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Summer 1997 Meeting

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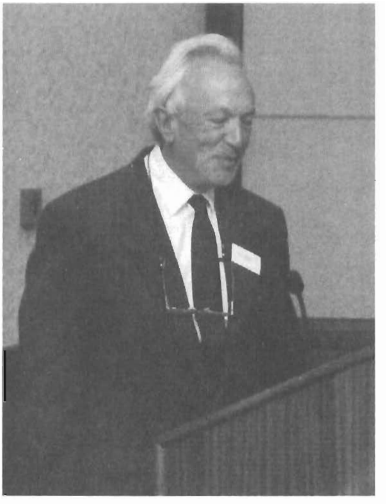

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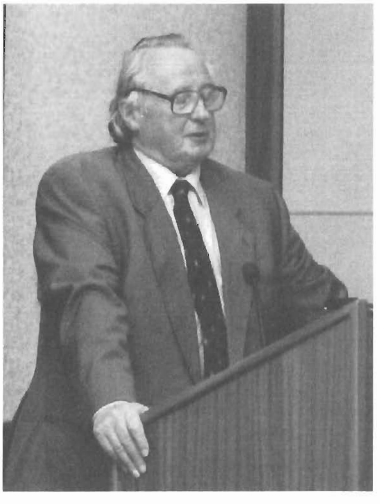

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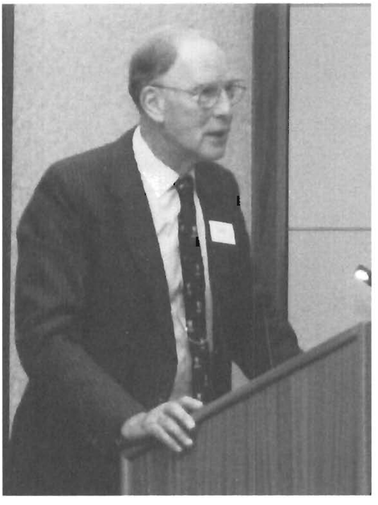

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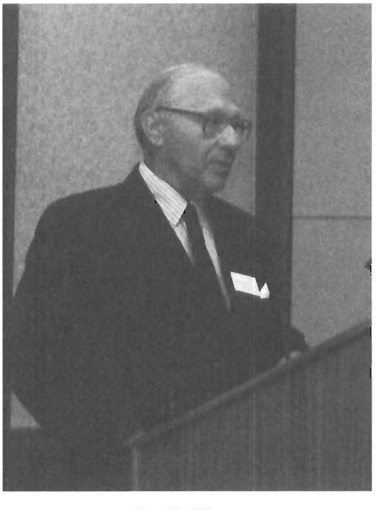

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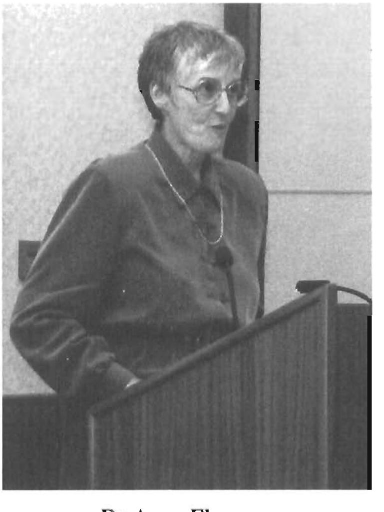

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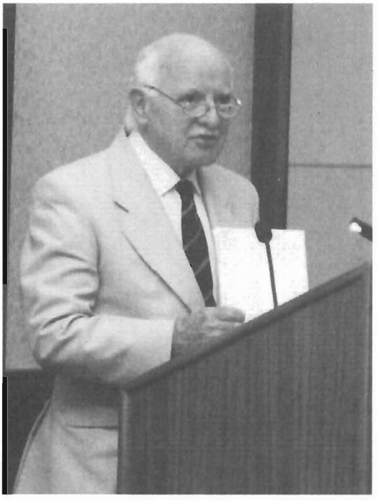

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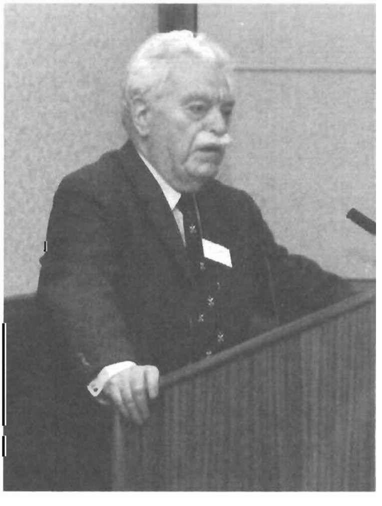

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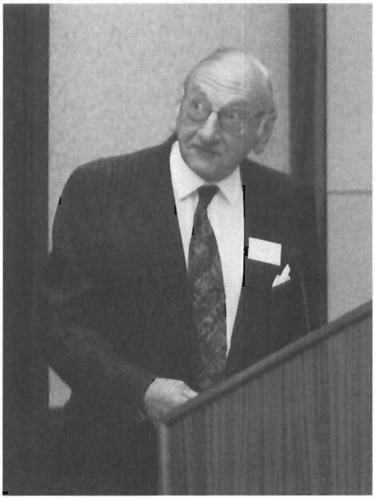

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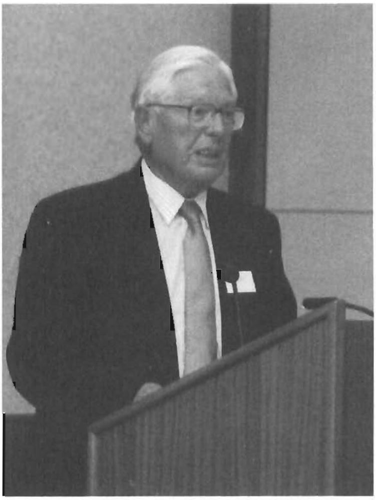

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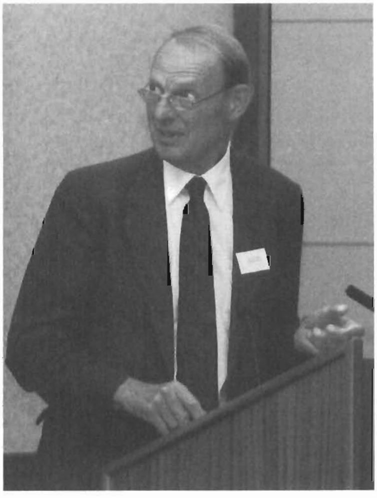

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TWO NUDGES TO PROGRESS

Professor T C Gray

I have two stories to tell. Both concern Liverpool University and doctors of initiative, who solved critical situations by nudging authorities into action and, by so doing, turned frustration and impending disaster into triumph.

The impressive gentleman in Figure 1, Dr James Campbell Brown, was Chairman of the Council of the Liverpool Infirmary Medical School and the Lecturer in Experimental Science; he was also the Public Analyst - a man of considerable stature in the town.

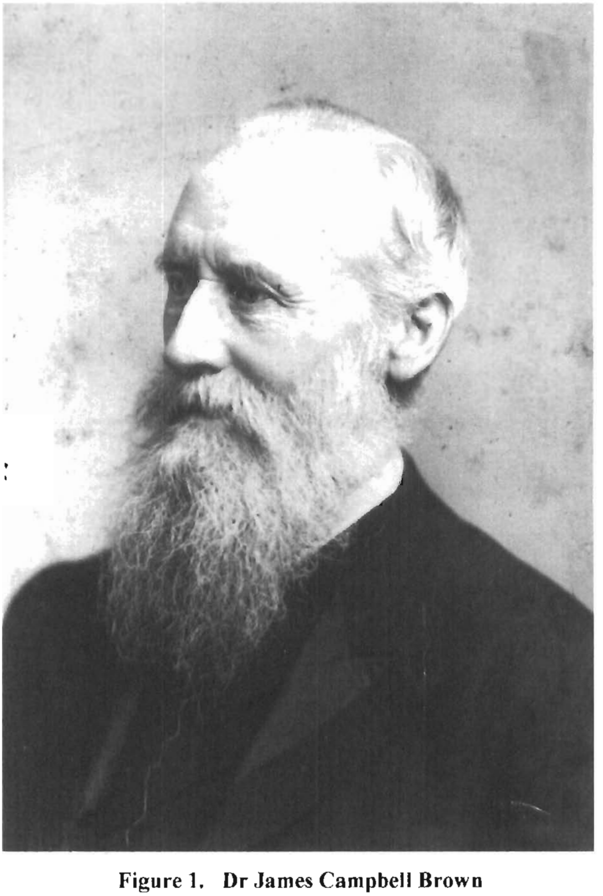

Figure 1. Dr James Campbell Brown

Until the middle of the nineteenth century, no institution in Liverpool had power to award degrees. For 43 years the University of London had allowed Liverpool Medical School students to sit its MB examination. In 1877, however, it was decided that students taking the London degree, in addition to the usual anatomy, physiology, botany and chemistry, must also have taken a course in, and pass an examination in physics.

