status of normal newborn infants (with special reference to the ductus arteriosus). *Pediatrics* 19: 431–437. Benson P F, Bonham-Carter R E, Smellie J M. (1961) Transient and intermittent systolic murmurs in newborn infants. *Lancet* i: 627–630].' Letter to Dr Daphne Christie, 14 December 2000.

<sup>140</sup> Farr V, Mitchell R G, Neligan G A, Parkin J M. (1966) The definition of some external characteristics used in the assessment of gestational age in the newborn infant. *Developmental Medicine and Child Neurology* 8: 507–511. Farr V, Mitchell R G. (1969) Estimation of gestational age in the newborn infant. *American Journal of Obstetrics and Gynecology* 103: 380–383.

<sup>141</sup> Apgar V. (1953) The Apgar score. A proposal for a new method of evaluation of the newborn infant. *Current Researches in Anesthesia and Analgesia* 32: 260–267. *idem* (1966) The newborn (Apgar) scoring system. Reflections and advice. *Pediatric Clinics of North America* 13: 645–650. See also page 73.

she gasped, cried at seven minutes after birth and survived – a perfectly normal, healthy child, alive at the age of 50, very lively, normal, healthy and six foot tall; birthweight 3lbs 13oz.

**Boyd:** An even longer follow up and using the ‘Corner’ ventilation. Thanks very much. We’ll move on in a minute, but one or two others want to come in.

**Dr Rodney Rivers:**<sup>142</sup> Some contributions which did come from Sweden at the end of the 1960s, early 1970s, were those relating to important investigations into the origins of the haemorrhages which were being seen both in the brains and the lungs of the premature babies that were surviving for short periods. A major question was whether these haemorrhages were explicable on the basis of an underlying haemorrhagic diathesis or whether some other mechanisms were involved in the initiation of these bleeds.<sup>143</sup>

Judith Chessells and Jonathan Wigglesworth were investigating these aspects at the Hammersmith and Judith was finding a number of babies with major coagulation abnormalities.<sup>144</sup> Hans Ekelund in Malmö was particularly interested in fibrinolysis<sup>145</sup> and whilst both at the Hammersmith and at University College Hospital we were seeing babies with what we called disseminated intravascular coagulation (DIC) – Hans was of the opinion that these letters would be better used to stand for ‘disseminated intellectual confusion’ which, I think, to some extent still applies today.

**Hull:** Could I just mention two things that I think ought to be included? The first is that incubators are designed on the concept of thermal exchange between the baby and the environment, and a lot of the early and important work was led by Kenneth

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<sup>142</sup> Dr Rodney Rivers FRCP (b. 1939) became involved in neonatal intensive care with Osmund Reynolds at University College Hospital, London, in 1970. He subsequently became interested in the investigation of babies with bleeding disorders with regard to the possible role of coagulation abnormalities in these conditions and was appointed to the post of Senior Lecturer at St Mary’s Hospital Medical School, London, with a principal interest in the newborn in 1978. He has served on several committees concerned with neonatal care and research, and was Chairman of the Appraisal Sub-Committee of the Thames Regional Perinatal Group, from 1993 to 1998.

<sup>143</sup> Professor Osmund Reynolds wrote: ‘Dr Rivers and his colleagues subsequently showed that bleeding into the lung was largely due to increased pulmonary capillary pressure and not a disorder of coagulation [Cole V A, Normand I C S, Reynolds E O R, Rivers R P A. (1973) Pathogenesis of hemorrhagic pulmonary edema and massive pulmonary hemorrhage in the newborn. *Pediatrics* 51: 175–187].’ Note on draft transcript, 1 February 2000.

<sup>144</sup> Professor Judith Chessells FRCP FRCPath FRCPCH (b. 1938) was Consultant Haematologist at the Hospital for Sick Children, Great Ormond Street, London, from 1973 to 1987, Honorary Consultant since 1988. She was Leukaemia Research Fund Professor of Haematology and Oncology at the Institute of Child Health, University of London, from 1988. See Chessells J M, Wigglesworth J S. (1970) Secondary haemorrhagic disease of the newborn. *Archives of Disease in Childhood* 45: 539–543.

<sup>145</sup> Ekelund H, Hedner U, Nilsson I M. (1970) Fibrinolysis in newborns. *Acta Paediatrica Scandinavica* 59: 33–43. Ekelund H, Hedner U, Astedt B. (1970) Fibrinolysis in human foetuses. *ibid.* 369–376. Dr Rodney Rivers wrote: ‘Hans Ekelund was a member of the Paediatric Department, Malmö, and of the coagulation laboratory there under the direction of Professor N C Nielsen. In 1972 he published his review “Fibrinolysis through intrauterine life and infancy”, based on his publications, in *Acta Paediatrica Scandinavica* from 1970 onwards.’ Letter to Dr Daphne Christie, 18 December 2000.

Cross and by Edmund Hey and his colleagues.<sup>146</sup> It's excellent, outstanding work. Edmund is not here and I am sorry, but he made a great contribution.<sup>147</sup>

**Boyd:** I have to say neonatal ward sisters were doing it long before the unit. I can remember Linda Collins, Anthea's predecessor, taking the jaundiced babies and wheeling them to the phototherapy unit, called the sun.

**Dr Pamela Davies:**<sup>148</sup> I think people underestimate the enormous number of hours that we spent on exchange transfusions. Colin [Normand] said he spent six months doing them, I spent years and years.<sup>149</sup>

**Smellie:** I don't think we can pass the bilirubin story by without mentioning John Bound and his demonstration that 30mg of vitamin K induced more kernicterus of prematurity than 1mg, which seemed therapeutically effective.<sup>150</sup>

**Barrie:** I thought I would just tackle your question of bronchopulmonary dysplasia and different sorts of ventilator. The story goes back to what I said earlier about resuscitation. I devised as a safety valve, the simple method of delivering positive pressure using a tube which dipped 40cm under water. The whole column was only 45cm, so it was not possible to exceed that pressure. In fact, the same system is still used in the modern Resuscitaire.<sup>151</sup> When I continued ventilating babies who wouldn't breathe on their own, I usually withdrew the tube in the water to 15cm. Even if they were finger-ventilated by a medical student for 24 hours, the pressure was limited and

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<sup>146</sup> See, for example, Cross K W, Flynn D M, Hill J R. (1966) Oxygen consumption in normal newborn infants during moderate hypoxia in warm and cold environments. *Pediatrics* 37: 565–576. See also note 14. Hey E N. (1969) The relation between environmental temperature and oxygen consumption in the new-born baby. *Journal of Physiology* 200: 589–603. Hey A N, Katz G. (1970) The optimum thermal environment for naked babies. *Archives of Disease in Childhood* 45: 328–334.

<sup>147</sup> Professor Harold Gamsu wrote: 'Their work on the zone of thermoneutrality for babies in incubators, clothed or unclothed, and related to gestational age and birthweight, is still of great clinical relevance.' Note on draft transcript, 25 July 2000.

<sup>148</sup> Dr Pamela Davies FRCP HonFRCPCH DCH (b. 1924) is a retired paediatrician with a special interest in neonatal follow up and infection. She worked as a junior hospital doctor and then Lecturer in the United Oxford Hospitals, and later as Consultant Paediatrician at the Hammersmith Hospital, London, from 1966 to 1982.

<sup>149</sup> Dr Pamela Davies wrote: 'Clarke's work on anti-D gammaglobulins eventually transformed the rhesus incompatibility situation; and the spare time gained by so many surely contributed to the development of further advances in neonatal care.' Note on draft transcript, 21 March 2000. Professor Osmund Reynolds wrote: 'Sir Cyril Clarke virtually abolished rhesus haemolytic disease of the newborn.' Note on draft transcript, 30 November 2000. See Anon. Professor Sir Cyril Clarke (1907–2000). *The Times*, 8 December 2000, page 25. See also Clarke C A. (1967) Prevention of Rh-haemolytic disease. *British Medical Journal* iv: 7–12. *idem* (ed.) (1975) *Rhesus Haemolytic Disease, Selected Papers and Extracts*. Commentaries by C A Clarke. Lancaster: Medical and Technical Publishing Co.

<sup>150</sup> It was Bernard Laurance in Derby who first reported hyperbilirubinaemia due to excessive vitamin K medication in 1955 [Laurance B. (1955) Danger of vitamin-K analogues to newborn. *Lancet* i: 819]. Information provided by Professor Peter Dunn, 15 January 2001. See also Bound J P, Telfer T P. (1956) Effect of vitamin-K dosage on plasma-bilirubin levels in premature infants. *Lancet* i: 720–722.

<sup>151</sup> An essential piece of equipment which is used by medical and midwifery staff to resuscitate the newborn. The Resuscitaire was designed and manufactured by a company called Vickers Medical Ltd, which came into being when Vickers Plc bought out a company called Oxygenaire, in about 1965. Shortly after that the first 'Resuscitaire' was introduced to the market. Edited from an e-mail from Anthony Flynn to Caroline Dux, 21 February 2001.

never more than 40cm. When other ventilators came along, I was much too scared of using high pressures and did not see bronchopulmonary dysplasia for a very long time – in fact not until much later when we started using sophisticated machines that could generate much higher pressures. I have always felt that excessive pressure is an important factor in bronchopulmonary dysplasia.

The tube in the trachea is also worth mentioning. The anaesthetists traditionally used rubber endotracheal tubes, which were the only tubes available for resuscitation before 1960. It soon became obvious to me that rubber tubes were not suitable. It was true you could boil them up whereas plastic tubing just melted, but the main problem with rubber tubes was that they had an intense irritant reaction on the larynx, especially after only a few hours and I very soon had to switch to plastic tubes. The question was, do you sterilize them and if so, how? In the beginning, I made my own tubes from large rolls of tubing that already had the right sort of curvature. I used to hide them in little paper packets in the radiotherapy department in the mistaken view that the irradiation would sterilize them. Although this was later shown to be bacteriologically unsound, there was no need to sterilize them at all because the fresh rolls from which I cut them had no pathogens and in any case were never re-used. Eventually the manufacturers started to make sterile disposable plastic tubes. For a long time, one modelled on my homemade tube was sold as the St Thomas' tube. The use of rubber tubes was, unfortunately, something that held resuscitation back for a very long time.<sup>152</sup>

**Boyd:** That's very interesting. Good example of those small things.

**Reynolds:** It was tin in the rubber that was rotting the larynx.

**Boyd:** I think at that point we should draw a line and spend a little while on the clinical outcomes and ethical debates in the 1960s and 1970s and, I think, Tom, you kindly offered to start.

**Oppé:** By the 1960s I was no longer involved directly in neonatal research nor even in the delivery of intensive care. But I had become Consultant Adviser in Child Health to the Department [of Health] and needed to be in touch with the rapid developments in neonatology. You have invited me to introduce the themes of outcome and ethics.

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<sup>152</sup> Professor Harold Gamsu wrote: 'It should be said that the development of reliable and disposable equipment was one of the major reasons for improvement in neonatal care. Sharp and fine needles, plastic syringes with the plunger moving smoothly in the barrel predictably, and soft fine indwelling feeding tubes and catheters all delivered sterile, played a major role. These developments went hand-in-hand with the availability of accurate microchemical analysis. In the 1950s, even the measurement of inspired oxygen concentration was messy and inaccurate. At the end of that decade, however, we could measure blood pH and glucose, and, in some labs, PCO<sub>2</sub>. As a result, correction of acidosis with bicarbonate and of hypoglycaemia with intravenous glucose became feasible and Robert Usher in Montreal was able to make some sensible recommendations for intravenous fluid therapy in the newly born.' Note on draft transcript, 25 July 2000. Professor Peter Dunn wrote: 'Robert Usher recently received the Apgar Award of the USA for the year 2000.' Letter to Dr Daphne Christie, 22 January 2001. See Usher R. (1959) The respiratory distress syndrome of prematurity. Changes in potassium in the serum and the electrocardiogram and effects of therapy. *Pediatrics* 24: 562–584. *idem* (1963) Reduction of mortality from respiratory distress syndrome of prematurity with early administration of intravenous glucose and sodium bicarbonate. *ibid.* 32: 966–975.



I agree that these subjects do overlap considerably because it was only when outcomes improved that several ethical debates were generated. I will mention three.

First, the impact of the successful treatment of haemolytic disease of the newborn by exchange transfusion. No sophisticated analyses or randomized trials were needed to show that this was an efficacious and acceptably safe operation. The hitherto passive attitude to neonatal care expressed as, 'Let's provide babies with tender loving nursing care, a bit of warmth and as much milk as you could' was swept away and thereafter it became morally justifiable to undertake active therapeutic intervention.

My second historical note is about the deep emotional concern with which some paediatricians viewed the survival of otherwise premature babies. I can think of Eric Burnard,<sup>153</sup> who sat for hours observing premature babies in Paddington, and of Robert Usher<sup>154</sup> in Canada and the USA, devoted to newborns. Then there was Kenneth Cross<sup>155</sup> – the physician turned physiologist – unable to have children himself who became driven to direct his life's work to the benefit of the newborn. At the top of the ladder there was the brilliant and influential Chief Medical Officer. It was widely believed that George Godber's<sup>156</sup> undoubted interest in maternal and child health was derived from familial medical problems.

The third point about outcomes was to my mind the early establishment of clinical audit. One reason for this was the equation put quite properly by the obstetrician, who asked, 'Is this baby going to be stillborn if we don't get it out, but if we deliver the mother prematurely, what is the chance of neonatal death?' This equation was important in diabetic pregnancies, haemolytic disease of the newborn, pre-eclampsia and placental insufficiency.<sup>157</sup> Such audits were best made locally and by collaboration between obstetricians, pathologists and paediatricians. Regional, national and international league tables provided important data about outcome related to birthweight, gestational age and neonatal death. As Chief Medical Officer, George Godber's formidable epidemiological knowledge was invaluable for raising the profile of neonatal paediatrics.

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<sup>153</sup> Eric Burnard FRACP FRCP (1916–1991) was an Australian neonatologist. He came to the UK in 1946 and held posts at Hammersmith Hospital, the Hospital for Sick Children, Great Ormond Street, London, and the General Hospital, Newcastle upon Tyne. In 1954 he joined the paediatric unit at St Mary's Hospital Medical School in London and in 1961 he went to Sydney, Australia, to set up a unit for newborn research at the Women's Hospital under the auspices of the Children's Medical Research Foundation. He remained there until he retired in 1981, continuing to work until 1989. See Stapleton T. (1994) Eric Dawson Burnard. *Munk's Roll* 9: 66–67.

<sup>154</sup> See note 152.

<sup>155</sup> See note 14.

<sup>156</sup> Sir George Godber KCB GCB DPH HonFRCS HonFRCGP HonFRSocMed FRCPsych FFCM (b. 1908) was Deputy Chief Medical Officer, Ministry of Health (1950–1960), Chief Medical Officer, Department of Health and Social Security, Department of Education and Science, and Home Office (1960–1973) and Chairman of the Health Education Council (1976–1978).

<sup>157</sup> See Christie D A, Tansey E M. (eds) (2000) op. cit. note 85, page 63. Professor Maureen Young wrote: 'Placental insufficiency is not a term very popular with the obstetric and gynaecology establishment. Small babies are "malnourished *in utero*" – their growth potential demand has not been matched by the maternal capacity to supply nutrients.' Letter to Dr Daphne Christie, 8 December 2000.

With demonstrable improvement in outcomes and more precise data about risks and benefits a number of new ethical issues emerged. The big ethical debates had philosophical roots between the imperatives of Kant with deontological absolutes, interpreted as the sanctity of human life at all costs, and the situational ethics proposed by Douglas Black<sup>158</sup> from a more utilitarian base. The Kantian ethic dictated that the live-born individual no matter of what maturity, physical formation or expected quality of life, was an end in itself and never to be considered simply as a means to any end such as the acquisition of knowledge or the ending of a futile life. The ethical debates that I recall during this decade included such issues as: to resuscitate or not to resuscitate the damaged infant, to provide intensive care or not to treat the infant with poor life expectancy, when is the fetus viable and when might futile treatment be abandoned?

The last subject I would mention with regard to the scientific rigour that underpinned intensive care is the recognition of the importance of the randomized clinical trial. It was Bill Silverman in the USA who convinced paediatricians, many of whom needed a lot of convincing, that the newborn deserved properly controlled trials and should not be subject to the clinician's hunch that he or she was doing good.

**Boyd:** Eva, from a more public health point of view, what did you feel?

**Professor Eva Alberman:**<sup>159</sup> Can I come to the public health point of view in a minute? I came to Guy's in 1960, to a new unit run by Paul Polani and set up by Ronald Mac Keith and Philip Evans. They had an immense interest in maturity of babies and the intactness of the neurological system. I was employed by Alison McDonald,<sup>160</sup> who carried out the first really good follow-up studies of low birthweight babies. You may remember she did a very large study, I think about 3000, I can't remember now, of babies of 2000g or less, and looked at the risk of cerebral palsy in babies with different characteristics, and also retrolental fibroplasia, which we haven't heard a lot about today.