The Liverpool Medical School had neither the personnel nor the equipment for such a course. Alarm bells were ringing loudly because Manchester's Owen's College was seeking the power to give degrees and that would be a lethal blow to the Liverpool School: it would lose its attraction to prospective medical pupils and apprentices with the result that the standard of medicine in the town would suffer.

Towards a University

Campbell Brown's nudge, made in 1877, was to persuade the Medical School to request from the city authorities the formation of 'a college for the cultivation of and practical teaching of the higher branches of knowledge, such as every other large centre of population in Britain possessed'. He then invited representatives of the town council and of the local Association for the Promotion of Higher Education to meet representatives of the Medical School Council in the Liverpool Medical Institution - the aim being to set in motion a plan for a University College. A suitable building, the vacated Lunatic Asylum, was available on ground owned by the Infirmary. That nudge had its ultimate reward in the foundation of a University College in the old asylum. The first academic appointment to it was to a Chair of Physics. The name of the physicist appointed was to become one to conjure with - Oliver Joseph Lodge; he was knighted and became a Nobel Laureate for pioneering the transmission of electrical waves. His work ultimately led to wireless telegraphy. Lodge stayed nine years in Liverpool, after which he became the first Principal of Birmingham University. The Medical School gave up its treasured independence to become a Faculty in University College and was therefore continuous with the present Faculty of Medicine. So - a nudge by the Chairman of the Medical School begat University College which, in a few years, was to develop into the University of Liverpool.

Sixty years later, a similar catalytic nudge was delivered, this time not by the Medical School, but by the Liverpool Society of Anaesthetists.

The first Anaesthetic Society in England was that in London; the second was the Liverpool Society. Its inaugural meeting was held in May 1930. At that time, anaesthetics were given by general practitioners and medically qualified ladies, some of whom were wives of surgeons and some combined anaesthesia with attendance at 'clinics'. At its foundation, the officers of the Liverpool Society were two male general practitioners, Drs O'Leary, the President, and R J Minnitt, the Honorary Secretary. The Society had been founded mainly on Minnitt's initiative but, percipiently, he preferred to be Honorary Secretary rather than President: the office of Hon Sec would give him a longer lasting opportunity to influence developments. In fact he remained Honorary Secretary until, twenty five years later, at the Society's Silver Jubilee, he allowed himself to be elected President.

Figure 2. Dr R J Minnitt

Minnitt was determined to contribute to the advance of anaesthesia. In 1925 he wrote a remarkable MD thesis on surgical shock, and the University recognised his ability and dedication by inviting him, in 1932, to become the first Honorary Lecturer in Anaesthesia. Two years later, he introduced his original 'Gas and Air' method of pain relief for self-administration by parturient mothers attended only by a midwife. For that he was awarded an Honorary Fellowship of the Royal College of Obstetricians and Gynaecologists. With a fellowship and a doctorate, he had become an anaesthetist of unique standing and was promoted to be the first statutory Lecturer in Anaesthesia in Liverpool University.

Two consequences followed, both of which, in Liverpool, were quite unheard of: an anaesthetist was invited to become a member of the Board of the Faculty of Medicine and, also against every Liverpool tradition, to serve on the Medical Board of his teaching hospital. Minnitt was now certainly in a position to influence developments in his specialty.

In 1942, when the 2nd World War was at its height, Churchill's government set up the Goodenough Committee, to plan the future of medical education. William Goodenough, a past Chairman of Barclays Bank, had been involved with developments in the field of medicine in Oxford which were being financed by Lord Nuffield. After two years of deliberation, his Committee made the proposal, then revolutionary, that Universities should establish full-time teaching and research chairs in clinical subjects. Medical Royal Colleges and Associations were invited to comment on these proposals and the Association of Anaesthetists was included.

Minnitt, on the Council of the Association, was asked to prepare, for the Goodenough Committee, a memorandum on the 'Proposed reorganisation of Medical Schools as it affected the teaching of anaesthesia'. In January 1943, he tried out his views on the Liverpool Society of Anaesthetists. In line with Goodenough, he suggested that: 'each University should have a Department of Anaesthesia and that this should be under one responsible Head. This would mean a Chair of Anaesthesia .... a whole-time appointment with a retiring age of sixty years on pension'. In character, he recommended that: 'the students should attend a course of lectures given during one term and the teaching of practical anaesthesia should be by apprenticeship and, for a period of time, Anaesthetic Clerks would be appointed to specialist anaesthetists'. As it was envisaged that, in the future, specialist anaesthetists would be available at any hour for urgent cases on rota, valuable teaching would thus be given to the anaesthetic clerks at the same time. Provision should also be made for the teaching of postgraduates who desired to specialise in anaesthesia and for refresher courses to be given to those practitioners wishing to keep up with advances in the specialty.

Liverpool University accepted the Goodenough proposals and, in October 1945, full-time clinical chairs were established and filled in medicine, surgery and in obstetrics and gynaecology. Astonishingly, Liverpool's most renowned specialty, orthopaedic surgery, was denied an established Chair, although it was the only university to have a degree in that subject. It was, however, given departmental status with a full time Director. Anaesthesia was not even mentioned.

In 1946 and early 1947, Readerships in Anaesthesia were established in the Universities of Leeds and Newcastle and it became obvious that postgraduate students and researchers in anaesthesia would gravitate to these and other academic departments unless an at least equivalent department were to be instituted in Liverpool. It was a situation, as far as anaesthesia was concerned, as critical as was that for the Medical School in 1877.

Towards a Department of Anaesthesia

The part-time anaesthetists were not keen on the appointment of a full-time academic, seeing it as a possible threat to their long-established rotas and independence. Time was passing: a Liverpool full-time anaesthetist, Dr Harbord, was appointed Reader in Leeds, but before he left, the Liverpool Society of Anaesthetists set up a committee of which I was a member, to deliberate on what could be done to persuade the Faculty of Medicine to establish an academic department. The result was a letter signed by Minnitt and Harbord, his Demonstrator, to the Dean of the Faculty of Medicine. Significantly, Minnitt signed the letter not as 'Lecturer' but as 'Honorary Secretary' to indicate the general support for his proposals of the Liverpool Society of Anaesthetists. The letter requested the rapid establishment of a full-time Department of Anaesthesia as there was a danger that the better anaesthetists would be attracted to situations where full-time departments were being established. This letter of 1946 was as significant a nudge for the development of anaesthesia in Liverpool as had been in 1877 the approach to the town by Campbell Brown, for the development of the University.

The Dean of Medicine referred this letter to the Faculty's Board of Clinical Studies for consideration. The Board was concerned about the reactions of the part-time anaesthetists and recommended that the Medical Boards of the teaching hospitals should be consulted, where the surgical members would be aware of the feelings of the part-timers. One thing Liverpool doctors would never tolerate was dictatorial interference with their terms of service. From the situation in the United States it could well appear that such interference might follow the appointment of a full-time Director. However, after persuasion by both the Dean and the Professor of Surgery, emphasising the importance of anaesthetic development for surgical progress and stressing that it was actually the anaesthetists' own Society which had pressed the Dean to take action, the Board of Clinical Studies reported favourably and the Faculty forwarded the proposals to the Senate and Council of the University. It was finally agreed that a 'Sub-Department of Anaesthesia be established within the Department of Surgery under the Headship of a whole-time Reader or Lecturer depending on experience'. However, sub-departmental status was not attractive: indeed, colleagues applying for such posts were regarded as rather letting the side down. I was fortunate enough to be accepted for the Liverpool post, but before accepting it I asked the Dean for an assurance that the Department would be completely independent of Surgery. Readers in the University were expected to be under professorial Heads of Departments; the situation was fraught. It was solved very satisfactorily when the Dean and the Professor of surgery, Charles Wells, gave an assurance that the Department would be independent, and were successful in persuading the university that, although a Reader, the incumbent should be the effective Head of the Department, allowed to submit his requests for funds directly to the Departmental Grants Committee and not through the Professor of Surgery as part of his surgical budget. This was a significant and unusual concession. Throughout my time as Head of the Department, at no time did the Professor of Surgery interfere or make any demands whatever - except for good anaesthesia when he was operating.

Acknowledgements

By courtesy of the Liverpool University Archivist, Mr Adrian Allen, this paper is based upon studies of Minutes (a) of the Liverpool Infirmary Medical School and of the Faculty of Medicine of Liverpool University and (b) of the Liverpool Society of Anaesthetists. The figures are reproduced from *For Advancement of Learning* by Thomas Kelly, with the kind permission of Liverpool University Press, from originals by the Central Photographic Department, Liverpool University.