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<sup>158</sup> Professor Sir Douglas Black Kt FRCP FRCPath FRCPsych FRCGP (b. 1913) qualified at St Andrews University in 1936 and was appointed to the Department of Medicine at Manchester University in 1946, becoming Professor of Medicine from 1959 to 1977, later Emeritus. He was Chief Scientist at the Department of Health and Social Security from 1973 to 1977, a member of the MRC from 1966 to 1970 and 1971 to 1977, Chairman of the MRC Clinical Research Board from 1971 to 1973, Chairman of the Research Working Group on Inequalities in Health from 1977 to 1980 and President of the Royal College of Physicians from 1977 to 1983. See *The Black Report*. (1980) *Inequalities in Health: Report of a research working group*. London: DHSS. Black D. (1987) *Recollections and Reflections*. London: The Memoir Club, British Medical Journal, especially pages 128–132.

<sup>159</sup> Professor Eva Alberman FRCP (b. 1929) had postgraduate training in epidemiology and in 1960 she joined the Paediatric Research Unit at Guy's Hospital, London. In 1963 she was seconded to join Neville Butler to work on the National Birthday Trust Fund Perinatal Mortality Survey and its follow up, the National Child Development Study. In 1972 she joined the London School of Hygiene and Tropical Medicine's Social Medicine Unit, and in 1979 was appointed to a Chair of Clinical Epidemiology at the London Hospital Medical College. After retirement she spent some time working at the Office of Population Censuses and Surveys.

<sup>160</sup> Professor Eva Alberman wrote: 'Professor Alison McDonald was a founder member of the Guy's Paediatric Research Unit in London and remained there until she moved to McGill University in Montreal, where she investigated occupational hazards to reproduction. Her monograph, *Children of Very Low Birthweight*, was published in 1967 by the Spastic Society Medical Education Unit in association with William Heinemann Medical Books Ltd. It described the neurological problems as well as the retrolental fibroplasia [now "retinopathy of prematurity"] in the survivors.' Letter to Dr Daphne Christie, 22 December 2000.

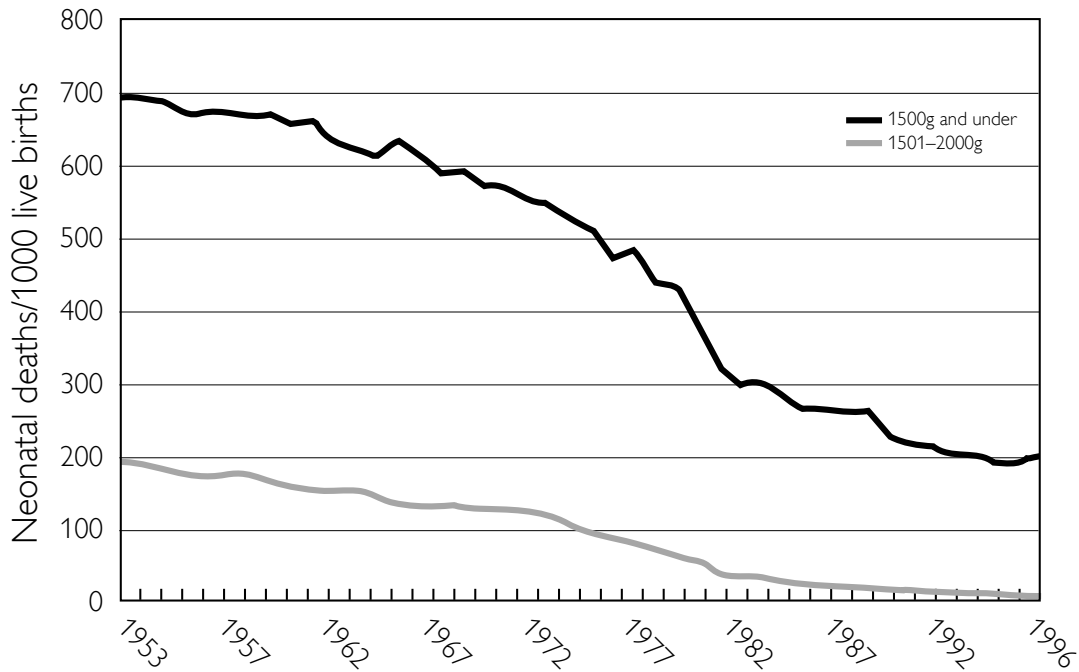


Figure 1. Neonatal mortality rate/1000 live births under 2000g, England and Wales, 1953–1996. Taken from Macfarlane A and Mugford M: *Birth Counts 1984 and 2000*. London: The Stationery Office. Tables A3.7 and A3.5.2. Change in birthweight groups in 1982: less than 1500g and 1500–1999g.

I was appointed to do a case control study of cerebral palsy, and on Alison's advice we divided these into the preterm and low birthweight and comparable controls, and normal birthweight and comparable controls. This was a very important distinction and little recognized in the early 1960s. Alison's study was started in 1959 when there was a lot going on in terms of outcome and ethical problems. One of the big balancing acts was between cerebral palsy and death. Moreover, in terms of public health, the epidemic of retrolental fibroplasia very much challenged the public health departments who, in the very early 1950s, set up the first collection of data on low birthweight in all local authorities and were obliged to make returns to the Department of Health, I think when George Godber was Chief Medical Officer. This first made it possible to determine the mortality of these babies and was the beginning of the public health interest in mortality and trends in mortality of low birthweight babies. Figure 1 illustrates the remarkable drops that have occurred since 1953 in the very low birthweight.

**Boyd:** Ann Stewart, did you want to comment? This is very much your area.

**Dr Ann Stewart:**<sup>161</sup> I was remembering that Cecil Drillien reported that the survival rate doubled, but there weren't any more intact survivors, and that is where our work began.<sup>162</sup>

<sup>161</sup> Dr Ann Stewart FRCP (b. 1930), as Senior Lecturer in Perinatal Medicine, ran the 'follow-up clinic' at University College Hospital, London, from 1968 to September 1996. She is currently Honorary Senior Lecturer in the Department of Paediatrics at University College London.

<sup>162</sup> op. cit. note 70. See also Drillien C M. (1967) The long-term prospects for babies of low birthweight. *British Journal of Hospital Medicine* 1: 937–944.

**Boyd:** Lilly, do you want to make any comment at this point?

**Dr Lilly Dubowitz:**<sup>163</sup> I think probably not quite at this point, but later, when we can compare what we were able to assess in the neonatal period, which didn't come until a bit later, and correlate that with survival and not only low birthweight and maturity, because I think that had been done by Drillien already.

**Boyd:** What I am not quite hearing at the moment on this clinical outcome, ethical debate, apart from Tom Oppé who has been very candid, is some reflection of the tensions in the early years as to what 'those immoral, obsessed, over-treating blighters in the neonatal unit are up to over-treating these infants, not letting them die in peace, and making sure they end up handicapped'. Who wants to come in on that?

**Reynolds:** Of course, this was absolutely in the forefront of everybody's minds and I just want to say how fortunate we were to have Ann Stewart who has been in charge of that study ever since 1968 and still is.<sup>164</sup> The thing as far as we could see in the early and middle 1960s, was that Cecil Drillien had published her work showing an extremely high incidence of disability in the survivors of very low birthweight, and there was a period of a few years when the conventional wisdom was that all these babies are damaged before they are born, so that anything you do to make them live, is inevitably going to produce a huge increase in damaged children in the community. This sort of jibed with the physiology and clinical observation in related work that was going on at the time, which was saying that these babies get hypoglycaemic and hyperbilirubinaemic and they can't breathe and they get acidotic and cold and I, among other people who were thinking in the same way, formed a hypothesis that maybe if you prevent all those things, the outcome is going to be a good deal better. Hence the programme starting in 1966, trying to prevent all those things. But yes, there was a great deal of scepticism and that is why the follow-up study was started. And, of course, you can't start off with a population survey of a region or something, you have got to start in a unit that's doing it all to ask the simple question, 'Are they mostly frightful, or are they mostly all right?'. That's the first question that had to be addressed. And so against a very large reduction in mortality, it turned out that the

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<sup>163</sup> Dr Lilly Dubowitz FRCP FRCPC (b. 1930) graduated from the University of Melbourne in 1956 and came to the UK in 1958 to train in endocrinology at University College and Hammersmith Hospitals, London. She got involved in paediatrics rather accidentally when she was asked to do a paediatric locum registrar post. Her interest in neonatal infant development was kindled by Ronald Illingworth and she has been working in this field ever since, first as a research fellow and then as Senior Lecturer. She continues to take an active interest in the integrated approach to the newborn nervous system combining imaging of the brain and electrophysiological studies with careful clinical assessment. See note 268.

<sup>164</sup> See Rawlings G, Reynolds E O R, Stewart A, Strang L B. (1971) Changing prognosis for infants of very low birthweight. *Lancet* i: 516–519. Stewart A L, Reynolds E O R. (1974) Improved prognosis for infants of very low birthweight. *Pediatrics* 54: 724–734. Roth S C, Baudin J, McCormick D C, Edwards A D, Townsend J, Stewart A L, Reynolds E O R. (1993) Relation between ultrasound appearance of the brain in very preterm infants and neurodevelopmental impairment at eight years. *Developmental Medicine and Child Neurology* 35: 755–768. Stewart A L, Rifkin L, Amess P N, Kirkbride V, Townsend J P, Millar D H, Lewis S W, Kingsley D P E, Moseley I F, Foster O, Murray R M. (1999) Brain structure, neurocognitive and behavioural function in adolescents who were born very preterm. *Lancet* 353: 1653–1657.

vast majority were okay,<sup>165</sup> so much so that the big babies that we ventilated, and the rhesus ones which Denys Fairweather was very involved in, were doing so well that we only followed them up for about three years.<sup>166</sup> It was just the tiddlers that were kept under long-term surveillance and subsequently it became important to set up regional rather than local statistics.

**Gamsu:** I can certainly remember that era. The difficulties that many of us had, working very hard as you have already heard, trying to keep these little babies alive, and then we were faced with the terribly depressing information in Drillien's book which showed how badly the babies were doing.<sup>167</sup> We had to sustain our enthusiasm, and particularly sustain the enthusiasm of the people we were working with, by telling them that there was a long interval between the publication of Drillien's study and collection of her data, and that in the interim there had been great changes in neonatal care. We were sustained in this, of course, by the evidence that was being produced by Ann Stewart and others, which certainly seemed to corroborate our optimistic impression that results had been improving in the interim. These studies also set the stage for everyone who was involved in neonatal work, to perform their own audit. Even though we recognized the shortcomings of doing hospital-based studies it was very important that these audits be established so that we at least knew our own local results. Of course, thank goodness, we have progressed on to more extensive regional studies now, from which one can draw a different set of conclusions without the disadvantage of restricting the follow up to a selected population.

**Reynolds:** I remember Cecil Drillien coming down in 1971 wearing a battledress, prepared to do battle with us, and sitting in with Ann [Stewart]. It's quite a funny story, but she didn't believe a word of it,<sup>168</sup> but then she did after she had talked with us.<sup>169</sup>

**Fairweather:** I want to come in again from the obstetric point of view, in relation both to the ethics and the clinical outcome. For antenatal analysis of the severity of rhesus disease we, as obstetricians, were performing amniocentesis and there was a lot of criticism because we were sticking needles into the pregnant uterus – a potentially risky procedure for both mother and fetus.<sup>170</sup> The technique progressed further when

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<sup>165</sup> op. cit. note 164.

<sup>166</sup> Stewart A, Turcan D, Rawlings G, Hart S, Gregory S. (1978) Outcome for infants at high risk of major handicap, in Elliott K, O'Connor M. (eds) *Major Mental Handicap: Costs and methods of prevention*. Ciba Foundation Symposium, 59. Amsterdam: Elsevier, 151–171.

<sup>167</sup> op. cit. note 70.

<sup>168</sup> op. cit. note 164.

<sup>169</sup> Dr Ann Stewart wrote: 'After we published our first paper in the *Lancet* [Rawlings G, Reynolds E O R, Stewart A, Strang L B. (1971) op. cit. note 164], giving our results, Cecil Drillien wrote to Os saying that she wanted to come and visit us. A date was fixed and she came in a sort of battledress, prepared to take us to pieces – she did not believe a word of what we had said! By the time we had spent some time together – and had a very good dinner – she came round to our point of view. And she has been a friend ever since! I had a card from her last Christmas. Sadly, she is going blind, so that is why she is not here today.' Edited from a letter to Dr Daphne Christie, 19 February 2000.

<sup>170</sup> MRC Working Party. (1978) Report: An assessment of the hazards of amniocentesis. *British Journal of Obstetrics and Gynaecology* 85: 21–34.

we went on to develop intrauterine transfusion to try to intervene even earlier to prevent intrauterine death from rhesus disease.<sup>171</sup> Again, there were a lot of ethical issues raised about that and these increased further when we began to use chromosomal analysis and other techniques for intrauterine fetal diagnosis of fetal abnormalities, thalassaemia, etc. This meant that there was quite a lot of opposition along the way while these developments were progressing.

**Davies:** I do agree that the infants who have been so well tended in recent years are turning out well. But neonatologists do have difficulty in realizing that because the survival of these very small babies is now so greatly increased, the actual number of disabled children is probably not less, may even very well be more, and I think that is an important point to remember.<sup>172</sup>

**Oppé:** I meant to mention two topics regarding research. One is to lay to rest the story that Kenneth Cross dismissed the importance of ambient temperature in the regulation of respiration in the newborn.<sup>173</sup> In fact, he was not aware of the fluctuations in ambient temperature caused, on the one hand, by intermittent opening of the windows to let out the smoke emanating from the research assistant's (me) pipe and on the other by a constant stream of mothers coming to see how the babies were doing in the plethysmograph or asking us to test their babies because they had heard that we only tested the really healthy ones. I was guilty of not monitoring the ambient temperature. It was about this time that the Medical Research Council asked its legal eagles to consider the ethics and legality of nontherapeutic research in children. The legal opinion was that although parents were perfectly all right as proxies for therapeutic research they had neither right nor moral justification to allow nontherapeutic research. Now this has never been tested in the courts and paediatricians, to their credit, went on plodding away, insisting that consent was an extremely important aspect of any sort of research but maintaining a slightly hypocritical position in that babies of low birthweight could be regarded as 'sick' and therefore could be investigated without the ethical problem of nontherapeutic research.

**Davis:** I want to introduce a rather different topic. Many will remember the demonstration by Aynsley-Green and Anand, that babies feel pain probably more than we do if their reactions to it are to be taken as an index.<sup>174</sup> I remember we first introduced indwelling arterial catheters simply because we couldn't bear watching babies heels being pricked quite so often, and I think we do want to bear in mind in the follow up that babies have been

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<sup>171</sup> Hamilton E G. (1978) Intrauterine transfusion for Rh disease: a status report. *Hospital Practice* 13: 113–117, 122–124.

<sup>172</sup> Professor Osmund Reynolds wrote: 'I don't think that neonatologists in general have difficulty in realizing this. The major aim of intensive care is, of course, to provide the maximum chances of survival for potentially normal children: on the whole, a pretty good job is being done – far more healthy children are surviving and the number of disabled ones is remaining comparatively low.' Note on draft transcript, 30 November 2000.

<sup>173</sup> See page 8.

<sup>174</sup> Anand K J, Sippell W G, Aynsley-Green A. (1987) Pain, anaesthesia, and babies. *Lancet* ii: 1210. Anand K J, Aynsley-Green A. (1988) Measuring the severity of surgical stress in newborn infants. *Journal of Paediatric Surgery* 23: 297–305.

through a rather hellish experience, sometimes in an incubator, being resuscitated and so on, and that probably this does have some permanent impact upon them.

**Alberman:** My baby was one of the ones that Kenneth Cross put in his plethysmograph. I found it an extremely distressing experience and I communicated this to my baby, who screamed all the way through and they had to stop it, so I don't think all mothers enjoyed this. This was fortunately a very healthy, lusty baby. But I would like to come back to follow up just for a minute, because I think there have been tensions, certainly between Cecil Drillien and Alison McDonald, and between University College Hospital and others. University College Hospital, because of its excellence – and it is and was excellent – certainly got the sickest babies, there's no doubt about that. I have always been worried that the follow up of babies of University College Hospital, which was superb, did not, as Lilly says, give a picture of what was actually going on in the country as a whole. It may be that the follow up of the University College Hospital babies gave a worse picture simply because they were such very sick babies.<sup>175</sup> The problem partly was administrative, because the follow up of babies is expensive, and it never stops, and the fundraisers hate it. The MRC, when I was on the board, was very unwilling to give money for follow up of babies, who were enrolled in randomized control trials, which I think was a disaster. The other way of handling this is by setting up registers of, for instance, babies with cerebral palsy or with other conditions that stem from early life. That has been a desperate struggle and only very few people have persisted, Peter Pharaoh being one of them.<sup>176</sup> We have to rely very heavily on registers from small countries, such as from Gothenburg in Sweden and the Western Australia register. This is something that has seriously held back our knowledge of the true ethical position.