THE LIVERPOOL COURSE

Dr G Jackson Rees
Formerly Consultant Anaesthetist, Alder Hey Hospital, Liverpool

In October 1947, Dr T C Gray was appointed by the University of Liverpool to the new post of Reader in Anaesthesia. This period was an important one for medicine in general and for anaesthesia in particular, for it was the run-up to the vesting date of the National Health Service. There were many anxieties at this time as to the place of the anaesthetist in the new health service. Dr Tom Boulton has kindly provided me with an outline of some of the steps taken to resolve these anxieties. The then President of the Association of Anaesthetists, Dr Archie Marsden had a close alliance with Lord Webb-Johnson, who was sympathetic towards Marsden's ambition to achieve a proper status for anaesthesia. He was, however, insistent that the first step should be the establishment of an examination structure which could be regarded as comparable to that for the FRCS or the MRCP. It was this view which led to the establishment of the two-part DA examinations. The first Part 1 examination was held in May 1948.

Thus when T C Gray took up his Readership in October 1947 the need was clear to him for post-graduate training of anaesthetists to meet the demands of the new examination structures. His interest in teaching had already developed, since before his appointment to the University he had held informal teaching classes for those wishing to enter the specialty. After appointment he lost little time in steering his plans through the committee structure of the Faculty of Medicine. This structure comprised a Board of the Faculty, reporting to which was a Board of Pre-clinical Studies and a Board of Clinical Studies. Reporting to the latter were Boards of Study for the main clinical divisions. There was not then a Board of Anaesthetic Studies.

Some ten weeks after taking up his office, Gray submitted to the Board of Clinical Studies a memorandum on anaesthetic training. The minutes of the Board meeting on 10 December 1947 include the following:

> 'That a committee consisting of the chairman, the Dean, Professor Wells, Mr Aldam, Dr Gray, Professors Newton, Sheehan and Woods, and two anaesthetists nominated by the Board of Clinical Studies, be appointed to consider the provision of post-graduate instruction for the training of anaesthetists.'

It is significant that the committee included the Professors of anatomy, physiology and pathology. The same meeting recommended a Board of Anaesthetic Studies be established. These recommendations were accepted by the Board of the Faculty on 16 January 1948. The new committee met on 19 February 1948. The attendance was regrettably poor; of the ten members appointed only five were present, including only one of the hospital anaesthetists. However, the form of the Liverpool course as it continued for many years was established at that meeting. The committee recommended the setting up, on an experimental basis, of a three-term course starting in October leading to the Part 1 of the DA in May and to the Part 11 in the following November. The autumn term should comprise: anaesthesia, 2 lectures per week; pathology, 2 lectures per week; physiology and physics, each 1 lecture per week; anatomy, dissection and observation; hospital practice, daily. The Lent term substituted pharmacology for one of the pathology lectures. The summer term had 1 lecture in medicine per week, and ward rounds in medicine and surgery. The course would be limited to 12 students, twelve months qualified from an approved university and having held a House Surgeon or House Physician post for six months in an approved hospital. The fee for the course should be £60. The first course was advertised in May 1948. There were 21 applicants, of whom 9 started the course in October.

It is not clear why only 9 rather than 12 were accepted. There is in existence a typescript listing the applicants with a tick opposite those selected, and there are only 9 ticks. In subsequent courses the numbers increased. Until the drift back to civilian life of demobilised service doctors, none of the Liverpool hospitals, teaching or municipal, had any junior anaesthetic staff. Rehabilitation training posts were established to bring ex-service people back into the hospitals in a supernumerary capacity for further training. It must have been difficult therefore, in the early planning of the course, to be certain of providing the clinical training. With the coming of the NHS in July 1948, a trainee staffing structure was acquired, with Junior Registrars (later designated SHOs), Registrars and Senior Registrars. Thus, by the time the course started in October there were enough Junior Registrar posts to accommodate all the course trainees.

The Reader had clearly seen it necessary to prepare the way for surgeons to accept in their theatres individuals being trained in anaesthesia. He wrote to all the surgeons in the hospitals involved explaining the new species and asking for their cooperation. I was able to find many of the replies, which were all helpful, although one expressed anxiety about the effect on the anaesthetic training of the undergraduates on his firm. When the second course was advertised the arrangements with the hospital authorities, the Board of Governors and the Regional Hospital Board, had become more formalised. Gray achieved agreement that the University should select the candidates for the course, and the hospitals would accept them for appointment to the Junior Registrar posts, of which there were at that time ten. There was also formal agreement that holders of these posts would be free of hospital duties to attend the lectures until 11am each day. This was perhaps the first time that the need for release for post-graduate teaching received official recognition by a hospital authority, and that an academic department was empowered to select junior staff for the hospitals of a Region.

The course was hugely popular. By 1952 the number of applicants far exceeded the 10 places available. To accommodate extra students, additional places were offered to those with financial support from outside the hospital service. This resulted in many overseas students on grants from their home governments, notably from Singapore, Malaya, Hong Kong and South Africa. Arrangements were made for these students to have supernumerary unpaid Junior Registrar posts to enable them to gain clinical experience.

Meanwhile on the national scene, things were moving forward. The Faculty of Anaesthetists had been formed and at the first meeting of the Board in 1948 Archie Marsden was elected Dean. Over the next four years the Faculty developed the format of the examinations for the Fellowship, the first of these taking place in October 1953. I well remember a conversation with Cecil Gray after he had been to a Board Meeting, when he told me of the plans for the very searching examination structure. He expressed the view that we were very fortunate in not having to subject ourselves to it! I think this was in early 1952, and on 10 March that year he produced yet another memorandum on post-graduate training.

In this memorandum he outlined the existing situation in Liverpool, paying tribute to the cooperation of the hospitals in the scheme. He then considered future developments. He recommended the course be extended to five terms, the first three on the lines of the old course, leading to the Part I of the FFA, followed by a Second Part course. These new arrangements, put into effect in 1954, demanded an increase in SHO posts. These were provided by the regional hospitals who were accommodating in both the time off and transport arrangements this scheme required.

Thus it was that the Liverpool course continued for many years, attracting many who subsequently became notable figures in anaesthesia. In these days of Calman the ideas involved in its formation may seem orthodox and mundane. Fifty years ago the concept was revolutionary and far-sighted and Liverpool set a pattern for post-graduate training which was later adopted by other centres and other specialties.

THE LIVERPOOL CONTRIBUTION TO THE DEVELOPMENT OF PAEDIATRIC ANAESTHESIA

Dr G Bush
Emeritus Consultant in Paediatric Anaesthesia
and Intensive Care, Liverpool.

Up to the early 1920s, the techniques of anaesthesia for infants and children were principally derived from adult practice and consisted of open ethyl chloride induction followed by maintenance with open drop ether or chloroform. Indeed in many district general hospitals these techniques were still practised as the standard method of anaesthetising children well into the 1960s.

Specialisation in anaesthesia for children was delayed by the second world war. However soon after the war, the need arose for the development of a safe and satisfactory technique for anaesthetising new-born and very young infants because of the progress being made in the techniques of operating on lethal congenital abnormalities such as oesophageal atresia and diaphragmatic hernia. Most children's hospitals at that time were served by a number of part-time anaesthetists who did not have the time or the expertise to undertake more specialised and challenging paediatric problems. Liverpool, with its three children's hospitals and multiple anaesthetists working in these hospitals, was no exception. Fortunately for the children of Liverpool and to paraphrase Sir Walter Scott: 'the hour had come, but also the man'.

Appointment of Dr Jackson Rees

Miss Isabella Forshall, who was the senior paediatric surgeon in Liverpool in 1948, recognised that a dedicated and innovative anaesthetist was essential if neonatal surgery was to be performed successfully. Dr Jackson Rees was at that time working in the University Department of Anaesthesia. He was then detailed by Dr, later Professor, Cecil Gray to go to Alder Hey Children's Hospital to pioneer new techniques for this work. As is now known, the rest is history. Miss Forshall also needed expert surgical assistance and she was able to recruit an enthusiastic and flamboyant helper, Peter Paul Rickham, who subsequently became Professor of Paediatric Surgery in Zurich.

Simple solutions are the most effective. Following his experience in adults using the Liverpool technique of controlled ventilation with relaxants, Dr Rees rapidly realised that this technique could be easily adapted to children using an anaesthetic circuit derived from the T-piece described by Dr Philip Ayre from Newcastle in 1937, by the addition of a small open ended reservoir bag to the expiratory limb.[1] This technique proved so successful that in the children's hospitals in Liverpool it came to be used in nearly all paediatric patients.

Within a year, Dr Alan Stead became the first of many dedicated, hard-working colleagues inspired by the example set by Dr Rees, to assist in providing the necessary cover for this time-consuming, challenging but highly rewarding work. Alan Stead, using extremely primitive equipment by today's standards, was able to show that compared with the adult, the new-born infant had a different response to muscle relaxants, being sensitive to the non-depolarising but resistant to the depolarising muscle relaxants. This pioneering work laid the foundation for the safe use of these drugs in paediatrics. Definitive evidence of the benefits of this basic technique and its very low complication rate was provided when Dr Gordon Pledger, a senior registrar at Alder Hey Children's Hospital in the 1960s, undertook an in-depth review of this method of anaesthesia, for which he was subsequently awarded his MD. This review was an early example of what is now known as a 'clinical audit'.