**McIntosh:** Another word about ethics. Ethics, I think, are related to perspectives, and perspectives change with both knowledge and people's perception of knowledge at the time. All parents now expect the best, they expect intensive care, etc. In Os's day there was not that expectation. By the time Malcolm Levene<sup>177</sup> and Rodney Rivers and myself came along, there was an expectation of survival and we could transmit

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<sup>175</sup> Professor Osmund Reynolds wrote: 'The University College Hospital follow up most emphatically did not give a "worse picture" otherwise we would not have forced on. The whole of our programme was based on our finding that most were doing well! See, for example, Stewart A L, Reynolds E O R. (1974) Improved prognosis for infants of very low birthweight. *Pediatrics* 56: 724–735. Stewart A L, Reynolds E O R, Lipscomb A P. (1981) Outcome for infants of very low birthweight: survey of world literature. *Lancet* i: 1038–1041.' Note on draft transcript, 1 February 2000. See also note 164.

<sup>176</sup> Professor Peter Pharaoh FRCP FRCPC FFPHM (b. 1934) was Professor of Public Health (formerly of Community Health), at the University of Liverpool, from 1979 to 1997, later Emeritus. See, for example, Pharaoh P O, Alberman E D. (1981) Mortality of low birthweight infants in England and Wales 1953 to 1979. *Archives of Disease in Childhood* 56: 86–89. Pharaoh P O, Cooke T, Rosenbloom L, Cooke R W I. (1987) Trends in birth prevalence of cerebral palsy. *ibid.* 62: 379–384. Hutton J L, Cooke T, Pharaoh P O. (1994) Life expectancy in children with cerebral palsy. *British Medical Journal* 309: 431–435.

<sup>177</sup> Professor Malcolm Levene FRCP (b. 1951) was Honorary Consultant Paediatrician at the Leicester Royal Infirmary and Reader in Child Health, University of Leicester Medical School (Senior Lecturer from 1982 to 1988) and has been Professor of Paediatrics and Child Health and Honorary Consultant Paediatrician at the University of Leeds Medical School since 1989.

this to parents with its optimism. Previously, parents and the general public just shrugged their shoulders at having a preterm baby but now they grabbed the optimism that we transmitted, because we had seen it. For the individual baby it would have been unethical not to give full intensive care. The original people working in neonatal intensive care were working on a sort of population ethics base, but those of us who were registrars and housemen were actually talking to the parents on personal terms about what might be possible, and the parents were often psyched up with that.

**Boyd:** I think that's a very interesting point. I thought for the next session we might mainly consider evaluation, and that probably needs to include protecting the brain, in so far as we are able, but I do also want to leave some time at the end for roll-out of the ideas we talked about in the first session and their developments into the wider NHS. So the second session should include particularly the development of neonatology and the wider NHS in the 1980s and 1990s.

**Professor David Harvey:**<sup>178</sup> I was thinking that we may not have said enough about how exciting it was at the Hammersmith in the middle 1960s and particularly to mention just two people. Peter Tizard,<sup>179</sup> I don't think has been mentioned, but was terribly inspiring to me as a trainee, and also Wilfrid Payne,<sup>180</sup> who after his retirement from Great Ormond Street came to the Hammersmith and introduced the micromethods that Jonathan [Wigglesworth] mentioned; the tiny amounts of blood that were needed to do chemical tests were a revelation.<sup>181</sup>

**Boyd:** Yes, I was very conscious of the Tizard absence. Does anyone want to pick that up any further than David, or any plus or minus aspects of the Hammersmith, just before we move on to evaluating the brain?

**Booth:** Only to say how very slow the Hammersmith was to develop paediatrics, and, of course, the reason was that as a postgraduate institution it was not expected to

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<sup>178</sup> Professor David Harvey FRCP FRCPCH (b. 1936) has been Professor of Paediatrics and Neonatal Medicine at Imperial College, London, since 1995 and Consultant Paediatrician, Queen Charlotte's and Chelsea Hospital, London, since 1970. His training in neonatology was as a houseman, research fellow, and registrar, at the Hammersmith Hospital, London.

<sup>179</sup> Sir Peter Tizard Kt DCH FRCP (1916–1993) was Medical Registrar and Pathologist, at the Hospital for Sick Children, Great Ormond Street, London, in 1947, and Assistant Director of the Paediatric Unit at St Mary's Hospital Medical School, London, in 1949. He was Reader in Child Health (1954–1964) and Professor of Paediatrics (1964–1972) at the Institute of Child Health, Royal Postgraduate Medical School, University of London, Professor of Paediatrics, University of Oxford (1972–1983), later Emeritus, and Fellow of Jesus College, Oxford (1972–1983), Honorary Fellow in 1983. See Davis J A. (1994) Sir Peter Tizard. *Munk's Roll* 9: 518–520.

<sup>180</sup> Professor David Harvey wrote: 'Wilfrid Payne FRCP (1894–1978) was chemical pathologist at the Hospital for Sick Children, Great Ormond Street (GOS), London. He developed techniques for the estimation of chemicals in tiny samples of blood. When he retired from GOS, he worked for three years at Queen Charlotte's Maternity Hospital, London, to establish normal ranges for chemicals in the blood of term infants. He then spent seven years at Hammersmith Hospital, London, undertaking similar studies in preterm infants.' E-mail to Dr Daphne Christie, 15 January 2001. See Cathie I A B. (1984) Wilfrid Walter Payne. *Munk's Roll* 7: 453–454.

<sup>181</sup> See page 22.



overlap with postgraduate centres in other parts of London. So there was really no need to develop postgraduate training at the Hammersmith in paediatrics, when it was already being done at Great Ormond Street.

The first professor at the Hammersmith was, in fact, Tizard and I don't know what date he came to the Hammersmith, it must have been about 1961. He really made a dramatic change in things and paediatrics and neonatology, his own particular interests, became terribly important within the scene at the Hammersmith. But I think Tizard's position was that he was very iconoclastic and when he went to Oxford he was extremely insistent that Scopes should become his successor.<sup>182</sup> I think we took the view that if you appointed Scopes, you would get the second best man, whereby we wanted to have somebody who might be the best on his own subject. And so Dubowitz was appointed and he's here and can comment if he wishes. But Tizard's position was quite clear, he objected to Dubowitz's appointment.<sup>183</sup>

**Oppé:** Just a quick word to say that we at St Mary's might have had neighbours from hell with University College Hospital on one side and the Hammersmith on the other. I can sincerely tell you that both Leonard Strang and Peter Tizard<sup>184</sup> were always supportive of our work and ensured that the units were complementary and not competitive.

**Boyd:** And just putting Tizard to bed, he had been at Mary's before and so he was a Mary's product in a sense.

**Davis:** He was a Middlesex man who came from Great Ormond Street as first assistant to Reggie Lightwood;<sup>185</sup> that's how he arrived at St Mary's. Then he left St Mary's for the Institute of Child Health and was posted to the Hammersmith, where they had a type of neonatal outstation and where later on he set up his neonatal research unit in reaction, I think, to not being appointed to the staff of Great Ormond Street as a neurologist. Most of his juniors were recruited for clinical studies in Geoffrey Dawes's Neonatal Physiology Unit in the Nuffield Institute in Oxford.

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<sup>182</sup> Professor Jon Scopes FRCP (d.1999) moved to St Thomas' Hospital, London, in 1973 where he established the neonatal intensive care unit and was Professor of Paediatrics there from 1975 to 1990. His PhD thesis was on the oxygen consumption of newborn infants and helped to establish the effective use of oxygen in premature babies. In 1972, he published with Sir Peter Tizard and others, *Medical Care of Newborn Babies*.

<sup>183</sup> After the Seminar a number of participants (including Dr Pamela Davies, Professor Victor Dubowitz, Professor Harold Gamsu, Professor Sir David Hull and Professor Osmund Reynolds) strongly objected to the comments made about Jon Scopes and Victor Dubowitz. Copies of their correspondence will be deposited with the records of this meeting in Archives and Manuscripts, Wellcome Library, London.

<sup>184</sup> See notes 66 and 179.

<sup>185</sup> Reginald Cyril Lightwood DPH FRCP (1898–1985) qualified in medicine from King's College Hospital, London, in 1921 and by 1939 he held honorary consultant appointments at the Hospital for Sick Children, Great Ormond Street, London, and at St Mary's Hospital, Paddington. He was appointed part-time director of St Mary's Hospital Medical School's Academic Unit of Paediatrics and later became Honorary Treasurer and then President of the British Paediatric Association. He made important investigations into metabolic disorders of infants, and descriptions of renal acidosis and infantile hypercalcaemia. See Oppé T E. (1989) Reginald Cyril Lightwood. *Munk's Roll* 8: 282–283.

**Professor Richard Cooke:**<sup>186</sup> I'll come back to Peter Tizard if I can in just a moment, because he was very much my mentor. Everybody has talked about centres of excellence and how great it was to work in them. My experience in neonatology began in 1972 as a senior house officer at the Central Middlesex Hospital. I had been refused a job at my *alma mater*, Charing Cross, by Herbert Barrie<sup>187</sup> and Hugh Jolly, and I was cast out to the outer wastes of London at the Central Middlesex, which had a huge delivery rate, and a large neonatal unit and no skills. The consultant was ill at the time on the cardiac intensive unit and remained there for six months during my first job. We had nobody covering apart from a senior registrar at the Middlesex Hospital, who never came out to the Central Middlesex. The registrar was the doctor who had done the house job six months before me, and the two of us together ran the neonatal unit, and all of the paediatrics there as well. Within an hour of arriving I had to intubate a newborn baby who wasn't breathing, having never intubated a child in my life before, and within a week had to put a child on a ventilator, having never seen a neonatal ventilator before. We were rescued by the Hammersmith Hospital, who came and collected sick babies rather officiously and carted them off.

What I want to emphasize is how difficult it was to get any form of training in neonatology, unless you were in one of the very few centres, which tended to keep themselves to themselves. Having been fired-up by the experiences of meeting these chaps coming like the cavalry from the Hammersmith, I got myself a job at the Hammersmith, but unfortunately, although I applied for the neonatal one, I got the general medical one with Victor Dubowitz, so I still didn't get neonatal experience. It was Pam Davies who was then the person who helped me most and sent me off to Oxford and Peter Tizard. That really brings me to talk about Peter as somebody who worked with him and under him, rather than worked with him as a peer. He was the most incredibly supportive person of his junior staff and his trainees and would do absolutely anything to help you in any way and every ward round was intensely intellectually stimulating. I can remember one of my earliest ones there, having spent the whole night trying to keep a tiny baby alive and fiddling around with this, that and the other, to have Dawes and Tizard come round and tear you apart on basic physiology, when you know jolly well that you were struggling to keep tubes in and get catheters in and all the rest of it. But he was very encouraging of his juniors to take up research and he encouraged almost everybody to *think* research, which was very refreshing to me then and it would be today I think, because there's so much concentration now on getting Certificates of Completion of Specialist Training [CCST] rather than getting into research, and having a research element to your training. He helped all of us tremendously there.

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<sup>186</sup> Professor Richard Cooke FRCP FRCPCH FMedSci (b. 1947) was Professor of Neonatal Medicine in 1988 (Personal Chair) at the University of Liverpool and later Professor of Paediatric Medicine from 1991. He was President of the British Association of Perinatal Paediatrics, from 1990 to 1992, and has been President of the Neonatal Society since 1997.

<sup>187</sup> Dr Herbert Barrie wrote: 'We obviously made a terrible mistake.' Note on draft transcript, 5 February 2000.

That really goes on to the big obsession then, which I think takes us into this session, which was 'bleeding into the brain'. Paediatric pathology was very successful then, with very high post mortem rates, and every baby we saw on the post mortem table had a big intraventricular haemorrhage. The belief then was that all of these children were dying from intraventricular haemorrhage. So the whole push was to look at this, and the feeling was that they were bleeding because they had abnormal circulation, an abnormal flow of blood to their brain. This was a fairly popular thought at that time, it certainly was in the Oxford circle, and I think also to some extent at University College Hospital, although they had one or two other ideas. The big push was to try to identify when a haemorrhage occurred. There had been attempts at post mortem to say that children who had had a lot of bicarbonate or a lot of ventilation were more likely to have a haemorrhage, but you didn't know whether the treatment had been given after the haemorrhage or beforehand. We got involved in trying to time intraventricular haemorrhage by injecting adult blood and then at post mortem working out how much was actually in the blood clot and getting an idea whether the blood clot had occurred either before or after we gave the blood. Later on people had ideas about using other methods to look at this. Very early attempts with ultrasound were unsuccessful. I can remember in 1976 trying to use one of these huge B-scanners<sup>188</sup> which hung from a great gantry and carting a baby off into the obstetric antenatal clinic to try to ultrasound her. It wasn't until much smaller, portable high-frequency scanners came around that ultrasound began to produce some results in the very late 1970s.<sup>189</sup>

**Boyd:** Thank you very much, Richard. I think this might be the moment to move on to David Delpy and ask how it all seemed from the physics side?

**Professor David Delpy:**<sup>190</sup> From the technical point of view. I am aware that we stopped the discussion at about 1970 and that a lot of the technical aspects of the work before that time had concentrated on ventilation. As mentioned, in particular in relation to the extreme variability of the blood oxygenation and the way that it changed dramatically with just very minor ventilation settings. I think, before we talk about the brain, that there were technical developments, in terms of blood gas monitoring, which really helped throughout the period of the early 1970s. These involved first the development of catheter tip PO<sub>2</sub> electrodes and then subsequently transcutaneous oxygen and carbon dioxide electrodes by the Huchs in Marburg and Patrick Eberhard in Basle.<sup>191</sup> The University College London developments on

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<sup>188</sup> See Christie D A, Tansey E M. (eds) (2000) op. cit. note 85, pages 5–10, 21–24.

<sup>189</sup> Morgan M E, Cooke R W. (1982) Timing of neonatal cerebroventricular haemorrhage with ultrasound. *Archives of Disease in Childhood* 57: 811. Morgan M E, Hensey O J, Cooke R W. (1983) Convexity cerebral haemorrhage in the neonate: *in vivo* ultrasound diagnosis. *Archives of Disease in Childhood* 58: 814–818.

<sup>190</sup> Professor David Delpy FRS (b. 1948) has been Hamamatsu Professor of Medical Photonics, Medical Physics and Bioengineering at University College London since 1992. See Christie D A, Tansey E M. (eds) (1998) op. cit. note 31.

<sup>191</sup> Eberhard P, Mindt W, Jann F, Hammacher K. (1975) Continuous PO<sub>2</sub> monitoring in the neonate by skin electrodes. *Medical and Biological Engineering* 13: 436–442. Huch A, Huch R. (1979) The development of the transcutaneous PO<sub>2</sub> technique into a classical tool. *Birth Defects Original Article Series* 15: 5–12.

catheter-tip electrodes were largely made by my previous boss, Dawood Parker, who just, by way of an anecdote, was developing an oxygen electrode for use in cardiac bypass circuits and was collaborating with Melrose at the Hammersmith Hospital.<sup>192</sup> However, he needed a big animal on which to do the testing of this enormous electrode which was about the size of this microphone (25 x 3cm),<sup>193</sup> and Os was working on fetal lambs and therefore had the ewe lying there essentially not doing much. Dawood persuaded Os to let him put his larger electrodes into the ewe while Os was studying the brains and the lungs of the fetus, and I think it was then that Os said to Dawood, ‘Why can’t we make a smaller version of this?’<sup>194</sup> In fact, the catheter-tip electrode<sup>195</sup> came about purely because Os was prepared to try to pull together a team of both physicists, electronic engineers, physiologists and clinicians. I think somebody has mentioned the strengths of this previously, this combination of skills all coming together and in a team who were prepared to question each other, where no one was all right or all wrong. Os was great at pulling together that sort of team, and University College Hospital really buzzed because of that combination. By the end of the 1970s, as Richard says, the brain was really what we were trying to concentrate on, and we held many ‘ideas’ sessions where everybody in the team was trying to suggest ways that we could use to look at the brain. The three front-runners that came out of this brainstorming were ultrasound, which Richard has mentioned, NMR spectroscopy, and infrared spectroscopy.<sup>196</sup> Along the way there were also a number of things that never came to fruition. I don’t know how many of you remember the cerebral function monitor and the great volume of electroencephalogram (EEG) monitoring that was being carried out, which interestingly is now coming back with more sophisticated analysis techniques and returning to its rightful place of prominence. There were also attempts to monitor intracranial pressure, because we thought it might in fact be transient rises in intracranial pressure – perhaps the infant fighting the ventilator – that were causing bleeds. We were sticking little tripods like little Eiffel towers over the fontanelle to try and use tonometry to continuously measure intracranial pressure. I remember trying to glue these things on to the head – it was a nightmare. It didn’t last the course.

The other technique that was very popular, and Peter Tizard and Peter Rolfe at Oxford were leaders in doing this in the UK, was transephalic impedance, trying to monitor

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<sup>192</sup> Parker D, Delpy D, Lewis M. (1978) Catheter-tip electrode for continuous measurement of PO<sub>2</sub> and PCO<sub>2</sub>. *Medical and Biological Engineering and Computing* 16: 599–600.

<sup>193</sup> Professor Osmund Reynolds wrote: ‘It had been used for measuring the PO<sub>2</sub> of Lake Windermere.’ Note on draft transcript, 30 November 2000.

<sup>194</sup> Professor Osmund Reynolds wrote: ‘I’m not sure about this: my recollection is that the electrode had already been miniaturized by the time we put it into sheep.’ Note on draft transcript, 1 February 2000.

<sup>195</sup> See Conway M, Durbin G M, Ingram D, McIntosh N, Parker D, Reynolds E O R, Soutter L P. (1976) Continuous monitoring of arterial oxygen tension using a catheter-tip polarographic electrode in infants. *Pediatrics* 57: 244–250. Pollitzer M J, Soutter L P, Reynolds E O R, Whitehead M D. (1980) Continuous monitoring of arterial oxygen tension in infants: four years experience with an intravascular oxygen electrode. *ibid.* 65: 515–522.

<sup>196</sup> See Levene M I. (1985) The role of NMR and other techniques in neonatal imaging. *Journal of Perinatal Medicine* 13: 259–264. See also notes 31 and 85.

changes in blood flow and blood volume by looking at the electrical impedance of the brain.<sup>197</sup> Anyhow, the thing that came through to the fore was ultrasound and Roland Blackwell, who is sitting next to me, will remember that and can tell the story much better than I can. But I found it amazing that for the best part of two years people were still trying to image the brain through the side of the head and struggling because of echoes from the bone, and yet we had this hole in the top of the head which we never actually shone the ultrasound through, or never thought to shine the ultrasound through. I suspect it was because the transducers themselves were so large that the idea of trying to mount something like this over a tiny fontanelle was ruled out of court.

**Cooke:** I believe I was the first person to demonstrate that the fontanelle could be used this way, and I certainly presented the first paper on it in September in Oxford in 1979<sup>198</sup> and then came to speak to you at University College Hospital at your invitation the following week. You then published the following week in the *Lancet*.<sup>199</sup> (We just wanted to check that you'd got the same answers that we had!) The only difference was that you were still using linear array and I was using a sector scanner. With a sector scanner you can peep through a keyhole, whereas with linear array you need a bigger space to look through, but I have to concede before I claim neonatal ultrasound, that it was, in fact, Karen Pape's work in 1978 and 1979 that really laid the foundation for this.<sup>200</sup>

**Lilly Dubowitz:** I think that the EEG has been useful all along and probably shown to be useful even before infrared spectroscopy, and has remained so. The second thing is that one of the things that David Delpy forgot to mention is that MRI [magnetic resonance imaging] has been incredibly useful even in neonates to show the extent of the lesions, which one could not completely do with ultrasound.<sup>201</sup> It was the correlation of these with the clinical findings which helped us to unravel quite a lot of things later.

**Delpy:** Have we moved on from ultrasound to MR and infrared yet?

**Boyd:** Let's stick with ultrasound for a little bit longer, because Osmund is passionate to make a comment.

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<sup>197</sup> Costeloe K, Smyth D P, Murdoch N, Rolfe P, Tizard J P. (1984) A comparison between electrical impedance and strain gauge plethysmography for the study of cerebral blood flow in the newborn. *Pediatric Research* 18: 290–295.

<sup>198</sup> See Rolfe P. (ed.) (1979) *Non Invasive Physiological Measurements*, vol. 2. London, New York, San Francisco: Academic Press. Cooke R W I. (1980) Diagnosis of periventricular haemorrhage by real time two dimensional sector scanning, in Rolfe P. (ed.) *Fetal and Neonatal Physiological Measurements*. Bath: Pitman, 344–355.

<sup>199</sup> Professor Osmund Reynolds wrote: 'This is not quite right. The University College Hospital letter to the *Lancet* [Lipscomb A P, Blackwell R J, Reynolds E O R, Thorburn R J, Cusick G, Pape K E. (1979) Ultrasound scanning of brain through anterior fontanelle of newborn infants. *Lancet* ii: 39], which included an image of a fontanelle scan, was published on 7 July 1979, alongside a letter from Richard which described his experience with fontanelle scanning [Cooke R W. (1979) Ultrasound examination of neonatal heads. *Lancet* ii: 38].' Note on draft transcript, 1 February 2000.

<sup>200</sup> Pape K E, Blackwell R J, Cusick G, Sherwood A, Houang M T W, Thorburn R J, Reynolds E O R. (1979) Ultrasound detection of brain damage in preterm infants. *Lancet* i: 1261–1264.

<sup>201</sup> See Christie D, Tansey E M. (eds) (1998) op. cit. note 31.

**Reynolds:** I wanted to say first, the reason why on earth did we need to go to such an extent for noninvasive investigation of the brain? The reason was to do with what the follow up was throwing up. Roughly speaking it turned out in the 1970s and 1980s that of less than 33-week gestation babies, over 80 per cent were doing well, up to 10 per cent were doing badly, and then there was a group in between.<sup>202</sup> Many other people were getting similar results.<sup>203</sup> The question was what was causing the trouble in those who were impaired and what could we do to prevent it, as well as prevent death. As David [Delpy] has said, Roland [Blackwell] had been in and out of the unit since the mid-1970s saying he thought that we were going to get a picture with ultrasound and Karen Pape came as a research fellow from the Hospital for Sick Children in Toronto. For logistical reasons, she couldn't come to us for a year, and went off very fortunately to work with Jonathan Wigglesworth who taught her the way around the brain. They wrote that wonderful book on haemorrhage and ischaemia in the neonatal brain at that time,<sup>204</sup> and then she moved over to us. Roland, who was masterminding all this from the physics point of view, will say something about this in a minute, but she led the clinical aspects of that study. We'd in fact set up three possible ways of looking at the brain which she could follow. We'd got transcephalic impedance, which of course is coming back now, and Doppler of the cerebral vessels, but also ultrasound, and she took that up and ran with it. The first paper was in 1979 in the *Lancet*,<sup>205</sup> where we said we could see intraventricular haemorrhage, ventricular dilatation, loss of brain tissue, but David is right about the fontanelle. We were trying to do the same cuts of the brain going up and down as for computerized tomography and transversely as well.

It was several months before we discovered the fontanelle, in early 1979, which shows how slow on the uptake one can be, and I have to say I can't remember the visit that Richard [Cooke] was talking about, who was clearly doing it all at the same time although we didn't know this. We were going round one Sunday morning and it was Tony Lipscomb (who sadly can't be here today) who put the probe on the top of the baby's head, and there was this wonderful picture of the brain. Because we used a 5-MHz probe, the image went right down through the brain, so you could see the third and fourth ventricles. We had, by chance, chosen an extremely suitable baby to do this on, because he had got a rather dilated ventricular system, but I am very aware that Richard was doing all this in Rotterdam at the same time. [**Cooke:** My images were actually published in 1980, because they are in the Proceedings].<sup>206</sup>

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<sup>202</sup> Stewart A L, Reynolds E O R, Hope P L, Hamilton P A, Baudin J, Costello A M de L, Bradford B C, Wyatt J S. (1987) Probability of neurodevelopmental disorders estimated from ultrasound appearance of brain in very preterm infants. *Developmental Medicine and Child Neurology* 29: 3–11.

<sup>203</sup> See Stewart A L, Reynolds E O R, Lipscomb A P. (1981) op. cit. note 175.

<sup>204</sup> Pape K E, Wigglesworth J S. (1979) *Haemorrhage, Ischaemia and the Perinatal Brain*. *Clinics in developmental medicine*, nos 69/70. London: Spastics International Medical Publications, Heinemann Medical Books.

<sup>205</sup> op. cit. note 200.

<sup>206</sup> op. cit. note 198.

**Professor Roland Blackwell:**<sup>207</sup> The reason we were scanning transversely was that we weren't primarily interested, at the time, in neonatal brains. Having obtained this brand new machine we were more interested in obstetric work. We suddenly discovered that we could see a great deal more detail in the fetal brain than ever before but we didn't know what we were looking at. So we went along to the neonatal department, and of course they were interested and we had a go at scanning the neonatal head.

Originally, and this would have been the beginning of 1978, we used a water stand-off between the probe and the head<sup>208</sup> because it was quite clear, as Richard said, you have got these long flat probes scanning a baby's curved head. We needed a stand-off to maintain the contact. We first filled a rubber glove with water for the purpose. It wobbled all over the place and was absolutely hopeless. We then made a small plastic tank with a polythene sheet as the base, which we rested on the baby's head and scanned through that. This was more stable but the nurses complained that we were drowning the babies when we tried to get this thing out of the incubator, so we abandoned it!

Later on, at the time that Karen Pape was there, we went back and tried contact scanning with plenty of contact gel and it all worked.<sup>209</sup> Karen was so excited, she was just ecstatic with the detail she could see, and from then on it all took off. I would have to say that Karen was the driver. It was incidental that we had gone back for a different purpose and suddenly we saw that this was just what was needed in the unit.

And off it went. We did a series of 35 babies, and published in the *Lancet* in June 1979.<sup>210</sup> Richard published his letter three weeks later in the *Lancet*, saying they had been scanning through the fontanelle. By the time of publication, as Os has said, so had Tony Lipscomb, and in July 1979 he published his letter in the same issue on scanning through the fontanelle.<sup>211</sup> Richard clearly had a much better machine for scanning through the fontanelle.

We were using a 5-MHz linear array, which was chunky, and difficult to get good contact, so it needed a lot of gel, but we were managing to scan through the fontanelle providing it was big enough. Scans were not particularly good through a small fontanelle but, if it was an inch or so across, then it worked well.

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<sup>207</sup> Professor Roland Blackwell FIEE FInstP FIPeM (b. 1943) has been at University College Hospital, London, since 1966 and is currently Head of the NHS Department of Medical Physics and Bioengineering. He was asked to evaluate the first commercially available ultrasound scanner and assisted in the development of many of the techniques that are now in routine use. As well as working in diagnostic ultrasound he also ran the department's Instrumentation Section, developing fetal monitoring, neonatal transthalamic impedance and intracranial pressure monitoring.

<sup>208</sup> The method is described in op. cit. note 85, pages 5, 17–19.

<sup>209</sup> op. cit. note 85, page 60.

<sup>210</sup> See Pape K E, Blackwell R J, Cusick G, Sherwood A, Houang M T W, Thorburn R J, Reynolds E O R. (1979) op. cit. note 200.

<sup>211</sup> Lipscomb A P, Blackwell R J, Reynolds E O R, Thorburn R J, Cusick G, Pape K E. (1979) op. cit. note 199.

The technique then flowed and, of course, it is still flowing. Ultrasound machines are getting astonishingly good because they now use very, very high frequencies compared with what we were able to use then, and enable visualization of much finer detail.<sup>212</sup>

**Victor Dubowitz:** I wanted to take the historical record one little step back, because I think the first window on the brain was really the CT scan. Papile had got ethical permission somehow to scan a large number of premature babies and what came out of that, which I think is very important, was that there were a lot of apparently well babies, who had big haemorrhages in their brains that she picked up on the computerized tomography (CT) brain scan.<sup>213</sup> That was a great source of inspiration to us subsequently to set up a study which I will mention in a bit more detail later. We were very fortunate at the Hammersmith in those days, because we were probably one of the few centres in the world that didn't have a CT scanner, so we were able to by-pass that completely, and go straight into ultrasound, which then became routine on our newborn unit and enabled us to apply it as a tool after University College Hospital and previously Richard Cooke had already identified it.

**Wigglesworth:** I was going to bring up the same point that Victor made. The reason that the Americans commenced using the CT scanner initially was related to the high cost of neonatal intensive care in the USA. At the time when, as Richard Cooke was saying, we assumed that the diagnosis of intraventricular haemorrhage was fatal, it was considered in some American units that a CT diagnosis of intraventricular haemorrhage would justify turning off ventilators in babies. I think that there must be an important message in that. Then when Papile showed that many apparently healthy preterm neonates had large haemorrhages there was a bit of a 'shock horror' reaction! Of course, in Britain in any case we didn't use CT scanners for newborn babies: we were still very worried about the radiation and all sorts of things, apart from not having the scanners! That was the background. So, as soon as ultrasound scanning was introduced it ushered in a totally new world and made the neonatologists start to concentrate on the brain, as they could now see what was happening in it, whereas previously the sight of the brain was the prerogative of people like me in post mortem rooms.

**Boyd:** David, you moved on to other imaging and monitoring notions.

**Delpy:** Other monitoring? As I previously said, the two other techniques that we had identified were NMR and infrared spectroscopy. Now NMR, we'd in fact looked at back around 1973, but not for imaging, but because Moon and Richards had published a paper showing they could measure pH in blood and also 2,3, DPG levels,

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<sup>212</sup> op. cit. note 85, for example, pages 48–49.

<sup>213</sup> Burstein J, Papile L A, Burstein R. (1979) Intraventricular hemorrhage and hydrocephalus in premature newborns: a prospective study with CT. *American Journal of Roentgenology* 132: 631–635.



by using phosphorus NMR.<sup>214</sup> So we'd had this rather impractical idea of having a little magnet that a baby's finger could be pushed into. However, we were again lucky because Doug Wilkie<sup>215</sup> was also at University College London and he, David Hoult, David Gadian and George Radda, in about 1974, had started looking at whole muscle, rat muscle, in NMR magnets. By the late 1970s, Doug Wilkie together with Joan Dawson, was aiming to use a 20-cm bore magnet to look at the arm during exercise.<sup>216</sup> So Os and Dawood Parker, my previous boss, talked to them, saying essentially, 'Look if you can get an arm in the magnet, we can get a baby in'. I remember that we applied to the Wolfson Foundation under its new Zuckerman initiative scheme to try to get an NMR magnet, as well as some funding for infrared equipment. In fact, they funded the infrared, but they didn't fund the NMR; probably because that was about £150 000 worth of magnet at the time.<sup>217</sup> So, we decided that if we were going to put in another, but this time successful, grant application, we had to get some preliminary data. So we did a series of six rabbit-brain studies up at Oxford Research Systems in Oxford, which involved dragging all of our monitoring equipment and animals at the crack of dawn all the way up to Oxford, and on one occasion staying the night in Os's cottage at Ginge. However, on the back of those animal studies, which we published in *Pediatrics*,<sup>218</sup> we were successful in getting the funding for an NMR magnet. Now the idea really was to go for spectroscopy, to look at brain metabolism. I think we thought that imaging was going to be so slow that we'd never be able to hold the infants sufficiently still to get good-quality images. Ultrasound was going to give us the imaging, and phosphorus spectroscopy was going to tell us about the brain metabolism.

Anyhow, in 1982, we did our first study using the magnet provided by the Wellcome Trust, the Muscular Dystrophy Group and Action Research,<sup>219</sup> and the special Trustees of University College Hospital. We had a baby come into the neonatal unit that had a suspected unilateral lesion, so we could compare one side of the brain with the other, because we didn't know what we were going to see. We knew what we saw in a rabbit,

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<sup>214</sup> Moon R B, Richards J H. (1973) Determination of intracellular pH by <sup>31</sup>P magnetic resonance. *Journal of Biological Chemistry* 248: 7276–7278. Professor David Delpy wrote: '2,3, DPG (2,3-diphosphoglycerate) is found at high levels in red blood cells (around 5mM) and affects the oxygen-binding capacity of the haemoglobin.' Note on draft transcript, 10 December 2000.

<sup>215</sup> Professor Douglas Wilkie FRS (1922–1998) held a Personal Chair in Experimental Physiology at University College London from 1965 to 1969, and was Jodrell Professor of Physiology and Head of the Physiology Department, from 1969 to 1979, then Jodrell Research Professor of Physiology (Emeritus), University of London, from 1979 to 1988. He married June Hill (see note 30) in 1949. See Woledge R. (1998) Professor D R Wilkie. *The Independent*, page 6.

<sup>216</sup> See, for example, Dawson M J, Gadian D G, Wilkie D R. (1978) Muscular fatigue investigated by phosphorus nuclear magnetic resonance. *Nature* 274: 861–866. See also op. cit. note 31.

<sup>217</sup> Professor Osmund Reynolds wrote: 'This eventually cost £250 000.' Note on draft transcript, 1 February 2000.

<sup>218</sup> Delpy D T, Gordon R E, Hope P L, Parker D, Reynolds E O R, Whitehead M D. (1982) Noninvasive detection of cerebral ischaemia by phosphorus nuclear magnetic resonance. *Pediatrics* 70: 310–311.