The success of the anaesthetic technique soon led to its application outside the operating theatre - in the neonatal surgical unit and equally importantly in the paediatric wards, for the treatment of respiratory failure, particularly in patients suffering from bronchiolitis due to viral or bacterial infection. Drs Frank Wilson and Ian Nesbit in the late 1950s recruited nurses and medical students to provide positive pressure ventilation for these infants on the wards throughout the 24 hours using a simple T-piece with the tail of the bag connected via a Y-piece to an underwater blow-off bottle. The publication of their work in the *British Journal of Anaesthesia* in 1958[2] was an important landmark in the development of intensive care in infants and children. They showed that tracheal intubation, either intermittently or sustained for short periods of a few days, could be used safely providing care and the correct-sized tracheal tube was used. They recorded the remarkable case of a neonate with tetanus at Alder Hey Children's Hospital where a tracheal tube had been retained in position for 34 days and bronchoscopy performed twice daily, without marked laryngeal oedema or any subsequent stenosis. Furthermore they reinforced the suggestion of Dr Rees that positive pressure ventilation was well tolerated in infants although they stressed that 'the pressure during the expiratory phase should be zero'. This was very difficult to accomplish with their ventilation circuit since they were, in fact, using positive end-expiratory pressure ventilation. It is conjectural, in the light of subsequent knowledge, whether their good results with 13 survivors out of 18 patients treated would have occurred if they had actually achieved a zero pressure during the expiratory phase. Wilson in 1958 also developed the Alder Hey tracheostomy tube, which facilitated positive pressure ventilation and assisted weaning from a tracheotomy.

Spreading the word

The late 1950s and early 1960s saw the dawn of specialised paediatric anaesthesia throughout the world, led by Dr Robert Smith of Boston, Dr Robert Cope and his colleagues from Great Ormond Street Hospital for Sick Children, London, Dr Digby Leigh from Los Angeles, Dr Alan Conn from Toronto, Dr Mary Burnell from Adelaide and Dr Margaret McClelland from Melbourne - and of course Dr Jackson Rees from Liverpool. Scientific symposia, and hospital visits by Dr Rees to many parts of the world led to an increasing awareness and appreciation of the Liverpool technique of paediatric anaesthesia. With his quick wit and remarkable clinical acumen, Dr Rees was a most popular and sought-after speaker and became an intrepid world traveller. Dr Peter Morris remarked in his citation at the 1992 presentation of the John Snow Silver Medal of the Association of Anaesthetists of Great Britain and Ireland to Dr Rees that, although he had been privileged to visit many countries, he always found that Dr Rees had been there at least twenty years previously! As a result of these visits, the Department of Paediatric Anaesthesia in Liverpool was proud to act as host to many visitors from abroad who were keen to see if the Liverpool technique was not only actually practised but also succeeded. A direct result of the spread of this teaching was a host of trainee anaesthetists from many countries who obtained junior posts at the Royal Liverpool and Alder Hey Children's Hospitals. Having been thoroughly indoctrinated they returned home, and there are now devotees schooled in the Liverpool technique in paediatric hospitals throughout the world.

The excellence of the training at the Liverpool Children's Hospitals was, of course, also recognised by trainees in this country. Many taking part in the postgraduate course organised by the University Department of Anaesthesia and from other centres, came to undertake training in paediatric anaesthesia. These trainees, during the course of their tenure, obtained comprehensive experience in all branches of paediatric anaesthesia and intensive care because of the large number of patients with a wide variety of surgical and medical conditions including emergency work, passing through the Paediatric Anaesthetic Department. At this time it is estimated that approximately 12,000 paediatric patients were being anaesthetised per annum.

During the 1960s and 70s, the Department pioneered a number of postgraduate courses in paediatric anaesthesia for trainees and consultants from the UK and abroad. As no national courses were then available, these were well attended and appreciated. By this time the Department had six consultants.

Scientific studies

The Liverpool technique led to numerous studies in collaboration with Dr Nightingale, investigating the clinical use of muscle relaxants in paediatric practice. Landmark papers have been published on relaxants in neonates, infants and children. Inevitably the major employment of these drugs has exposed complications, but it is noteworthy that despite the regular use of tubocurarine, as far as I recall, we never had a case of bronchospasm, nor of the neostigmine-resistant curarisation which was so dreaded in the adult in the early 1960s. Since suxamethonium in single or intermittent doses was frequently used for operations lasting up to 20 minutes, a series of important responses were reported in association with this agent. These included the lesser incidence of muscle pains in younger children, the cause, hereditary pattern and management of children who develop prolonged neuromuscular block, the susceptibility of burned patients to develop cardiac arrest, the dangers of arrest in patients with progressive muscular dystrophy of the Duchenne type, the biochemical effects of its administration during halothane anaesthesia and the increased incidence of dreaming which could be reduced by prior administration of tubocurarine.

Whilst it was appreciated that with spontaneous respiration a high gas flow into the T-piece circuit was necessary to prevent re-breathing, the precise gas flow requirements in conjunction with the 'Jacksonian' type of controlled ventilation had not been determined. Meticulous work by Tony Nightingale in 1978 based on his studies estimating the carbon dioxide output in anaesthetised children led to the practice of using a derived formula during controlled ventilation to achieve a steady mild hypocarbia. Tony Nightingale is still the UK representative on the International Standards Organisation seeking greater uniformity and safety in paediatric equipment.

One of the greatest advances in paediatric intensive care has been the widespread use of prolonged tracheal intubation. Dr Rees has, in a previous lecture to this society, drawn attention to the pioneering work in this field by Dr Keith Sykes in South Africa, Dr

Brandstatter from Beirut and Drs Allen and Steven from Adelaide in 1964. Once this work was published, its importance was immediately recognised world-wide. Dr Rees was most impressed by its clinical application and following his return from Australia in 1964, he devised a special tracheal tube which became the standard method for all children requiring prolonged airway protection in the Liverpool Children's Hospitals.

Reference has already been made to Dr Rees' observation in 1958 that positive pressure ventilation was well tolerated in infants. Following further clinical observation, often in the middle of the night, he became convinced that an expiratory resistance was not only well tolerated but was of great benefit. He stated at the World Congress of Anaesthesiology in 1986 in London that:

> 'In abnormal lungs having a high airway resistance, an expiratory retard is desirable. An expiratory resistance of 5cm H_2O can make a large difference to the oxygenation in these circumstances. This can be appreciated if one looks at the type of ventilation exhibited by an infant in respiratory distress. As he pulls down his diaphragm, the upper part of his chest collapses. Then he closes his glottis and holds air in his chest whilst he redistributes the air from one part to another, producing a grunting noise. He is deprived of this mechanism for achieving adequate distribution of air if he is intubated and I believe that the application of expiratory resistance is invaluable in a great number of cases.'

The increase in arterial oxygenation following the institution of a continuous positive airway pressure was confirmed some years later by research workers in San Francisco. This was a truly remarkable contribution to paediatric respiratory physiology arising from astute clinical observation.

Liverpool paediatric anaesthetists have been at the forefront in welding together anaesthetists in the United Kingdom and other paediatric centres throughout the world, culminating in the inauguration of the Association of Paediatric Anaesthetists of Great Britain and Ireland in 1974 and in 1989 the Federation of European Associations of Paediatric Anaesthesia. In 1993 the Third European Congress was held in Liverpool.

I have highlighted just some of the contributions made by the many involved in anaesthesia in the Royal Liverpool Children's Hospitals at Myrtle Street and Heswall and Alder Hey Children's Hospital during the last 50 years. Their work of course continues, improving the safety and acceptability of paediatric anaesthetic practice.

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THE BLEASE BROTHERS*

Dr T H L Bryson
Retired Consultant Anaesthetist, Liverpool Maternity Hospital

John and Dick Blease were two Merseyside brothers who were motor engineers in the years before World War II. They set up business in Moreton on the Wirral where they were successful in repairing and maintaining the cars of the local residents.

One of their customers was a doctor who combined general practice with an interest in clinical anaesthesia. He had designed an anaesthetic machine and sought the help of the Blease brothers to make the machine and help sell the apparatus. One of the brothers, John, became very interested in the machine and learned how to induce and maintain anaesthesia in order to promote its sales.

The local surgeons soon recognised his anaesthetic skills and he was called to administer anaesthetics at the local hospitals. Indeed, during the war he became a mainstay of emergency anaesthesia in Birkenhead and carried a document describing him as an emergency anaesthetist to enable him to pass through the road blocks which were set up during the blitz.

After the war, John gave up motor engineering and set up his own company to design and build anaesthetic equipment which still exists at the present time and has recently won the Queen's Award for Export Achievement. This required him to leave Merseyside and move to London. However, on retirement, he returned to live at Heswall, Wirral, continuing his hobby of repairing and building clocks and watches until his death in 1985 aged 79.

The Liverpool Society of Anaesthetists in 1983 paid tribute to this remarkable man who made a great contribution to the development of anaesthesia by electing him to Honorary Membership of the Society.

* Summary only, at author's request. Ed.

SAMPSON LIPTON AND THE PAIN FOUNDATION

Dr D Bowsher
Retired Hon.Consultant Neurologist, Pain Relief Service

Sam Lipton, who died of malignant secondaries from an unknown primary on 6 December, 1994, was the moving spirit behind the Pain Relief Foundation and its Research Institute. He was born in Liverpool on 18 April 1922, and educated at the Liverpool Institute and the University of Liverpool; he qualified in medicine in 1944 at the age of 22. He was appointed Consultant Neuroanaesthetist to the (then) Mersey Regional Neurosurgical Unit in 1950, at the early age of 28. He gained the DA in 1949 and the FFARCS in 1954.

From the beginning he took an interest in postoperative pain and was soon called upon for advice in chronic pain problems on the Unit. Because of his gregarious nature, his interest in pain soon became known in the large general hospital (Walton Hospital) to which the Regional Neurosurgical Unit was attached; his advice was sought by other consultants, particularly orthopaedic surgeons and oncologists.

Within a year or two Sam was putting aside one or two half days a week for consultation on, and treatment of chronic pain cases. These he treated for the most part by nerve blocking techniques, analgesics having already been used by other consultants without success. By 1953/54, he decided to set up a separate Pain Relief Service, Europe's first clinical service for the relief of chronic pain. As it grew, he began by the late 50s or early 60s to encounter considerable difficulties with the byzantine administration of the National Health Service, who objected that there was 'no precedent' for such a service. In characteristic style, Sam cut the Gordian knot by having 'Centre for Pain Relief' printed above 'Regional Neurosurgical Unit' on the hospital's headed notepaper. As soon as the administrators began to see letters on this notepaper they, equally characteristically, assumed that the service must exist, as it had its own headed paper! Within a year or two, during one of the National Health Service's administrative reorganisations, the name was sanctified and Dr Lipton was officially named as its full-time Director, at which time he ceased giving anaesthetics.

One of the key features of Sam's enthusiastic personality was that as soon as he heard of a new method he went off to learn about it, then came back and tried it out. Thus, he performed nearly 1,000 percutaneous cordotomies in the course of his career. As soon as he heard of trans-sphenoidal injection of alcohol for pituitary destruction being performed in Rome, he rushed off to learn about it and quickly introduced it into our therapeutic armamentarium. His interests were not confined to 'conventional' medicine. In 1972/73 our Centre was the first National Health Service clinic to use acupuncture for pain relief. This was done at the same time as we began to insert stimulating electrodes over the dorsal columns of the spinal cord. When more cautious colleagues said they had heard of therapies such as insertion of electrodes or use of unconventional drugs, he insisted that we tried them on the next available case. Lack of recognised surgical training never deterred Sam! We were able to employ a medically qualified acupuncturist for one session a week, so continued with this form of therapy for many years. A year or two after the introduction of acupuncture, we got a 'healer' to come down from Scotland and demonstrate his amazing powers - which included relieving the pain of tennis elbow in cynical Sam! But a few years later, a part-time lay healer was found to join the team of the Pain Management Programme by Sam's former Senior Registrar and successor, Chris Wells, as Director of the Pain Clinic.

Although Sam obtained some small grants from drug companies and the (then) Mersey Regional Research Committee, he was never a fundamental researcher on his own. However, he encouraged others to undertake research on his patients, and did all he could to facilitate it. He was always willing to prolong procedures so that recordings could be made, or to find suitable patients for a project investigating some particular aspect of pain.

By the late 1960s, other doctors were beginning to take an interest in the treatment of chronic pain, and started to come to Walton Hospital to learn from Sam. He became famous for his precept: 'See one, assist at one, do one' as a method of teaching pain relieving techniques. At the same time, he began to travel all over the world to learn new methods himself, and frequently gave invited lectures on his own methods and experience; he thus built up a huge international network of clinical pain relievers who exchanged ideas and experience, though without any formal organisation. During the 1960s he devoted much time and thought to the organisation of his own and other pain relieving services. He recruited health professionals with skills other than his own: physiotherapists, neurologists, neurosurgeons, orofacial specialists, psychologists, psychiatrists, physical medicine specialists all worked officially or unofficially in his Centre for Pain Relief, thus building up the service.

Sam's reputation as a pain reliever grew steadily. By the middle of the 1970s, only two thirds of patients at the Centre for Pain Relief were 'local', the other third were referred from other parts of the British Isles and overseas. He wrote extensively on his methods, many of which, because of their pioneering nature, could be regarded as clinical trials. Later he spoke on the radio and appeared on TV programmes, in which he was a 'natural'. When an organisation for pain relieving clinicians (The Intractable Pain Society of Great Britain and Ireland) was formed, he became its President in the second year of its existence. He later (1984-1991) served as President of the World Society of Pain Clinicians.

Honours began, rightly, to accrue to Sam. In 1981, he was Hunterian Professor at the Royal College of Surgeons; in 1982 he was awarded the Merseyside Gold Medal for outstanding achievement and in 1984 he was appointed an Officer of the Order of the British Empire (OBE) for services to medical science. In 1986 he received the Pask Certificate of the Association of Anaesthetists, for outstanding contributions in the field of anaesthesia and analgesia. In 1987 his alma mater, the University of Liverpool, awarded him the degree of MD *Honoris Causa*. He was a founder member of the International Association for the Study of Pain, and served on its International Committee and in 1989 he was elected one of its first Honorary Members.

By the 1970s, formal courses of instruction had begun at the Centre for Pain Relief, in addition to the ever increasing number of 'attachments' for visitors from Britain and abroad. It would not be an exaggeration to say that the majority of British pain relieving physicians, and a goodly number from many other countries, received some or all of their training from Sam.

We have noted that Sam was always active in collaborative research with colleagues in basic and clinical sciences. During the second half of the 1970s, he began to formulate the notion of setting up a research institute for the investigation of *human* chronic pain. He argued that such an institute should be associated with the Centre for Pain Relief, which was attended by an ever increasing number of patients, and had become (perhaps always was, given its long history) the largest pain relieving clinic in Europe. It was mainly through his initiative that in 1978/79 the Pain Relief Foundation was set up as a charitable trust by Sam and his colleagues, David Bowsher and John Miles. Because of the fame of Sam Lipton's name in pain relieving circles, it was possible at an early stage to obtain a substantial priming grant. With the help of this money, added to smaller sums which had been received as fees for teaching courses or as donations for research, the Foundation's Pain Research Institute was able to open its doors and begin work the following year - embodying another favourite precept of Sam's: 'Do not waste time messing about with Committees - get on with it and do something'.

From the beginning of the Pain Relief Foundation's Pain Research Institute, Sam Lipton went untiringly round the country raising money for its activities, in addition to his work as Medical Director. As a Trustee, he insisted that the Foundation support research and education *outside* its own Institute, as well as within it, thus making it possible for the Foundation to offer research and education grants through the (British) Pain Society. He continued actively to participate in and encourage all the research and educational activities of the Pain Research Institute, as well as to give unstintingly of his time and energy in the direction of its affairs until a few weeks before his death.

Were it not for John Bonica (who died in September 1994) on one side of the Atlantic and Sam Lipton on the other, it is unlikely that pain relief as a clinical discipline and The International Association for the Study of Pain as a clinico-scientific forum would ever have come to exist in their present states.

Sam retired a little early from the NHS. While continuing to play an active role as Medical Director of the Pain Research Institute, he also managed to gain a BA in Mathematics at the Open University in 1986. Sam was married to Gloria (née Fox) in 1954. She qualified as a solicitor, having taken a law degree as a mature student at Liverpool University, and worked in the Crown Prosecution Service until shortly before the unexpected onset of his final illness. They have two sons who are both medical graduates of Manchester University and now consultants in the Health Service.

JOHN DUNDEE IN LIVERPOOL

Dr J Riding
Formerly Consultant Anaesthetist, Liverpool Health Authority

Those of us who knew John Dundee during his period in Liverpool universally recall him as a colourful, remarkable and unforgettable figure. The students who attended the post-graduate courses on which he lectured from 1951-58 will each retain vivid memories of this unusual personality.

John Wharry Dundee was born at Larne in Northern Ireland on 8 November 1921. After education at Ballyclare High School, he graduated at Queen's University, Belfast in 1946. As a student he played in a dance band and was a part-time member of ENSA between 1941 and 1944. It is believed that these activities helped to finance his studies.

After house appointments at the City and County Hospital, Londonderry, he was appointed resident anaesthetist at that hospital in 1948, and obtained the D A (Ireland). A year later he made his way to Liverpool, like many graduates from N I. Sir Ivan Magill, who was a house officer at the Stanley Hospital, Maurice Burrows, who joined the post-graduate course and H H McWilliam, the legendary medical superintendent at Walton Hospital, to which John came as Registrar in 1949 were a few of the distinguished migrants.