<sup>219</sup> Action Research [formerly known as Action Research for the Crippled Child (see page 59)] was founded in 1952 in the UK and supported the pioneers of ultrasound scanning. It has also been involved in the development of the British polio vaccine and rubella vaccine.

but we turned out to have chosen the right baby at the right time and Os managed to persuade the parents to agree to the study. From that flowed our knowledge, of secondary energy failure and that the brain metabolism is not necessarily destroyed by an acute asphyxial episode, but that there is a cascade of effects that are triggered by the acute insult.<sup>220</sup> Obviously there is a whole range of people here who can talk more about the way the NMR has developed, and in particular the Dubowitzs and David Edwards can talk about the imaging, but if I can, I will just complete the University College London side of the story. The original Wolfson Foundation application had been for NMR and for infrared. Infrared had been originally described by Franz Jobsis in 1977, who, in a *Science* paper showed he could trans-illuminate a cat head of about 4.5cm diameter.<sup>221</sup> Dawood Parker and Linda Soutter, who was a scientist working with us at the time (and had previously done a lot of work on the intravascular oxygen electrode),<sup>222</sup> met Franz the following year at a meeting in Nijmegen, and he said, ‘I am getting my infrared instrument made commercially by Edwards Laboratories, do you want to be involved in trying to use it on babies?’ And we said, ‘Yes, great, we will be one of the clinical centres’. So for two years we waited for this instrument to arrive from America, but it didn’t. They didn’t come through with the goods, and so in the end we put together an application to the Wolfson Foundation to build our own. We got it funded and I got a very good research worker, Mark Cope, to join us and he built what became the infrared system marketed by Hamamatsu Photonics, but that was developed here at University College London. The grant award was part of the Zuckerman initiative,<sup>223</sup> and just as an aside, and as an indication of the way British industry has consistently missed out on good ideas, it was a requirement that we have an industrial backer for Zuckerman funding and our industrial backer was Vickers

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<sup>220</sup> Cady E B, Costello A M de L, Dawson M J, Delpy D T, Hope P L, Reynolds E O R, Tofts P S, Wilkie D R. (1983) Noninvasive investigation of cerebral metabolism in newborn infants by phosphorus nuclear magnetic resonance spectroscopy. *Lancet* i: 1059–1062. Hope P L, Costello A M de L, Cady E B, Delpy D T, Tofts P S, Chu A, Hamilton P A, Reynolds E O R, Wilkie D R. (1984) Cerebral energy metabolism studied with phosphorus NMR spectroscopy in normal and birth-asphyxiated infants. *ibid.* ii: 366–370.

<sup>221</sup> Jobsis F F. (1977) Noninvasive, infrared monitoring of cerebral and myocardial oxygen sufficiency and circulatory parameters. *Science* **198**: 1264–1267.

<sup>222</sup> *op. cit.* note 195.

<sup>223</sup> Professor David Delpy wrote: ‘My recollection was that Lord Zuckerman chaired a committee that produced a report to the Government (in about 1980), which essentially said that universities needed to work much more closely with industry to transfer academic ideas into commercial products. The Wolfson Foundation took this up by announcing a grant award scheme (chaired by Lord Zuckerman) [The Wolfson Technological Projects Scheme] which required the university applicants to have industrial partners involved with the application. In general, the idea was that the Wolfson would fund the first two or three years of a programme, with the industrial partners taking this over as the ideas successfully completed the laboratory phase of their development. My ex Head of Group, Professor D Parker, submitted an application for the development of the NIR spectrometer with Vickers Medical Ltd as the industrial partner. The grant was awarded (Wolfson Reference Z/81/21) for three years, but during this period, Vickers Medical decided they did not want to take up the development, so we had to find an alternative industrial partner, and Hamamatsu Photonics stepped in.’ E-mail to Dr Daphne Christie, 17 January 2001. A copy of a letter from Mr Paul Ramsbottom, Assistant Executive Secretary of the Wolfson Foundation, London, to Dr Daphne Christie, dated 29 January 2001, which provides some information about the scheme, will be deposited with the records of this meeting in Archives and Manuscripts, Wellcome Library, London. See Rotherham L. (1984) *Research and Innovation. A record of the Wolfson Technological Projects Scheme 1968–1981*. Oxford: Clarendon Press.

Medical. Under the Zuckerman initiative, Wolfson provided the first two years of funding and the industrial partner was supposed to take up the third year and then market the device. At the end of the first two years, Vickers Medical pulled out and said that it was too much of a 'blue sky' development since there would be no product within a year. So as a result, our infrared spectroscopy developments went over to the Japanese.

**Boyd:** They have given up the Rolls Royce as well! Thank you very much, David, that's very interesting. You mention several people. Pat, do you want to come in? What's your perspective?

**Dr Patricia Hamilton:**<sup>224</sup> I arrived at University College Hospital in 1983 when they had just done the rabbit work and were starting the babies, and it was a terribly exciting time, because it was clear this technique (MRS) was going to work. It was looking at the condition of birth asphyxia where previously we had just sat and supported the baby and wondered if we were doing the right thing or not. So it was very exciting to be involved in this, and to be involved in taking the babies down to the magnet. I would like to pay tribute to the Physics Department at University College London. We had these amazing pieces of equipment, the transport incubator was specially designed, because, of course, everyone said you can't put a baby in the magnet, they disappear entirely into the bore of the magnet, how are you going to monitor them with nonmetallic means? And all these questions were solved by that department. And the first near-infrared spectrophotometer was about the size of a wardrobe, it looked as if it was built with Meccano and so on, but it worked. It was all terribly exciting, particularly the NMR spectroscopy because you could see this spectrum gradually being accumulated, and you could see that the technique was working and that it was going to start to answer the questions we had asked of it.

**Reynolds:** I want to focus our attention back on why we needed these big machines. First, we knew that haemorrhage and ischaemia were the two major perinatal insults to the brain, but we knew that from CT and from what Jonathan Wigglesworth had been showing. Ultrasound was extremely good at showing us haemorrhages, so we followed everybody up, and discovered it was only the big ones in brain tissue and those that caused a block, leading to hydrocephalus, that caused trouble.<sup>225</sup> Follow up showed that the other haemorrhages went away and didn't leave any notable or possibly any sequelae at all, so all those guys who had been switching off ventilators because of the CT showing small haemorrhages, as I think Jonathan has already said, had something to think about. But of course the problem was that the follow up then revealed, ours and

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<sup>224</sup> Dr Patricia Hamilton FRCP FRCPCH (b. 1951) worked as Senior House Officer on Professor (then Dr) Dunn's Neonatal Unit. She subsequently completed a two-year neonatal fellowship in Vancouver and worked at University College Hospital, London, from 1983 to 1987. She was involved in work on magnetic resonance spectroscopy (MRS) and near-infrared spectrophotometry and in follow-up studies of preterm babies. She is now Consultant Neonatologist at St George's Hospital, London, and Honorary Secretary of the Royal College of Paediatrics and Child Health in London.

<sup>225</sup> See, for example, Thorburn R J, Lipscomb A P, Stewart A L, Reynolds E O R. (1981) Prediction of death and major handicap in very preterm infants by brain ultrasound. *Lancet* i: 1119–1121. See also op. cit. note 202.

everybody else's, that it wasn't haemorrhage that was the major cause of trouble – it was jolly common, but most haemorrhages went away – it was the ischaemic lesions. So the reason why we sat down with our medical physics colleagues and people in physiology and anatomy and all around the place, was to see if we could find noninvasive ways of getting at cerebral ischaemic lesions early enough to be able to do something about them. Because you couldn't see them early on, of course, with ultrasound, and that's why we went for magnetic resonance spectroscopy and discovered this business of secondary energy failure, which is important, because it can be modelled in animals, and you can try preventive strategies and apply them back to the baby. For example, mild hypothermia is rather effective, whereas magnesium doesn't seem to work at all,<sup>226</sup> which was contrary to accepted wisdom at the time. And that's also why we went for the near infrared;<sup>227</sup> these were noninvasive ways of looking at the antecedents and prognostic significance of ischaemic lesions in the brain, and of testing out preventive strategies.<sup>228</sup>

**Lilly Dubowitz:** It's very interesting, because these things sort of went hand in hand. The spectroscopy beautifully showed up the physiological changes. The first neonatal MRI on a child with a large haemorrhagic infarction was done at the Hammersmith in 1983. The beauty and advantage of MRI was that you then could follow the brain development by using the same technique for follow up. For instance, the surprise was that in a large haemorrhage, the myelination was not at all disturbed, or only slightly around the lesion, while with an infarct, or particularly with periventricular leucomalacia, the myelination was completely disrupted and this gave some of the explanations why children with haemorrhage developed relatively well, while the children with leucomalacia did relatively badly.

**Cooke:** Could I take a slightly different angle and come slightly nearer the end of the 1990s? I think one of the most important things that we have begun to realize is that lots of different units are doing different things, sometimes reinventing the wheel, and that the dissemination of information produced has not always been as good as it

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<sup>226</sup> Thoresen M, Penrice J, Lorek A, Cady E B, Wylezinska M, Kirkbride V, Cooper C E, Brown G C, Edwards A D, Wyatt J S, Reynolds E O R. (1995) Mild hypothermia following severe transient hypoxia-ischaemia ameliorates delayed cerebral energy failure in the newborn piglet. *Pediatric Research* 37: 667–670. Penrice J, Amess P M, Punwani S, Wylezinska M, Tyszczyk L, D'Souza P, Edwards A D, Cady E B, Wyatt J S, Reynolds E O R. (1997) Magnesium sulphate after transient hypoxia-ischaemia fails to prevent delayed cerebral energy failure in the newborn piglet. *ibid.* 41: 1–4.

<sup>227</sup> Wyatt J S, Cope M, Delpy D T, Wray S, Reynolds E O R. (1986) Quantitation of cerebral oxygenation and haemodynamics by near-infrared spectroscopy. *Lancet* ii: 1063–1066.

<sup>228</sup> Professor Osmund Reynolds wrote: 'One of the most important aspects of ultrasound and magnetic resonance spectroscopy was that they helped provide a good idea about prognosis in individual babies. See, for example, *op. cit.* note 202. See also Azzopardi D, Wyatt J S, Cady E B, Delpy D T, Baudin J, Stewart A L, Hope P L, Hamilton P A, Reynolds E O R. (1989) Prognosis of newborn infants with hypoxic-ischaemic brain injury assessed by phosphorus magnetic resonance spectroscopy. *Pediatric Research* 25: 445–451. Reynolds O. (1996) Causes and outcome of perinatal brain injury, in Magnusson D. (ed.) *The Lifespan Development of Individuals* (Nobel Symposium). Cambridge: Cambridge University Press, 52–75. In the majority, in whom the prognostic indicators were good, one could be reasonably reassuring to the parents, but when they were bad – for example, large haemorrhages or severe energy failure – one could discuss with parents how far intensive care should or should not be pursued.' Letter to Dr Daphne Christie, 1 February 2000.

should be, or the understanding of it. The best example of this was in the use of antenatal steroids, which has probably contributed more than anything else, except perhaps mechanical ventilation. In 1972 it was quite conclusively shown that antenatal steroids in preterm mothers produced a dramatic improvement in the outcome of those babies subsequently born preterm.<sup>229</sup> Although numerous small studies were done following that, because New Zealand was considered to be a rather primitive backwater and didn't have ventilation and so on, this was thought nonapplicable to our own situation. There was a very poor take up of antenatal steroid use through the 1970s and 1980s and it was only with the introduction of systematic review of information available from clinical trials that a sufficiently convincing picture could be put forward so that the use of antenatal steroids became very widespread and almost routine in this country in preterm labours. The effect of antenatal steroids is far larger than most of the other effects of all the great discoveries that people have been talking about today, and has done far more for everyday neonatology than any of the clever things we can do by looking into brains. It really has.<sup>230</sup>

And second to that, I suppose, comes the whole surfactant story, the earlier part of which was alluded to, but really nothing happened until people started doing controlled clinical trials. I think the introduction of the controlled clinical trial has been one of the greatest breakthroughs over the last 20 years or so. Neonatology has moved from doing interesting things in lambs, and extrapolating them to sick babies, to doing appropriate studies in sick infants with controls. That is one of the most important developments we have had and I think it has been ignored.

**Gamsu:** Just a small correction to what Richard [Cooke] has just said. It wasn't in any sense disparagement of New Zealand's paediatrics that led to other trials being done. It was just a feeling that for such an important subject, more than one trial should be done. And, of course, we did mount a multicentre trial in this country,<sup>231</sup> which became part of the meta-analysis of many trials, which contributed to our understanding of the effect of steroids. But it wasn't done in the spirit of disparaging New Zealand paediatrics.

**Cooke:** The point I wanted to make was that the original trial was reasonably powered and actually showed a convincing result. Most of the subsequent trials were underpowered and unable to show that convincing a result. They were all over the place and only when they were put in a meta-analysis and a systematic review, could an extremely powerful argument be made. Even then, it took five years for the Royal College of Obstetricians and Gynaecologists to issue a one-sentence instruction to

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<sup>229</sup> Liggins G C, Howie R N. (1972) A controlled trial of antepartum glucocorticoid treatment for the prevention of the respiratory distress syndrome in premature infants. *Pediatrics* 50: 515–525.

<sup>230</sup> Avery M E. (1995) Historical overview of antenatal steroid use. *Pediatrics* 95: 133–135.

<sup>231</sup> Gamsu H R, Mullinger B M, Donnai P, Dash C H. (1989) Antenatal administration of betamethasone to prevent respiratory distress syndrome in preterm infants: report of a UK multicentre trial. *British Journal of Obstetrics and Gynaecology* 96: 401–410. Crowley P. (2000) Prophylactic corticosteroids for preterm birth (Cochrane Review), in *The Cochrane Library*, issue 4. Oxford: Update Software.

their members to say perhaps it's a good idea to think about steroids and it wasn't until the mid-1990s that the recommendation guideline came.<sup>232</sup>

**Reynolds:** I agree with what you say about steroids, but one of the reasons people didn't take them up initially, I think, was because of evidence at that time from Dobbing and others which said they reduced the number of adult brain cells in the rat.<sup>233</sup> I am not, of course, saying they shouldn't be used, because they are obviously doing wonderful things, but some important endocrinologists say that there may be trouble in later life, conceivably premature ageing, which is what happens in certain animal species. One has got to have it at the back of one's head that these things can happen. As I say, there is just a slight frisson there.

**Gamsu:** That point, of course, bedevils all neonatal research – the problem of taking the long view about what we do. I do think that we should try to take the long view of our actions, but I don't think we should anticipate the worst. [**Reynolds:** No. I quite agree, I wasn't saying one shouldn't use them, I was just saying one has got to be aware of these things]. But it does emphasize the need to do properly controlled trials, with proper follow up and there has perhaps been more study of the use of steroids and follow up of children who have been given steroids, than almost any other treatment in neonatology.

**Victor Dubowitz:** I wanted to bring up one aspect in relation to the imaging and other technology and the controlled studies again, as it's important. There's often a tendency for the technology to be an end in itself but we'd always looked upon the technology as a good tool in a sense for honing up our clinical acumen and clinical abilities. One of the early studies we set up – I think it was about 1979, when Malcolm Levene was with us – was to do a prospective blind controlled study, of ultrasound versus clinical assessment.<sup>234</sup> He did all the ultrasound imaging and Lilly independently did the clinical assessment, and neither communicated with each other or with the neonatal unit, which was a bit of an ethical problem, but we didn't want to start influencing the management of the children just on the basis of what was seen on the ultrasound. It was only after 100 cases in fact, and after the code was broken, that they compared their data. We then found that certain predictive things at a clinical level that would be useful, and I think there's been this ongoing approach, with many different aspects and modalities of technology, in parallel with clinical assessment.

**Alberman:** Can I come to what I think is one of the most topical questions that has been raised by the imaging possibilities, and that is the argument that has largely been brought up by litigation, namely the timing of the actual injury? My impression is that

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<sup>232</sup> The Royal College of Obstetricians and Gynaecologists. (1996) *Antenatal Corticosteroids to Prevent Respiratory Distress Syndrome*, Guideline no. 7. London: The Royal College of Obstetricians and Gynaecologists.

<sup>233</sup> See De Souza S W, Adlard B P. (1973) Growth of suckling rats after treatment with dexamethasone or cortisol. Implications for steroid therapy in human infants. *Archives of Disease in Childhood* 48: 519–522. Dobbing J, Sands J. (1973) Quantitative growth and development of human brain. *ibid.* 48: 757–767.

<sup>234</sup> Dubowitz L M, Levene M I, Morante A, Palmer P, Dubowitz V. (1981) Neurologic signs in neonatal intraventricular hemorrhage: a correlation with real-time ultrasound. *Journal of Pediatrics* 99: 127–133.

although we are now able to time some injuries, there is still a lot of doubt about others, and it is, of course, a very critical question when it comes either to litigation or to efforts made to keep these children alive, assuming that all the damage was done early on and that you don't add to it during the neonatal period.

**Hull:** Can I put a historical twist on that?

**Boyd:** Yes, if you put a historical twist, it's then admissible.

**Hull:** I remember, I think I may have been Secretary of the Neonatal Society at the time, that Action Research<sup>235</sup> asked us to organize a conference, and it was held in the Royal College of Obstetrics and Gynaecology in about 1972. It dealt with the causes of the main disabilities, cerebral palsy, mental retardation, blindness and deafness and was interdisciplinary; it had neonatologists, paediatricians, obstetricians and geneticists, and the idea was to channel Action Research money to support paediatric research, particularly in the neonatal area, and possibly some obstetric research. What came out from the papers of that conference was that by far the largest proportion of those disabling conditions were essentially nothing to do with what happened during labour or delivery or in the newborn period, and a great deal more to do with the genetics and other environmental factors, and Action Research then decided not to publish the papers. Obstetricians and neonatologists have had a lot of money over the past because they believed they were going to avoid these terrible conditions, but they are not responsible for a major fraction of them.