John Hargreaves, at that time chief anaesthetist at Walton recalls how quickly he saw that John was 'an exceptionally able anaesthetist', a 'highly beneficial influence on the rest of the staff, especially the juniors' and a 'regular powerhouse'. His 'high principles, colossal energy and immense enthusiasm' were early in evidence and marked him out for rapid advancement.

These characteristics observed by John Hargreaves were evident to all those with whom he came into contact throughout his years in Liverpool. What impelled him to take up a career in anaesthesia, I have been unable to establish. The question is of interest because many ambitious graduates aspiring to a career in clinical medicine were more attracted to what were then regarded as the major specialties of medicine, surgery and obstetrics.

Word of the young man's exceptional abilities and original mind quickly spread and in 1950 Cecil Gray appointed him Lecturer in the University Department. He had by this time passed the D A (England). The postgraduate course of that year, of which I was a member, attended his lectures with pleasure and profit for he was a lively, humorous and kindly teacher whose material was always well prepared and up-to-date and was delivered with enthusiasm and lucidity. He maintained an informal atmosphere and possessed the gift of encouraging comment and opinions from the more reticent members of the class. A special interest in pharmacology was clearly evident at this early stage in his career, although he lectured most capably on a diversity of topics, including refrigeration analgesia and anaesthetic apparatus.

In many ways his most valuable role was as supervisor of abstract and discussion groups. Each member of the course was given a topic, provided with selected references, asked to study the literature and then to prepare an abstract for circulation to the class. The member subsequently presented the results of his or her survey and these were discussed by the group, often at length and vigorously. In this way, over several years, John introduced young people to the study of journal literature and to the elements of speaking before an audience - both activities being quite new to most students at that time. As a clinical teacher, he was excellent, imparting information easily and continuously. Whilst testing a trainee's knowledge constantly (for he was rarely silent!) he did so in such a fashion that we enjoyed working with him in the operating theatre.

John's interest in research was evident from a very early stage. His thesis on aspects of thiopentone anaesthesia led to the award of the degree of M D of The Queen's University, with commendation, in 1951. He had already published work before this, and thereafter a stream of papers on clinical and laboratory research and clinical reports poured forth throughout his years in Liverpool, continuing by the end of his career to a total of more than 500.

During the 1950s, his principal interest lay with thiopentone and other barbiturates. Such aspects as the influence of bodyweight and sex on dosage requirements, the phenomenon of acute tolerance, the effects of renal and hepatic dysfunction and the importance of redistribution all led to publications. As Professor R Clarke has stated, John was one of the earlier workers in the field of pharmacokinetics before this term was widely used. These studies led to the appearance in 1956 of his monograph *Thiopentone and other barbiturates*, described by Professor Mushin in his review as ..probably the most important contribution to the literature on the thiobarbiturates'.

Intravenous anaesthetics were not by any means his only field of interest and he published work on muscle relaxants, adrenal insufficiency, dystrophia myotonia and phenothiazines amongst other subjects. With L F Tinckler he drew attention to the exaggerated and sometimes alarming response to injection of pethidine in patients suffering from severe liver damage. As non-barbiturate intravenous agents were developed, so his studies widened.

Much of his time was devoted to the work of the Neurosurgical Unit at Walton Hospital. When the French work on artificial hibernation appeared, he was quick to see how this might be adapted to permit safer arterial hypotension for the better performance of intracranial surgery and especially that for subarachnoid haemorrhage. The technique he developed, and the results obtained in 50 cases, were published in 1956. Although now superseded, it represented a valuable advance at that time. With Cecil Gray and others he had already published an account of the use of hypothermia with autonomic block in general surgery.

John Dundee was a regular speaker at the Liverpool Society of Anaesthetists, his first appearance being in 1950, when just 29, on anaesthesia for intestinal obstruction. His appearance at the LS A became a keenly awaited annual event. Perhaps of unusual interest in so young a man was his attraction to the history of anaesthesia. In 1952 he presented a well-researched and illustrated paper on David Waldie and his role in the story of chloroform anaesthesia, which was later published. In the following year he spoke on artificial hibernation. He spoke also at the Section of Anaesthetics of the RSM, and to many local societies, often on abnormal responses to thiopentone. The newly introduced anti-hypertensive drugs, corticosteroids and tranquillisers were of great interest to him. He reviewed the subject of drugs influencing the responses of patients to anaesthetics in 1958, in a paper which had great practical value at that time.

In 1955, he travelled to Philadelphia to spend a year as research fellow at the University of Pennsylvania and as staff anaesthetist at the University Hospital. During that fruitful year, apart from publications arising from research, he delivered some half dozen papers to learned societies in the United States and Canada. In the year after his return, he submitted a thesis for the degree of Ph D Liverpool. I well recall the day of the viva voce examination as he waited in the office we shared. The normally ebullient and cheerful John fell prey to doubts as he prepared to be examined by Cecil Gray and the formidable Gar Pask. Happily, all went well.

A less well-known aspect of his contributions to anaesthesia whilst in Liverpool was his keen interest in the management of chronic pain. In about 1952 he assumed the running of the clinic started by Cecil Gray a few years earlier. He rapidly established excellent relationships with surgeons and physicians, particularly Dr Eric Baker Bates. He established, contrary to the then current opinion, that local analgesia could sometimes be effective in providing worthwhile, and occasionally permanent relief in non-malignant conditions. I recall a patient with a recurrence of tic douloureux who had had almost ten years without symptoms following Gasserian ganglion blockade using lignocaine. Neurolytic drugs he found were all too often effective for disappointingly short periods. He was always alert to the possibilities of new techniques. When Robert Maher, the Rochdale physician, published his technique of using phenol by spinal injection, he lost no time in arranging a visit to study the matter at first hand. Immediately, Maher's technique was adopted and was used in selected cases for the next 25 years.

John was fearless and became expert with the needle. It will be recalled that spinal and regional blocks were not widely used in the 1950s. This may be explained by the Woolley and Roe case of 1953, the serious complications following the use of Efocaine, and the advances in quick and convenient general anaesthetic techniques. It is horrifying to recall that blocks of the Gasserian ganglion, the coeliac plexus and the lumbar sympathetic chain were performed in the outpatient clinic, without radiological control, and without the precautions against infection regarded as normal today.

His deep interest in the pharmacology of analgesics led to extensive study of their use for chronic pain, a field of medicine exciting little general interest at that time. He promoted the value of oral analgesics, especially for cancer pain. Strong analgesics asserted in the laboratory to be equipotent were, he stressed, not necessarily equipotent, nor associated with equivalent side effects, such as dizziness and nausea, in the individual patient. This point was clearly confirmed by the results of trials of analgesics made in each patient suffering pain of malignant origin. He was constantly concerned with the brevity of action of strong analgesics. As new groups of drugs such as phenothiazines, tranquillisers and anti-depressants appeared, so he studied the possibilities of extending analgesic action by combining one or more of these drugs with conventional analgesics. Geoffrey Burton recalls 'his astute ability to categorise and label the degrees of disability which a patient showed before, during and following some type of therapy', thus enabling him to obtain values for use in statistical comparisons. A paper summarising his experience of the use of drug combinations over a five year period were published in 1957.

A sympathetic, approachable and optimistic manner ensured that he was very popular with patients attending his clinic, some of whom enquired after his welfare years later. This fortunate constellation of attributes was much needed in a clinic of last resort. One of John's outstanding features was a tireless restless energy. This was combined with a fierce, though largely concealed, ambition, great self-confidence and an insatiable scientific curiosity. Again, as Geoffrey Burton put it, he was 'apparently able to put in' about 24 hours per day with a negative amount 'left over for sleep'. He was popular with senior and junior colleagues, though he was outspokenly critical of anything approaching disinterest or idleness. His good humour, practical kindness and special concern for overseas post-graduates were greatly appreciated. He would, for example, offer to relieve juniors who had been too long on duty and would spend time generously to help and advise in the preparation of lectures or on setting up research projects.

John could be a formidable opponent and occasionally displayed a brisk temper. A famous story concerns his appointment to the session at which a particularly difficult ENT surgeon worked. On arrival at 9am, John was confronted by the surgeon demanding that only open ether should be used. An altercation ensued and by 10.30am John was back in the Department, having been to the Regional Hospital Board office to resign the session.

For him, material for research was to be found everywhere, and each patient, it seemed, merited an entry of some sort in the research notebook he invariably carried.

He and his wife, Sally, lived in a flat above Dr Sellwood's general practice surgery in Walton, Liverpool, very near to Walton Hospital. John undertook surgeries to help out in the general practice and to help meet the rent. He was thrifty in private life and yielded to few in the matter of how far a pound could be made to stretch. Leisure activities could be strenuous as when he and his wife took up the then popular pastime of square dancing. He took a keen interest in football. Photography was also one of his interests. He photographed (and perhaps travelled on) the last tram journey in Liverpool. A deeply religious man, his convictions profoundly influenced the conduct of his life. He was a capable church organist and played other musical instruments including the accordion to great acclaim at the Department of Anaesthesia Christmas parties.