**Boyd:** I think I am hearing a bit of a subtheme, what I might call the Luddite subtheme. I wouldn't disagree with it, from Richard Cooke and now from you, David, that actually some of the excitements we have been discussing this afternoon, are a little bit off the side from the bulk of the population. Is that what you are saying?

**Fairweather:** This gives me a chance to put an oar in again, because in my time at Aberdeen in the late 1950s the work that Dugald Baird put me on to with Raymond Illsley – and which we published – was a study of the obstetric and social origins of mental and physical handicap.<sup>236</sup> This came about because Baird felt that a lot was being attributed to what was happening to the fetus in the course of pregnancy or during labour and delivery. He wanted to find out whether problems identified in the infant later were related to obstetric complications or management. So this idea about the origins of damage or disability again stems partly from the initiatives that Baird took to set up multidisciplinary studies.

**Reynolds:** Coming back at David [Hull] isn't the right way of putting it, but, of course, it is accepted that the vast majority of disabled infants are disabled largely

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<sup>235</sup> See note 219.

<sup>236</sup> Fairweather D, Illsley R. (1960) Obstetric and social origins of mentally handicapped children. *British Journal of Preventive and Social Medicine* 14: 149–159.

because of genetic influences. But, if you are dealing with small, ill babies, who are surviving in ever-increasing numbers, with a high risk of haemorrhage and ischaemic lesions in their heads, you had better do your absolute damned best to understand why those lesions are caused and prevent them in so far as it is possible. I think, on the whole, people in this field have been reasonably successful in that the vast majority of surviving infants coming out of intensive care units are normal infants. A much smaller proportion are not, but that smaller proportion has remained reasonably constant. So the main gain is a big increase in normal infants. One has got to keep the proportion of damaged ones as small as one possibly can, and that's why we need all these things like head imaging and all that,<sup>237</sup> but that's a different argument from saying that in the community at large the majority of disabled children are disabled for genetic reasons.

**Lilly Dubowitz:** I think one of the problems has been that one always wanted to associate birth asphyxia and its consequences with only one event. What is really happening at the moment, that when we are able to time the event, the ischaemic damage does occur around the time of delivery, but there are antecedent events which will define which of the children are going to be susceptible and which are not. The causes are therefore multiple and not single.

**Boyd:** I think we should, in a moment, move on to our final issue, which is the development of neonatology in the wider NHS in the 1980s and 1990s, but just before doing so, there may be topics that we haven't picked up on that people feel we should pick up on. I am particularly conscious of the nutritional aspect and Pam [Davies], that's something you might like to think about, whether you want to say anything about that. Are there other topics people think we should pick up?

**Booth:** I think for the historians it would be very interesting to hear something about the way in which research in this field has been supported, whether or not the Medical Research Council took it on board early on, was it supportive? I happen to know that Tizard's work, for example, was largely supported, I think, by Nuffield, and by Action Research for the Crippled Child.<sup>238</sup> What were the funding bodies and was the funding adequate? Did you have to fight very hard for it, and did you line up people from other disciplines to support you in your work?

**Boyd:** Thank you very much, that's an important issue. I think what we will do is we will go into the business of developing neonatology and I will come back to those two points, when people have had a chance to reflect on them. And David, I think you kindly agreed to think about the wider NHS.

**Hull:** We have heard that by the beginning of the 1980s neonatal medicine was well advanced. We knew what was needed to create a sympathetic environment with warmth, comfort, safety, protection from infection, minimal handling, within the

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<sup>237</sup> See note 228.

<sup>238</sup> Later known as Action Research (see note 219).



family setting, with family involvement. We appreciated the need to replace the functions of the placenta as soon as possible with early feeding down a plastic tube into the stomach if necessary, supplemented with intravenous nutrition if required. We knew to monitor and address metabolic fluctuations, glucose, electrolytes, bilirubin, and the need to monitor the safe delivery of oxygen. Success increasingly depended on initiating the premature functioning of the bowel and the lungs, and that was critical to survival, but to do it often caused harm to gain the benefit. With this sensitive care, more and more premature babies survived.

I agree with Ross [Mitchell] that it was the demonstration that they could survive that made it clear to all that far more babies might survive if quality care was more generally applied. The interests of the babies were addressed. Before birth with steroids, during delivery with the mode of delivery, and immediately after birth the babies were taken instantly into a more sympathetic setting. I think this realization, possibly more than anything else, led to the increasing survival. Potentially viable infants were arriving in the nursery in much better shape. That was in the beginning of the 1980s. If we look at Figure 1 [page 38], that was when the larger premature babies survival rate was improving impressively. The concern at the beginning of the 1980s was that not all infants in the UK, who would benefit from this care, were actually having it. The position roughly stated at the beginning of the 1980s was that most maternity units in the UK had special nurseries, with incubators, they could give tube feeds, they could apply phototherapy, and therefore they could, to some extent, meet the needs of most small babies. Only a few units, mainly in university regional centres, were well equipped and had experienced nurses and doctors.

With the reports of the successes, the clinicians who were responsible for the special nurseries in district general hospitals, saw the need to expand their services, and therefore a lot of new special-care baby units were built in maternity units in general district hospitals. But the clinicians still needed to transfer babies for some neonatal *intensive* care, that is, those requiring prolonged ventilation or surgery, to the regional centres. As I understand it, the regional centres were initially funded out of hospital budgets, but by the 1980s the Government had recognized the need for special funding, and it set up a tertiary regional service. Neonatal care is expensive and it is demanding on nursing and medical time and needs a lot of expensive equipment. In the current language, they were high-cost, low-volume, services. And over the 1980s the supply never met the need.<sup>239</sup> Often there was no room at the inn, babies were not getting in and it was a cause of public concern.

One of the reasons for this was the increasing demand for neonatal intensive care over the 1980s. I would be interested in what other people have to say, but I think there were two main reasons. The first was developments in the management of respiratory

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<sup>239</sup> Professor Osmund Reynolds wrote: 'The problem began quite early in the 1970s and provided the major stimulus for the House of Commons Select Committee Enquiry (see page 63).' Note on draft transcript, 1 February 2000. See also *op. cit.* note 56.

failure, with better monitoring, better ventilator systems, the use of surfactant and the use of prenatal steroids. Thirty-four per cent of 32-week infants require ventilation; that's from a population study in 1990–95. The second was the realization that some of the very immature babies previously considered not to be viable under 28 weeks' gestation also survived if they were ventilated. In this group 95 per cent required ventilation, and they required it for 19–20 days on average and that introduced a considerable demand.<sup>240</sup> They survived not only because of ventilation, but because extra fluids were given to match the high transepidermal water loss.

The Royal College of Physicians had a working party, on which some of you served. It reported in 1988, and advocated that neonatal intensive care should take place in regional centres.<sup>241</sup> But in 1990 the NHS management arrangements were changed and regional services were to go. That meant that the neonatal intensive care services were no longer going to be supported on regional funds. On behalf of the independent body that was set up then – the Clinical Standards Advisory Group (CSAG) – David Field and I were asked to look at the impact of the new management arrangement on neonatal intensive care.<sup>242</sup> We asked the Purchasing Authorities about their services. Many of them did not know if they had, or where they obtained, neonatal intensive care for their population. Some of them actually said that they didn't need that sort of thing. Many of the Provider Trusts didn't know whether they provided neonatal intensive care or not and were vaguely hoping that the block contracts would sort it out. Obviously, this had to change.

The health service for newborn babies includes four elements. The 24-hour resuscitation, the routine examination, the special care for minor problems, as well as intensive care. Wherever babies are born there is the need for the first three of those elements. By 1994–95 an element of the fourth, that's neonatal *intensive* care, was being practised in most maternity units, and only the very immature and those requiring surgery, on the whole, were transferred to regional centres. Of course, the debate arose whether that was in the best interests of the infants, and there were some early studies suggesting that it was better that they went to the regional centres. David Field and I failed to find any evidence that the babies did better in regional centres

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<sup>240</sup> Clinical Standards Advisory Group (CSAG). (1993) *Neonatal Intensive Care: Access to and availability of specialist services*. London: HMSO. *idem* (1995) *Neonatal Intensive Care: Access to and availability of specialist services. Second report*. London: HMSO.

<sup>241</sup> Royal College of Physicians, London. (1988) *Medical Care of the Newborn in England and Wales*. London: Royal College of Physicians. Professor Osmund Reynolds wrote: 'This was first advocated much earlier, in the Sheldon Report 1971 (op. cit. note 247), Oppé Report 1974 (op. cit. note 248) and Short Report 1980 (see note 56).' Note on draft transcript, 1 February 2000. The Liaison Committee of the British Paediatric Association and the Royal College of Obstetricians and Gynaecologists also produced a report in 1978 on how to improve perinatal care. See British Paediatric Association/Royal College of Obstetricians and Gynaecologists. (1978) *Recommendations for the Improvement of Infant Care during the Perinatal Period in the UK*. Liaison Committee Discussion Document (Dunn P M, Chairman). London: British Paediatric Association/Royal College of Obstetricians and Gynaecologists. See also Dunn P M. (1984) Special and intensive care of the newborn in the South Western Region, 1980–1982. *Care of the Critically Ill* 1: 10–14.

<sup>242</sup> op. cit. note 240.

than they did in the smaller units for those infants that the smaller units elected to treat. In other words it seemed to us that the selective referral system seemed to be working reasonably well.

But something else was happening around the 1990s and afterwards. The first was that the survival figures were levelling off, there wasn't much change. The improvement in the pre-viable infants had occurred during the 1980s. The second was there wasn't an increasing need for neonatal intensive care. The number of ventilator days, or whatever measure one uses, wasn't increasing, it had levelled off. And so it was that Dr Chapple who analysed the London scene said, 'All paediatricians are now trained in neonatal intensive care' and she went on to say, 'It is now extremely rare for there not to be a cot available in a recognized neonatal intensive care unit'. In other words the problems in the 1980s seemed to be going away. To balance that, we thought that in our report we ought to record that on Christmas 1995, and Christmas is always an emotive time to talk about babies in care, a baby was born in a maternity unit in the Midlands and nine neonatal units who offered neonatal intensive care were asked to take the infant but were unable to do so.<sup>243</sup> There will always be times when the regional units won't be able to take another baby.

Now, in general, there is a high standard of care and the achievements, the outcomes, are good. It seems to me, and this is a personal view, the challenge is to provide neonatal care so that it is a safer experience for the infants, it is less obtrusive, it is more gently provided, and it leaves the infants with fewer scars and the families with happier memories of the care their babies received in their first days of life.

**Boyd:** Thank you very much, David. I think we would all resonate to that. Now in the discussion, I would like us to stick not to what in a sense is politically desirable, but does the history as described by David feel right?

**Gamsu:** It was very interesting to hear that review of services provided for neonatal care. I really can't understand, however, how the conclusion was reached that there were sufficient facilities for neonatal intensive care in the London regions, when those of us who were very personally involved in the provision of that care, were reminded every day how few facilities were available, how many babies had to be turned away, and that applied not only to the neonatal intensive care units themselves, but to those hospitals that were trying to get babies into those units. In fact the impression, and it is only an impression, that we had, was that the position in London was probably worse than the position in any other place. We were constantly being told about London that, 'Oh well, in the metropolitan regions you are very well provided for' and that was said by people from the DHSS and elsewhere, and in fact was very far from the truth. Speaking to my colleagues who worked in units outside London, we seemed to be in a more deprived situation,

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<sup>243</sup> op. cit. note 240.

having to refuse babies far more often.<sup>244</sup> So I honestly cannot see how the conclusion was reached that we were well provided for.<sup>245</sup>

Concerning David Hull's last point, I'm sure that we would all agree that the provision of neonatal intensive care in no way precludes sympathetic handling of babies and their parents. In fact a lot of the incentive for that sympathetic handling came from those who were involved in neonatal intensive care.<sup>246</sup>

**Reynolds:** I would like first to say that I thought that was a masterly account of the way I saw most of it too. But the first idea about regionalization was in the Sheldon Report,<sup>247</sup> I sat on the Committee – and on most of the others as well. George Godber received the Sheldon Report with great sympathy. It was published in 1971, and it said that every region ought to have one major centre where most of the intensive care goes on, and everybody else ought to be tooled up to some extent. And then Tom Oppé chaired a report in 1974 (which I sat on too),<sup>248</sup> which said why doesn't everybody implement the Sheldon Report, because nothing had happened. It was still two years before the Sheldon Report was circulated for action to the regional health authorities in 1976, whereupon the Social Services Select Committee of the House of Commons undertook a major enquiry into perinatal and neonatal mortality under the chairmanship of Mrs Renée Short; that sat from 1978 to 1980 and it was a really big thing.<sup>249</sup> It accumulated a tremendous amount of data. In the neonatal field it became clear that the major regional centres were, by then, being overwhelmed, and a recommendation of what became known as the 'Short Report' was that you had got to have some regional structure, managed structure, to deal with this overwhelming of the major centres. That's where the recommendation came from, that each region ought to

<sup>244</sup> Professor Osmund Reynolds wrote: 'I absolutely agree with that: for many years University College Hospital had to refuse admission to more babies than it admitted.' Note on draft transcript, 1 February 2000.

<sup>245</sup> Professor Harold Gamsu wrote: 'There has been a recent paper [Parmanum J, Field D, Rennie J, Steer P. (2000) op. cit. note 250] which shows that intensive care units still have to transfer babies out because of pressure on their own overstretched facilities.' Note on draft transcript, 17 December 2000.

<sup>246</sup> Professor Harold Gamsu wrote: 'Pierre Budin had shown in Paris at the turn of the century that mortality of babies decreased substantially when they were cared for by their mothers. Much later, Kahn and Wayburne in Johannesburg showed the same [Kahn E, Wayburne S, Fouche M. (1954) The Baragwanath premature baby unit – an analysis of the case records of 1000 consecutive admissions. *South African Medical Journal* 28: 453–456]. Klaus and Kennell in Cleveland subsequently demonstrated the importance of early maternal contact and its effect on the immediate, and subsequent welfare of the child [Klaus M, Kennell J H. (1970) Mothers separated from their newborn infants. *Pediatric Clinics of North America* 17: 1015–1037]. Freedom from pain, the provision of comfort and the promotion of sleep are further aspects of care we have come to recognize.' Note on draft transcript, 25 July 2000. See Budin P. (1907) *The Nursling*. London: Caxton. See also Richards M P M. (1978) Possible effects of early separation on later development of children – a review, in Brimblecombe F S W, Richards M P M, Robertson N R C. (eds) Separation and special care baby units, ch. 2. *Clinics in Developmental Medicine*, no. 68. London: William Heinemann Medical Books, 12–32.

<sup>247</sup> Sheldon Report. (1971) Report of the Expert Working Group on the Special Care of Babies. *Department of Health and Social Security Reports on Public Health and Medical Subjects*, no. 127. London: HMSO.

<sup>248</sup> Oppé Report. (1974) *Report of the Working Party on the Prevention of Early Neonatal Mortality and Morbidity*. Health Circular HC(76) 40. London: DHSS.

<sup>249</sup> Professor Osmund Reynolds wrote: 'The three specialist advisers were Eva Alberman, Richard Beard and myself.' Note on draft transcript, 1 February 2000. See *Perinatal and Neonatal Mortality*. (1980) op. cit. note 56.

have one big perinatal centre but also three to five so-called level-2s geographically dotted around the regions, with a proportion of regional funding. Also, that all the smaller maternity hospitals ought, of course, to be able to do the basics, and minimize the number of mothers and babies that got shifted around. By the time the Thatcher reforms came into effect in 1990, all the regions in the country except one had got funded systems of that sort up and running, or in the late stages of planning. Because of the geography in a few regions it was preferable to run a two- (rather than three-) level system. But then when the funding was abolished, of course chaos broke out and we were all told that we had got to compete with everybody else. I still think it would make much more sense to have some kind of managed regional structure for this field, because I still don't like – even though far more paediatricians are trained in the field, of course – the idea of a 700g or 800g baby being cared for as a part-time occupation of a possibly general paediatrician somewhere, but no doubt I am getting old fashioned.

It wasn't just the neonatal regional services; it was all regional services that were abolished as part of those so-called 'reforms'. The fall-back position was some form of what one called accreditation to start with but you are not now allowed to use that word at the Department of Health, so you have to call it appraisal. Rodney Rivers, who is here, has carried this out very successfully in the Thames Regions, so that the purchasers can be given a good idea of the quality of care to be expected in all the London hospitals, to guide them about where babies get sent.<sup>250</sup>

The final point is, if you haven't got any kind of managed structure, how do you arrange a proper spread of units around the country so that sick babies are within reasonable reach of one?