For John Dundee, his period in Liverpool, first at Walton and then at the University Department, was a crucial stage toward achieving his constant goal of returning to The Queen's University of Belfast. It was an immensely fruitful period, for his own career, and for the beneficial influences he brought to bear on so many young anaesthetists. He was ever conscious of his indebtedness to Cecil Gray, for encouraging his academic development in every way possible and for making available every facility for the conduct of research including collaboration with members of the Department of Surgery. In return, John's loyalty and devotion to the Department never wavered and his contribution to the Liverpool scene was outstanding.

When John Dundee returned to Belfast as Head of Department, all were sorry to see him go. Yet we knew that the time had arrived for the next step in what was to prove a remarkable career.

DAVID WALDIE AND THE CHLOROFORM SCENE IN LIVERPOOL

Dr Anne Florence
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As Liverpool featured at the dawn of the chloroform age it is appropriate, in the sesquicentenary of James Simpson's use of chloroform in midwifery and surgical practice, to explore the Liverpool scene and, once more, attempt to tell the story of David Waldie whose work almost certainly contributed to Simpson's success in November 1847. Waldie received scant recognition from his contemporaries, particularly Simpson, but subsequently gained considerable coverage in the popular press. For many years the mention of anything remotely connected with anaesthesia, Simpson or Linlithgow was invariably followed by correspondence about Waldie. Alas, much that was written is inaccurate, highly speculative and frequently without foundation. With the help of letters written by Waldie and other material to be found in the archives of the Liverpool Medical Institution, this dissertation aims to clarify the life of an early pioneer to whose researches humanity owes a great debt.

David Waldie was born on 27 February 1813 at the Cross, Linlithgow, above the shop in which his father ran a chemist and druggist business eventually inherited by David's younger brother, George. David Waldie was educated at Linlithgow Grammar School before proceeding to the Royal College of Surgeons of Edinburgh where he received his diploma in 1831. This was the year in which Samuel Guthrie, an American army surgeon, attracted by the description of chloric ether which he found in Silliman's *Elements of Chemistry*, set out to prepare this chemical. Accounts are inaccurate, but it has been suggested that Guthrie produced pure chloroform by distilling alcohol with chlorinated lime. Almost simultaneously, Souberain prepared a similar compound which he named bichloride of lime and in 1832 Liebig prepared chloride of carbon which became known as perchloride or terchloride of formyle. This sweet-tasting liquid with an agreeable smell had a specific gravity of 1.480, a boiling point of 141^{o} F and evaporated readily at room temperature. It was fully soluble in strong spirit but only sparingly soluble in water. In 1834 Dumas accurately determined the composition of this chemical and gave it the name chloroform. However, it continued to be referred to as chloric ether or perchloride of formyle for many years.[1]

There is no documented scientific record but it is apparent from correspondence available in the Liverpool Medical Institution that chloric ether was introduced into medical practice in this country around 1836 by Dr Richard Formby, a physician at Liverpool Royal Infirmary. He used it to treat hysteria. Between 1838 and 1839 Dr Brett, principal chemist in the laboratories of Liverpool Apothecaries' Hall at 4 Colquitt Street, received a prescription for an unfamiliar compound, chloric. He found the formula in the *United States Dispensatory* and used it to produce a 'spirituous solution' which became rapidly popular amongst the physicians of Liverpool, in particular, Dr Formby.

Waldie - the chemist

After qualifying, David Waldie practised for a short time as a surgeon and apothecary at 67 High Street, Linlithgow. He was, however, principally interested in chemistry and abandoned his medical career to become a chemist at Apothecaries' Hall, Liverpool, between 1839 and

1840. He immediately came into contact with the impure chloric ether which had been prepared by Dr Brett. When he succeeded Brett as senior chemist, Waldie found that his method of preparation yielded a product which contained a high proportion of undecomposed spirit. It was not of uniform strength and frequently had a disagreeable flavour. Waldie experimented with this liquid and subsequently perfected a method of separating and purifying the active constituent, chloroform, which he washed thoroughly before dissolving it in a small quantity of pure spirit. He thus prepared a liquid of uniform strength and quality with a specific gravity of 1.500. He made this available to the physicians of Liverpool and subsequently reported that:

> 'Those members of the medical profession who are in the habit of using it, prefer it greatly to sulphuric ether, as possessing all its remedial value and being very much more agreeable'.

Waldie quoted Dr Imlach's description of its use in the treatment of severe facial neuralgia:

> 'It removed the pain and produced sleep and the next night it was so much better that none was required. It was repeated five times on alternate nights and the health, strength and appetite became much improved.'[2]

Unfortunately, Waldie's work was interrupted by a fire which destroyed the warehouse and laboratories of Apothecaries' Hall on 17 July 1846. Perhaps hampered by this catastrophe, Waldie did not publish or even publicise his method of preparation of pure chloroform. At this time he was obviously aware that Jacob Bell, a London chemist had, in early 1847, prepared impure chloric ether for use as a substitute for sulphuric ether, for which he claimed success. In March 1847, another chemist, Furnell, recommended that Holmes Coote, a surgeon at St Bartholomew's Hospital, try an available preparation of chloroform. This trial ended in failure. Waldie attributed these failures to the fact that the preparation used was composed principally of alcohol.[2]

Waldie and Simpson

In October 1847 during a visit to Scotland, Waldie met his old friend and college contemporary, James Simpson. The Scotsman was already familiar with chloric ether. Following his marriage to the daughter of a Liverpool shipowner, Simpson paid frequent visits to that city and became acquainted with many of the physicians. It was well-known that Simpson had experimented with vapours for some time in his quest for a volatile substance which would induce insensibility to pain. It is therefore not surprising that Dr Formby had drawn his attention to chloric ether around 1845.[3] In an account of his meeting with Simpson, Waldie wrote:

> 'Being well acquainted with the composition and volatility, agreeable flavour and medicinal properties of chloroform, I recommended him to try it promising to prepare some on my return to Liverpool.'

It is possible that Waldie described the method of preparation of the pure form with Simpson. Alas, before Waldie could provide the chloroform, Simpson procured some and discovered the effect of its inhalation. In the company of at least two of his assistants 'some chloroform, which a local chemist had prepared, was tried out by chance on the night of 4 November 1847'. The exact source of this chloroform in uncertain. Simpson attributed it to Mr Hunter of Messrs Duncan, Flockhart and Company. On 10 November 1847, Simpson described the use of chloroform in obstetric and surgical practice, to the Medico-Chirurgical Society of Edinburgh. This communication was subsequently published in a pamphlet entitled: *'Notice of a New Anaesthetic Agent as a Substitute for Sulphuric Ether in Surgery and Midwifery'*.[4] On 14 November, Simpson wrote to Waldie: 'I am sure you will be delighted to see part of the good results of our hasty conversation'. On 29 November, Waldie addressed a meeting of the Liverpool Literary and Philosophical Society on the subject: 'Chloroform: the new agent for producing insensibility to pain by inhalation'.[3] It is also recorded that both Simpson and Waldie were present at a meeting in Liverpool in December 1847 at which chloroform was discussed. For a short time after this Waldie continued the preparation of chloroform in the attic of 87 Bold Street, the residence of his friend John Abraham, one of the founders of the pharmaceutical firm Clay & Abraham. Waldie and John Abraham obviously indulged in self-experimentation with chloroform the results of which were vividly described by Mrs Abraham and discussed in the many letters which Waldie subsequently wrote to both John Abraham and his daughter. And so Waldie and Abraham confirmed the anaesthetic properties of chloroform. There, Waldie's interest in chloroform ended for 22 years.

On only one occasion did Simpson publicly acknowledge that Waldie had recommended to him the perchloride of formyle. That he was not, at least initially, perturbed by Simpson's failure to acknowledge his contribution was probably a reflection of Waldie's character; he was a man unwilling to seek notice or fame for himself. His deep religious convictions can be seen from his pamphlet entitled *The Ultimate Manifestation of God to the World*, published in 1847.

In 1870, following the death of Sir James Simpson, Waldie featured in both the medical and public press. True recognition of his rôle in the discovery of chloroform appeared in Simpson's obituary in the *Lancet* of 13 May 1870 which read:

> 'At last Simpson acting on a hint supplied him by Mr Waldie, a chemist in Liverpool, made a series of experiments with chloroform, and so succeeded in assuring himself of its efficacy that he did not hesitate to proclaim it to the world as the long sought for yet finally discovered anaesthetic.'[5]

The true story of the introduction of chloroform into anaesthetics

Soon after, on 23 May 1870, a story was published in the *Daily News* of London which suggested that David Waldie had discovered the effects of chloroform on animals while a chemist and bookseller in Linlithgow. It was alleged that a little dog which had sniffed some chloroform in a saucer on the floor of the shop keeled over unconscious, apparently dead. However, after a time, the dog regained consciousness. This story was immediately refuted by Waldie's younger brother, George, the chemist and bookseller in Linlithgow, as sheer fiction. His protest to the *Daily News* was not published but a brief inconspicuous acknowledgement of the error appeared a fortnight later. This fictitious tale stimulated George Waldie to publish a pamphlet entitled: *The True Story of the Introduction of Chloroform into Anaesthetics* which contained David Waldie's original paper of 27 November 1847 and a restatement of the facts which outlined in greater detail the events leading to Simpson's discovery. Waldie also deplored the fact that he had been unable to prepare more chloroform on account of the destruction of his laboratory. Otherwise he would have discovered the anaesthetic properties himself. His feelings are strongly reiterated in a letter which he wrote to John Abraham in July 1970.