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<sup>250</sup> Dr Rodney Rivers wrote: 'The notion that it might be possible to establish a system of appraisal of neonatal services within the Thames regions arose from the publication in February 1992 of the House of Commons Health Committee Report on Maternity Services (op. cit. note 56). No authoritative process of accreditation under government aegis had followed from this report and the Thames Regional Perinatal Group (TRPG) therefore took it upon itself to set up a subcommittee to explore the possibility of a process of peer appraisal. We have heard how the inability within the Thames regions of being able to guarantee that a baby would be admitted to a level-3 unit for intensive care had resulted in the widespread introduction of intensive care cots in district general hospitals throughout the regions. The process of appraisal involved the valuing of the neonatal services of each of these NHS hospitals where neonatal care was taking place against a set of ascribed values. These values included criteria that were considered important if sufficient ongoing experience was to be provided for nursing and medical staff, and took into account proposals that had been made by the British Association of Perinatal Medicine in regard to staffing levels that were required if the provision of round-the-clock availability of staff with a sufficient level of training and expertise that was to be achieved. The aims of the process were to improve the care available to high-risk babies by ensuring the provision of what was then considered to be a safe level of service, and to enable the consultants working in these units to provide purchasers and trusts with details of the equipment and staffing requirements that were needed to meet the appraisal criteria, if they so wished...Virtually all units were visited and reports issued by the end of 1998: the appraisal process has resulted in improvements in equipment, nurse staffing establishments and training levels, and in medical cover of many units.' Edited from a letter to Dr Daphne Christie, 30 March 2000. See Milligan D W. (1997) Neonatal intensive care provision in the United Kingdom 1992–3. British Association of Perinatal Medicine. *Archives of Disease in Childhood* 76: 197–200. Parmanum J, Field D, Rennie J, Steer P. (2000) National census of availability of neonatal intensive care. *British Medical Journal* 321: 727–729. Professor Harold Gamsu wrote: 'The London Perinatal Group was brought into being at an informal meeting of neonatal paediatricians in the late 1970s who resolved to find ways to improve neonatal services in London. Subsequently the group evolved into the Thames Regional Perinatal Group and included representatives from all the Thames Neonatal Intensive Care Units.' Note on draft transcript, 17 December 2000.

**Boyd:** We won't have a debate about whether the Thatcher government was a mistake or not, but we will ask Jonathan Wigglesworth for his comments.

**Wigglesworth:** I want to get back to David Hull's analysis of the rise in demand for neonatal intensive care services in the 1980s and ask about the causes. I seem to think that one reason for this was the increasing popularity of maternal fertility treatments which resulted in an enormous increase in the number of higher multiple births, all of whom needed intensive care.

**Oppé:** Just a note about the Sheldon Report. George Godber<sup>251</sup> set up the Expert Working Group on the Special Care of Babies in response to an impassioned letter, or short article, from Kenneth Cross, making the accusation that infants in special care baby units were being starved of oxygen in order to prevent retrolental fibroplasia, but in doing that it was wrecking their brains from anoxia.<sup>252</sup> It was this, together with George Godber's passion for babies, if I can put it that way, that set up the Expert Group which really said intensive care was something that should happen only in places where babies can be cared for intensively. And then there was a lot of argy-bargy about the finances required for how many intensive cots, but I won't go into that. But I think that's important.

Another important point about intensive care for babies within what you might call 'regional hospitals' or 'nonspecialist centres', was the impact of various regulations on the training of preregistration and registration house physicians. A great many paediatric posts were being put into paediatrics as part of vocational training for general practice and many were, of course, unsuitable people, either in motivation or in work load, to actually participate in intensive care. One of the reasons for regionalization was that you could have a dedicated staff and not involve inexperienced people in the care of premature babies.

A final point was that in the list of Civil Service documents that have been mentioned, the Court Report on the Child Health Services did have a very powerful chapter on neonatal care, in which it got the soundbite, 'This is a holocaust which the National Health Service should not put up with'.<sup>253</sup>

**Reynolds:** There's one important number to give. As part of the beginning of the investigation for the Short Report which started in 1978, surveys right around the whole country were done, and it was discovered that there were only 12 paediatricians in England and Wales who spent the majority of their time working with neonates. How do you set up a service if there is nobody actually trained? It was one of the huge constraints on spreading neonatal care around at that time.

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<sup>251</sup> See note 156.

<sup>252</sup> Cross K W. (1973) Cost of preventing retrolental fibroplasia? *Lancet* ii: 954–956. See also note 14.

<sup>253</sup> Court Report. (1976) *Fit for the Future*. Report of the Committee on Child Health Services. London: HMSO.

**Hull:** I apologize for unduly provoking Harold [Gamsu], for I knew his views when I quoted Dr Chapple. But the difficulty we had with our report was actually identifying where the service fell short and the indices we adopted when a baby travelled further than the nearest neonatal intensive care unit, babies were transferred out of the place where they were born, if they were in a unit that ought to provide neonatal intensive care, or if twins were split up. We gained evidence that all these were happening in the UK and it was unsatisfactory, but there wasn't a great deal of evidence in 1994–95 from the London area that that was actually happening there. We couldn't find any evidence that babies never ultimately found an appropriate home, but they often travelled too far, beyond the nearest unit. I think that if you are going to do something about it, you've got to get the evidence that some babies are missing out.<sup>254</sup>

We recommended strongly in both reports that you couldn't leave neonatal intensive care to 'market forces',<sup>255</sup> that there had to be some sort of structure in the country, so that babies could get the best deal out of the limited resources available. We made that very clear. But it didn't include the notion that all neonatal intensive care should be done in the regional centres, but rather it should be done where it is most appropriate to do it. As far as Jonathan [Wigglesworth] is concerned, again I couldn't quote everything, but the Royal College of Physicians' Report does say that one of the other reasons for the rise is the increase in the number of twins at that particular time, and multiple births, but I don't think it was a major contribution to it.<sup>256</sup> I think the biggest contribution was that more babies were being ventilated and the very small babies needed an awful lot of ventilation. And as far as my statement about gentle care, I don't think Harold did misunderstand me, my point is that neonatal intensive care has got to be provided without it being such a frightening experience. I am aware of the work that people in this room have done to try to promote that.

**Boyd:** Well I have to say, just as a puff for you, that visiting your unit in Nottingham always struck me as a very good example of that.

**Corner:** Very little has been said today about the nursing side of things. One of the important things that was set up in the late 1960s was the nurse training in special and intensive care of the newborn. In recognition of the centres where this should be done, I travelled from Lands End to somewhere north of Leeds, looking at units all over the place with a nurse, who was a specialist, to decide which units were suitable

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<sup>254</sup> Professor Harold Gamsu wrote: 'Members of the London Perinatal Group and hospitals in the four Thames regions collaborated with the Emergency Bed Service to record all attempted neonatal referrals to intensive care for a six-month period in 1979/80. Only 40–65 per cent could be accepted. In 1983 the situation was unchanged [see Gamsu H R. (1983) Neonatal intensive care in the four Thames regions, in *Neonatal Intensive Care. A dilemma of resources and needs*. Report of a one-day conference 1 December 1983. London: The Spastics Society, 13–20]. The main reasons for refusal of admission then, as now, were too few places and too few nurses.' Note on draft transcript, 19 January 2001.

<sup>255</sup> Professor Osmund Reynolds wrote: 'As stated also in the 1992 Select Committee Report by a committee with a Conservative majority chaired by Nicholas Winterton, and in spite of the edicts of the Thatcher reforms (this is one reason why Winterton got fired...).' Note on draft transcript, 1 February 2000.

<sup>256</sup> *op. cit.* note 241.

for the training of nurses in neonatal intensive and special care. One of the things that we found outstanding was that some units appeared to be very adequate, and this really arises out of having them in all major district general hospitals, because in some there was not enough clinical practice in those particular hospitals to justify running a nursing course there. For instance, a hospital that only had, for example, one exchange transfusion in six months, or something like that, didn't give the nurses sufficient experience. So, in fact, we turned down a few quite well-known units, because they were not dealing with enough babies to give the right experience. And in a region like the South-West region, where distance counts enormously, this was quite a problem. This question of moving babies is quite important, but you have to weigh up whether your movement of the baby will give a high level of expertise to help the baby survive, and in particular, the nursing care, because without expert nursing care none of the babies would survive.

**Boyd:** Thank you very much for that. I wonder if Caroline [Dux], Mae [Nugent] or Anthea [Blake], any of you from the nursing profession, want to come back on any of that from a historical perspective in particular.

**Blake:** I can remember when I first started at University College Hospital that a lot of the hospitals with prem units did run a course of their own, but these were not standard across the whole of the country and so if you did your training at one hospital it wasn't necessarily recognized in another hospital. The training that Beryl mentions with the Joint Board of Clinical Nursing Studies tried to standardize the content of the nursing courses across the country, so that wherever you did your training, you had covered the same basic curriculum.<sup>257</sup> Of course, the amount of clinical activity, as Beryl says, was very important, because unless you see a thing several times, it is very difficult to remember what to do, so having a certain critical mass and experience helps you to build up that knowledge.

In 1978 the Neonatal Nurses Association was formed<sup>258</sup> with the specific remit of trying to spread good practice between units. Because there was only one neonatal

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<sup>257</sup> Professor Osmund Reynolds wrote: 'The course run by the Joint Board of Clinical Nursing Studies was based quite largely on one that had been established for several years at University College Hospital, London.' Note on draft transcript, 30 November 2000.

<sup>258</sup> Miss Anthea Blake wrote: 'The Neonatal Nurses Association owes its formation to the vision of Beryl Chadney, then Nursing Officer in the Children's Division of the Department of Health and Social Security. Both the 1974 Oppé Report (op. cit. note 248) and the 1976 Court Report (op. cit. note 253) had drawn the Department's attention to the deficiencies of provision for neonatal care and the fact that the perinatal mortality rate was well above some other developed countries. A personal survey of units across the country led Beryl [Chadney] to conclude that there were four areas that could be improved: nursing practices needed to be reviewed and updated; nurse training in the specialty was inadequate; better use of trained staff was needed; and communication between units required urgent attention. To this end, in 1977 she invited six senior nurses from across the country to consider addressing these issues by setting up a national study conference (which was held in March 1978 at University College Hospital, London) and organizing neonatal nurses into a national group, later an Association. From this small beginning, the Association now has around 2500 members, produces the bi-monthly *Journal of Neonatal Nursing* and is actively involved in matters of central policy making.' Letter to Dr Daphne Christie, 6 January 2001. See Chadney B. (1994) How it all began: The history of the Neonatal Nurses Association. *Journal of Neonatal Nursing* 1: 6–11.



unit in a hospital, and only one senior sister in each unit, it was difficult for them to share ideas. We were working in a speciality that was very hard pressed and you often didn't get all of your days off, and it was difficult to be funded to go to study days, and there weren't many of them anyway. That was the reason for setting up the Neonatal Nurses Association, with the remit of sharing ideas and trying to have a national forum for discussion of good practices. As Richard [Cooke] was saying, it's no good one unit having a good idea if they don't share it, or if they have got a problem, not trying to find out what other places are doing to answer the problem. So I think that the Neonatal Nurses Association has helped nursing to develop its practice in many ways. Of course, throughout the 1970s and 1980s the nursing training courses became more rigorous and more in-depth, with a much better basis of physiology, there is more technology to learn, and we've become increasingly aware of our professional accountability. Some of the things that we did in the 1960s and 1970s our own professional body would not probably countenance these days, and for good reason. At the time when we did them, they seemed like a good idea. Maybe now with hindsight and perspective, we see that we were skating on very thin ice on occasions. Now we are a little better prepared. I don't know if the others would agree.

**Miss Caroline Dux:**<sup>259</sup> I would just like to come in on that. I worked in 1980–81 in a small, special care baby unit at a district general hospital, prior to coming up to University College Hospital, and at the time if we had a preterm baby, the only way to ventilate was to hand ventilate on a Resuscitaire and wait for a squad to arrive from a bigger unit. And then – we thought we were very grown up – we received our first ventilator, it arrived in a cardboard box, and we put it together in the equipment room, literally with the instructions in front of us, and we learnt to use it, myself and the paediatrician, on the job. But we did that from a point of ignorance and with hindsight I am horrified what we did, but at the time we thought we were doing it for the best, for the baby. We didn't know anything else, we didn't have facilities for doing blood gases on the unit. They had to go up to the big people's ITU right at the other end of the hospital compound. It was a big district general hospital and we didn't have ultrasound, we didn't know what we were doing to brains, but we felt if we could ventilate a baby, we must be doing something good. This was right at the beginning of the era of every small unit being able to ventilate. I was horrified when I came to work at University College Hospital to realize what we had done. At the time we thought it was in the best interests of the babies, but it was really kit medicine at its finest.

**Boyd:** I have to say, having worked at University College Hospital in the 1960s, I can remember ventilating babies in just the same amateur way. Perhaps it would have been better if I had phoned Osmund up. That was a very interesting contribution. I am going to ask Pam if she would like to say something about nutrition.

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<sup>259</sup> Miss Caroline Dux RN RM RNT CertEd FE (b. 1955) worked on the Neonatal Unit at University College Hospital, London, in the 1980s before taking up her post as Sister on the Neonatal Unit at the Whittington Hospital, London, in 1983. She developed her interest in teaching by undertaking appropriate postgraduate training. After many years as a tutor at Bloomsbury and Islington College of Nurse Education she returned to the clinical field, working again on the Neonatal Unit at University College Hospital, London, in 1996.

**Davies:** In the 1950s, it was generally felt that preterm babies, the most immature of whom could neither suck nor swallow, would be more safely starved in the first days after birth because of the dangers of aspiration. In addition, in 1949 Clement Smith<sup>260</sup> and others in Boston, USA, were influential in promoting the view that such babies were oedematous so that extra fluid was unnecessary; and later, in 1962, that they had enough stored fat, glycogen and tissue protein available for catabolism to prevent them dying. I think he was wrong there, but he did change his views later.<sup>261</sup>

Victoria Smallpeice<sup>262</sup> at Oxford disagreed with this view – she held that the placenta nourished the baby, usually adequately, until the moment of birth, and that it was illogical to cut off the supply of food in this way. She found some support for her views in discussion with others at an International Congress of Pediatrics. She knew, too, that the Professor of Surgery at Great Ormond Street, Andrew Wilkinson,<sup>263</sup> disliked postoperative starvation of newborn infants, believing it created metabolic chaos. In 1962, Smallpeice started feeding babies who weighed 1000–2000g at birth early, with expressed breast milk. The relatively newly available polyvinyl feeding tube passed into the stomach was a great advance over the teaspoon and ‘fountain pen’ dropper.<sup>264</sup> An enthusiastic young nursing staff showed that even ill babies could be fed small amounts frequently from soon after birth with indwelling tubes strapped in place. We did not do a controlled trial but compared results with babies nursed at the Churchill Hospital where delayed feeding was continued as before. I soon realized I was doing fewer exchange transfusions for hyperbilirubinaemia on the early-fed infants at the Radcliffe Infirmary, that symptomatic hypoglycaemia as defined then was not seen, and birthweight was regained sooner.

In 1965 Wharton and Bower published from the Sorrento Hospital, Birmingham, the results of a controlled trial of infants fed early and later; they confirmed hyperbilirubinaemia and hypoglycaemia were less common in the early-fed but found more of them died.<sup>265</sup> We should record here that a pioneering public health doctor,

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<sup>260</sup> See note 14.

<sup>261</sup> Dr Pamela Davies wrote: ‘So in this country and in the USA, but not always in Europe, fluid was withheld after birth for varying periods, sometimes up to four days, and in one extreme case I will always remember, for 111 hours.’ Letter to Dr Daphne Christie, 21 March 2000.

<sup>262</sup> Dr Victoria Smallpeice FRCP (1901–1991) was first Physician in Charge and Clinical Director to the Children’s Department, United Oxford Hospitals, Oxford, and Consultant Paediatrician to the Oxford Regional Hospital Board, from 1947 to 1966. She was a member of council of the British Paediatric Association, from 1959 to 1962, and was elected an honorary member in 1970. She was President of the Paediatric Section of the Royal Society of Medicine from 1965 to 1966. See Davies P A. (1994) Gwladys Victoria Smallpeice. *Munk’s Roll* 9: 479–482.

<sup>263</sup> Professor Andrew Wilkinson CBE FRCSE FRCS (1914–1995) was Nuffield Professor of Paediatric Surgery, Institute of Child Health, University of London, from 1958 to 1979, later Emeritus. He was Surgeon at the Hospital for Sick Children, Great Ormond Street, London, from 1958.

<sup>264</sup> Smallpeice V, Davies P A. (1964) Immediate feeding of premature infants with undiluted breast milk. *Lancet* i: 1349–1352.

<sup>265</sup> Wharton B A, Bower B D. (1965) Immediate or later feeding for premature babies? A controlled trial. *Lancet* ii: 769–772. See also McCance R A. (1982) Early physiological work at Sorrento: recollections of the 1930s, in Wharton B A. (ed.) *Topics in Perinatal Medicine* 2. London: Pitman Medical, 17–19.

Dr Victoria Mary Crosse, had opened the country's first special nursery for premature infants in 1931 in the grounds of the Sorrento Maternity Hospital.<sup>266</sup>

I think, nevertheless, there was a gradual change to early feeding from 1962; and then as infants greater than 1000g began to survive in increasing numbers, that sort of initial feeding was superseded by total parenteral nutrition. I am very sorry Jonathan Shaw isn't here to talk about it. He did an enormous job in this very technically demanding aspect of feeding, and I am sure things now are infinitely better and easier.<sup>267</sup>

**Boyd:** Thank you, that was a very helpful contribution. Very quickly, Os, and then we are just going to say how the system was funded.

**Reynolds:** I want to make two points. First, some of the babies that Cecil Drillien followed up had no food for nine days, no fluids for five days; the mind boggles about what must have been the bilirubin levels, and hypoglycaemia wasn't known about at that time, and it's amazing to me that any of them actually turned out okay.<sup>268</sup>

The second is, I was going to say something about Jonathan Shaw too, because he introduced total parenteral nutrition through long silastic catheters. It was a conceptual leap at the time because he based the mixture on Elsie Widdowson's data on accretion of minerals and other substances in fetal bodies as they grew.<sup>269</sup> So he was supplying what they would have got *in utero* had they remained *in utero*, but doing it intravenously, and he conquered all the difficulties about, for example, getting the calcium right; these things are very difficult, and it was a huge conceptual leap.

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<sup>266</sup> See note 8.

<sup>267</sup> Dr Pamela Davies wrote: 'No one has really mentioned that the first decade or so of paediatric entry to newborn nurseries was accompanied by several disasters before vital lessons of developmental physiology and pharmacology were learned the hard way. These include retinopathy of prematurity (excessive levels of oxygen), grey baby syndrome (chloramphenicol), kernicterus (sulphonamide, vitamin K) and yellow staining of primary (and very occasionally secondary) dentition (tetracycline). In this context I think that prolonged follow up of very low birthweight infants should be mandatory and should persist into their child-bearing years. There needs to be confirmation of the safety of many of the investigative and therapeutic aspects of modern neonatal intensive care in the long term. Dates of introduction of new departures should always be carefully recorded.' Letter to Dr Daphne Christie, 21 March 2000. See note 269.

<sup>268</sup> Professor Harold Gamsu wrote: 'As far as I can recall, she [Cecil Drillien] did not discriminate between the growth-restricted or appropriately grown low birthweight baby. Though earlier authors (for example, Budin) had pointed out that not all low birthweight babies were preterm, it was only in the 1960s that Peter Gruenwald drew our attention to the entity of poor intrauterine growth [Gruenwald P. (1963) Chronic fetal distress and placental insufficiency. *Biology of the Neonate* 5: 215–265] as did Michael Dawkins in 1968. Reliable charts which related birthweight to gestation appeared at this time. An accurate estimate of gestational age was required and this was provided by clinical examination using a combination of neurological and morphological features [for example, Dubowitz L M, Dubowitz V, Goldberg C. (1970) Clinical assessment of gestational age in the newborn infant. *Journal of Pediatrics* 77: 1–10]. This gave rise to a new verb, "Has the baby been Dubowitz'd?". Later, Campbell was able to date the gestational age of the fetus using cranial ultrasound measurement and following this to measure fetal growth patterns [Campbell S. (1969) The prediction of fetal maturity by ultrasonic measurement of the biparietal diameter. *Journal of Obstetrics and Gynaecology of the British Commonwealth* 76: 603–609].' Letter to Dr Daphne Christie, 17 December 2000. See also note 85.

<sup>269</sup> Shaw J C. (1973) Parenteral nutrition in the management of sick low birthweight infants. *Pediatric Clinics of North America* 20: 333–358. *idem* (1988) Growth and nutrition of the very preterm infant. *British Medical Bulletin* 44: 984–1009. See also note 34.

**Stewart:** I want to tell you about the strictures on feeding. If you were under 5lbs, you got starved for one day, and so on, until you got to 2lbs 8oz, when you got starved for five days.

**Boyd:** Does anyone want to make any comment about the funding sources? We will allow ourselves two or three minutes for that in response to Chris [Booth]'s challenge about that.

**Victor Dubowitz:** If I can just make a brief comment. When I came to the Hammersmith, succeeding Peter Tizard, it looked as though all the carpets were just about being pulled out at the time – the Nuffield support had come to an end, there was some support from Action Research and that was coming to an end. Everybody seemed to be on soft money, there was only one established post, apart from the new Chair that they established, and it really was tough having to apply and re-apply. We had some sympathetic support from the MRC, certainly two successive three-year grants for cerebral blood-flow studies, which attracted Frances Cowan. I don't know exactly which year that was, and then the Wellcome Trust gave us a large programme grant at one stage to study something that was raised earlier on. Simon Godfrey was trying to develop a continuous blood oxygen-monitoring system that automatically adjusted the baby's oxygen level, to try to get an optimum level,<sup>270</sup> and there were numerous other grants in between. But it certainly wasn't easy and there wasn't ready money available to go round.

**Reynolds:** It was a big problem in the 1960s, but once things start happening then funding bodies become much more friendly. I remember the fastest grant that we ever got was when we showed a good image of the brain with ultrasound in 1978.<sup>271</sup> The turnaround time was two weeks for acceptance from the MRC and that later became a programme grant and later still we added a programme grant from the Wellcome Trust. I think now it's become a lot more difficult and there are people here who will be suffering, but my understanding is that perinatal care is a priority of neither the MRC nor the Wellcome Trust, and that's serious. Action Research seems to be plugging a lot of gaps right now.<sup>272</sup>

**Fairweather:** Under the difficulties of funding, nobody has mentioned that one of the big difficulties came after you had done research showing that a new approach or technique was beneficial and should be incorporated as part of routine management – namely achieving the actual takeover from research to NHS funding. An example, that Os will remember from University College Hospital, was the antenatal diagnosis

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<sup>270</sup> Collins P, Levy N M, Beddis I R, Godfrey S, Silverman M. (1979) Apparatus for the servocontrol of arterial oxygen tension in preterm infants. *Medical and Biological Engineering and Computing* 17: 449–452.

<sup>271</sup> op. cit. note 200.

<sup>272</sup> Professor Osmund Reynolds wrote: 'And, of course, one must not forget the role of charities in supporting the clinical care of babies, something we've not discussed, but should have. The main charity is BLISS (Baby Life Support Systems) which has supplied equipment to nearly all the special and intensive care units in the country and has also supported the training of doctors and nurses. BLISS celebrates its 21st anniversary this year.' Note on draft transcript, 30 November 2000.

of thalassaemia – where at one point the service was going to cease totally because I insisted that I couldn't continue to fund this on research monies, because it was no longer research, having become an accepted, necessary form of investigation. The decision was reversed only by involvement of the local population, for we were sitting in the middle of a very large Greek Cypriot population who relied very much on the service, and only their vociferous pressure brought about a last-minute change by the region to provide NHS funding.

**Oppé:** Just as a quick response to Christopher Booth. In my opinion it was always quite difficult to get adequate funding for scientific neonatal research. For one thing, a whole lot of people used to say, 'Oh, dear little infants, all the charities support you, no problem,' but the fact is most of the parent groups and the charities were interested in service or in treatment, and not in prevention or basic physiology. The MRC caught us paediatricians, I think, in a sort of catch-22 situation.<sup>273</sup> They said, 'We'd love to give more grants but we're not getting good enough applications,' but the problem was that they didn't really have anybody in the corridors of MRC power who was a paediatrician or could reasonably, I think, look in comparative terms at the paediatric applications. So it has, historically, been quite difficult to get funding, and I have alluded earlier on in this discussion to a slight problem, which is the legality of research unless it is of direct therapeutic benefit.<sup>274</sup>

**Boyd:** I am not going to try to sum up, which would take another four hours, except to tell Osmund that regionalization is back in something called OATS, which is 'out of area treatment scheme',<sup>275</sup> which will be just as problematic as the old regional services were.

I think we should thank, first of all, Tilli and her team for putting this together. I think it has been a super afternoon, at least from where I sit. Secondly, to thank Os as Adviser and the Wellcome Trust for funding the occasion, and finally thank you all for coming. It's you that have made it, and it is particularly nice to see our nursing colleagues, our science colleagues, our clinical colleagues, all mixed up together, which is what neonatology has been doing for the past 40 years, and our heavier physics colleagues, the heavy metal. Thank you all very much indeed.

**Tansey:** May I thank you all very much for coming. It has been a great privilege for us all who are not part of this field, to listen to your reminiscences and to hear your debates, and I would particularly like to thank Robert for his excellent and punctual chairing.

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<sup>273</sup> Catch-22 – A no-win situation. 'Orr would be crazy to fly more missions and sane if he didn't, but if he was sane he had to fly them. If he flew them he was crazy and didn't have to; but if he didn't want to he was sane and had to.' Heller J. (1961) *Catch-22*, ch. 5. Leicester: Charnwood.

<sup>274</sup> See page 41.

<sup>275</sup> Professor Robert Boyd wrote: 'A transient NHS funding mechanism introduced when the "internal market" of the 1990s was dismantled following the election of a Labour government in 1997.' Note on draft transcript, 13 December 2000.

## GLOSSARY

### Amniocentesis

A procedure in which a needle is placed transabdominally into the amniotic cavity in order to remove fluid for analysis. It is often used in the antenatal diagnosis of chromosomal abnormalities and genetic disorders.

### Anoxia

A total lack of oxygen supply to the body tissues.

### Apgar score

Developed by the American anaesthetist, Virginia Apgar (see note 82), this is a scaled score of a newborn's physical condition based on five measures (heart rate, respiration, muscle tone, colour and reflexive responsiveness). A maximum of two points is given for each, often measured at one minute and five minutes after delivery. *op. cit.* note 141.

### Apnoea

The cessation of breathing, often temporary in the newborn.

### Asphyxia (or suffocation)

Asphyxia in the newborn is due to respiratory failure bringing about lack of oxygen and failure to get rid of carbon dioxide. In the severe case, the baby not only fails to breathe, but the circulation is also compromised.

### Asphyxia pallida

An old term that describes a baby with severe and prolonged **asphyxia**, associated with acute pallor. Inevitably, such a baby will need immediate resuscitation.

### Atelectasis

The failure of the lung to expand. It occurs in **premature** babies when the cells lining the air sacs (alveoli) are immature and unable to produce the wetting agent (**surfactant**) with which the surface tension of the alveolar lining layer is overcome.

### Bronchopulmonary dysplasia

A chronic lung disease of newborn babies, particularly low birthweight babies, often caused by trauma resulting from artificial ventilation of the lungs with oxygen under pressure. It frequently occurs after recovery from **respiratory distress syndrome**.

### Computerized tomography (CT)

A technique which revolutionized medical imaging in the 1970s, bringing new insights into the anatomic basis and history of many diseases. See, for example, *op. cit.* note 213.

### CT

See **Computerized tomography**.

### Continuous positive airway pressure

A technique for breathing spontaneously against raised airway pressure.

### Endotracheal (tracheal) intubation

The insertion of a soft polyvinyl tube into a baby's trachea via the mouth or nose, to support breathing.

### Fontanelle

A gap in the bones at the apex of the skull. Newborn babies are born with a fontanelle, which disappears as the bones in the skull fuse; this is usually complete at around 18 months of age.

### Haemolytic disease of the newborn

The condition was usually caused by rhesus positive cells from the fetus with a rhesus positive father finding their way into the circulation of the rhesus negative mother, usually at birth, and inducing antibody formation to what is for her a foreign antigen. In the next pregnancy her antibodies are transferred to the fetus across the placenta (a normal protective process) and attack the baby's red cells if they are rhesus positive, inducing haemolysis and causing anaemia and jaundice. This sequence of events is now preventable by giving women antibodies to rhesus positive cells at delivery, thus preventing her sensitization. Some cases of haemolytic disease result from maternal transfer of naturally occurring antibody to her fetus, such as may occur with an A or B group fetus and an O group mother. See also **kernicterus**.

### Hyaline membrane disease

See **Respiratory distress syndrome**.

### Hydrocephalus

This is usually the consequence of obstruction of the outflow of cerebrospinal fluid from the cerebral ventricles before the skull sutures close resulting in the enlargement of the head.

**Hyperbilirubinaemia**

Dangerously high levels of bilirubin in the circulation cause the baby to be jaundiced. Hyperbilirubinaemia and **kernicterus** used to occur in premature infants who received large doses of vitamin K (op. cit. note 150), as well as in **haemolytic disease of the newborn**.

**Hypocalcaemia**

Low blood calcium, leading to vomiting and uncontrollable twitching of muscles if severe.

**Hypoglycaemia**

A deficiency of glucose in the bloodstream, which in the newborn baby is usually manifested by apnoea and fits in small-for-dates babies.

**Hypoxaemia**

A reduction of the oxygen concentration in the arterial blood.

**Hypoxia**

Insufficient oxygen in the body to support normal metabolic requirements.

**Ischaemia**

An inadequate flow of blood to a part of the body, often due to hypotension in the newborn.

**Kernicterus**

Kernicterus may occur when there is a high level of unconjugated bilirubin in the circulating blood such as in **haemolytic disease of the newborn**, but much more commonly in **premature** babies who tend to have a deficiency of liver enzymes for conjugation of bilirubin. A high level of bilirubin consequently occurs in the blood of the immature infant and, at certain levels, passes into brain cells and interferes with the biochemical changes in the cells, so that this can cause their death. As a result of the damage to brain cells, cerebral palsy may develop, with associated involuntary movements.

**Low birthweight infant**

The birth of a baby weighing less than 2.5kg (5lbs 8oz).

**Nuclear magnetic resonance (NMR) imaging [or magnetic resonance imaging (MRI)] and NMR spectroscopy (or MRS)**

The absorption or emission of electromagnetic energy by nuclei in a static magnetic field, after excitation by a suitable radiofrequency magnetic field. The peak resonance frequency is proportional

to the applied magnetic field. The signals from the tissue under examination can be interpreted as images (NMRI, MRI) or spectra providing biochemical information (NMRS, MRS). See, for example, op. cit. note 196.

**Necrotizing enterocolitis**

A serious disease affecting the bowel during the first few weeks of life, more common in **preterm** babies. The abdomen distends and blood and mucus appear in the stools. Intestinal necrosis and perforation may ensue.

**Periventricular leucomalacia**

Lesions in the periventricular regions of the brain, thought to be due largely to cerebral ischaemia.

**Plethysmograph**

A device for measuring volume, usually that of blood supply, in a part of the body.

**PO<sub>2</sub>**

Partial pressure (P) of oxygen (O<sub>2</sub>) measured in KPa.

**PCO<sub>2</sub>**

Partial pressure (P) of carbon dioxide (CO<sub>2</sub>) measured in KPa.

**Pre-eclampsia**

An obstetric condition occurring in the second half of pregnancy, characterized by hypertension, proteinuria and usually oedema.

**Preterm (premature) birth**

The birth of a baby before 37 weeks of gestation (calculated from the first day of the mother's last menstrual period). Very preterm is birth before 33 weeks.

**Respirator**

See **Ventilator**.

**Respiratory distress syndrome (hyaline membrane disease)**

The condition develops in a newborn infant when the lungs fail to expand after birth due to deficiency of **surfactant**. It is most commonly seen in **premature** infants. Breathing is rapid, laboured and shallow, and hyaline material collects in the terminal airways. The condition is treated by intensive nursing, intravenous fluids and oxygen, with or without positive pressure by a **ventilator**.

**Retrolental fibroplasia (or retinopathy of prematurity)**

This condition is most often seen in the extremely **preterm baby** especially, but not exclusively, in those given supplemental oxygen. It may resolve spontaneously or, more rarely, may lead to severe scarring, retinal detachment and blindness.

**Surfactant**

A wetting agent consisting of a complex mixture of compounds (including lipids, protein and carbohydrates) that prevents the air sacs of the lungs from collapsing by reducing surface tension. Its absence, as in the immature lungs of **premature babies**, leads to **atelectasis** and **respiratory distress syndrome**.

**Thalassaemia**

A genetically determined blood disease caused by an unbalanced production of haemoglobin chains with resultant anaemia, widespread in the Mediterranean, African and Asian countries.

**THAM**

See **Trihydroxyaminomethane**.

**Tonometry**

The technique of noninvasively monitoring the pressure inside an organ by flattening part of its wall to remove lateral stresses so that the internal and external pressures are equal. In the context of this discussion, the skin over the fontanelle is flattened to enable the intracranial pressure to be monitored.

**Transcephalic impedance**

Measurement of the electrical impedance of the head in order to detect changes in blood volume.

**Trihydroxyaminomethane (THAM)**

A drug that was used to counter metabolic acidosis in infants with **respiratory distress syndrome**.

**Ultrasound**

Sound waves, or mechanical vibrations, beyond the range of human hearing [one to 20 million vibrations per second (in the range of 1–10 MHz)]. By transmitting extremely short pulses of ultrasound into the body and detecting the origin of the echoes, detailed anatomical images can be built up. Ultrasound scanning of the neonatal brain produces a real-time image.

**Utero-placental insufficiency**

A reduction in the transfer of nutrients and oxygen from the mother to the fetus caused by a pathological condition at the interface separating the maternal from fetal tissues.

**Ventilator**

A piece of equipment that is manually or mechanically operated to maintain a flow of air into and out of the lungs of a patient (baby) who is unable to breath normally.





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