India and Linlithgow

By this time, David Waldie was a successful analytical and manufacturing chemist in Barnagore, Calcutta. He left Liverpool in 1853 to become a chemist with Malcolm & Co in Calcutta but found it difficult to work in such an unenterprising company and so moved to Barnagore. Finally, in 1878, he formed his own company, the Kasipur Chemical Works, where he remained until his death on 23 July 1889. He is buried in the Scottish Cemetery on Karaya Road, Calcutta, where his gravestone can still be found. His factory survived. Just 40 years ago it was recorded that the activities of Waldie's factory had changed but the sound traditions which David Waldie so firmly established had inspired the industry he founded and today the Waldie name is associated with high quality and sound business methods.[6]

Waldie had been an enthusiastic member of the Asiatic Society in Calcutta. On his death, the President paid the following tribute:

> 'David Waldie does not seem to have received full credit for his share in one of the most important discoveries of the age. A man of retiring and unassuming ways ...... he undoubtedly did much to promote chemical science in this country.'

Figure 1

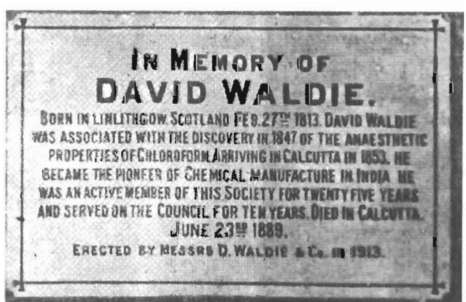

Figure 2

In January 1913 a bronze plaque was erected at the house in which he lived while in Linlithgow. (Figure 1) It shows a relief of Waldie with scales and retort with the inscription:

> 'David Waldie, Surgeon, L.R.C.S.E. and Chemist. Born at Linlithgow, 1813. Died at Calcutta 1889. A pioneer in anaesthetic research. To him belongs the distinction of having been the first to recommend and make practicable the use of chloroform in the alleviation of human suffering.'

A smaller plaque in the vicinity suggests incorrectly, that he made these discoveries in that house. In 1922, wholesale chemists, friends and admirers of David Waldie presented the Linlithgow Loving Cup to the Town Council of the Royal Burgh of Linlithgow. This cup, in the shape of a chemist's mortar with its ladle representing a pestle, became an integral part of the annual Linlithgow ritual of the 'Riding of the Town's Marches', an event still extant. Unfortunately, it incorrectly proclaims that Waldie was the discoverer of the anaesthetic properties of chloroform. A memorial plaque erected in Calcutta (figure 2) bears the accurate inscription: 'Waldie was associated with the discovery in 1847 of the anaesthetic properties of chloroform'.

Acknowledgement

I an indebted to the staff of the Library, Liverpool Medical Institution, for making the archival material available to me.

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EPISODES FROM THE LIFE OF A D WALLER

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The purpose of this paper is to give some insight into the character of Augustus Waller. There is no full biography of him and he left few personal papers but enough can be found to make at least a partial assessment of him as a personality. Four facets of his life have been selected for discussion: the influence of his father; marriage and family; the discovery of the human ECG and the University of London Physiological Laboratory.

The influence of his father

His father was Augustus Volney Waller (1816-1870), a physiologist who has a place in medical history through the eponymous Wallerian degeneration of nerve. He spent part of his life in France, qualified in medicine at Paris and returned to work there after a spell in practice in London and research in Germany. His last years were spent in Switzerland. His son, Augustus Désiré Waller, was born in Paris in 1856 and grew up in a cosmopolitan environment. He spoke English, French and German and absorbed the scientific culture of the family. Young Waller was only 14 when his father died and the family moved from Geneva to Aberdeen, possibly for financial reasons since very little was provided in the will. There he attended school and university qualifying in medicine in 1878. His professor of physiology was the little-known George Ogilvy whose only apparatus was a few microscopes for histological demonstrations. Fortunately, the lack of stimulus did not deflect Waller from his chosen career as a physiologist. He commenced his working life in the footsteps of his father by obtaining an MD degree from Aberdeen, and then sought postgraduate experience at the Mecca of physiology, the laboratory of Ludwig at Leipzig.

The heart of British physiology lay in the triangle of Oxford, Cambridge and London and it was in London, with its many medical schools, that Waller sought the first rung on the physiological ladder. He started as a BMA research student with Burdon Sanderson at University College in 1881, and proceeded as lecturer at the medical schools of the Royal Free Hospital (1883) and St Mary's Hospital (1885) before establishing his own, independent laboratory within the University of London in 1902, where he remained.

During his career he was active in research (with a leaning towards electro-physiology), in teaching (he wrote a book of practical exercises and a full-length textbook of physiology) and in the scientific establishment (as represented by the Physiological Society, the Royal Society and the British Association). Emulating his father, he too was awarded the Montyon Medal of the French Académie des Sciences (1885), was appointed FRS (1891) when only 35, and was elevated to the rank of professor (1912). His filial respect is seen in the dedication of his textbook: *To the memory of my father Augustus Waller MD FRS. Emigration of leucocytes: degeneration and regeneration of nerve; cilio-spinal region; vaso-constrictor action of the sympathetic.* Although others had contributed to the growth of knowledge of these subjects, Waller senior had undoubtedly made some important and lasting discoveries which were a matter of pride to his son. Young Waller referred to himself, perhaps in mock humility but certainly with affection, as being THE Wallerian degeneration thereby implying that his own achievements stood second to those of his father. Waller believed that it was the task of physiologists to uncover new basic truths about body function which would be turned into medical advances by the scientifically-minded hospital clinician. This was not exactly how his career developed but it was an ideal which owed much to his father's example.

Both father and son had an interest in anaesthesia. Waller senior studied the effect of chloroform on cutaneous absorption and investigated 'vagal compression' as an alternative to chloroform for acute procedures. A family tragedy which might have had some influence on Waller junior was the death of his niece from chloroform in 1903 when only 21. Waller also saw himself as a link in a physiological dynasty but, as will be seen, this was an ambition which was not fulfilled.

Marriage and family

In 1885 Waller married Alice Mary Palmer (1859-1922), the daughter of George Palmer, a wealthy biscuit manufacturer. They met when she was a medical student at the Royal Free Hospital and she gave up her studies to get married. She brought with her a substantial cash settlement and a large detached house in its own grounds in St John's Wood, London. There were cooks, housemaids and nursemaids and a private laboratory where the Physiological Society met in its early days. It was to be a family home for them and their five children for the rest of their lives. Their neighbour was the painter Alma Tadema, whose house, unlike Waller's, still stands. As became his new status, Waller had family portraits painted by Tadema and others. He also introduced from Paris the sculptor Alexander Zeitlin who made portrait busts of him and two of his children, Jack and Frances. His wife and elder daughter were presented at Court which indicates his new place in society.

Family life mixed with scientific life most intimately. Travel to scientific meetings at home and abroad often involved the children and was combined with summer or winter sports when possible. There were plays, parties, balls and scientific visitors to entertain. Waller's interests spread to bulldog breeding and motor cars (he was among the first to incur a speeding fine in Regents Park).

Typical of the family involvement is the recollection of Mary Waller that her mother on one occasion instructed the children to choose what they wanted to take on a seaside holiday adding: 'and don't forget, Father has bagged the galvanometer'. It is not surprising that such a full varied home life did not readily lead to marriage; only two of the four adult children married, late in life, and both were childless. More surprising is that despite their early experience of physiology, often as subjects for their father's experiments, none of the children made their mark as a physiologist, despite some efforts to do so. George, the eldest son, went in for town planning but made a gesture to his father's work by leaving his body to St Mary's; Mary came nearest to inheriting her father's mantle by taking physics at Bedford College and making a career of teaching medical physics at the Royal Free ; the other two sons, William who qualified in medicine at Oxford, and John who took botany at Cambridge, both spent a few years in the Department of Physiology at Liverpool but made no contributions to the subject. Both retired in their early thirties to live on the private means coming from their mother's estate. With no grandchildren there was to be no Wallerian dynasty. The youngest child, Frances Alice, was drowned in a shipping accident when only twelve.

Figure 1. Bronze bust of A D Waller at St Mary's Hospital Medical School by Zeitlin, 1901. Reproduced with permission

The fullness of his home and scientific life combined with his financial independence might have limited Waller as a physiologist by making him free to follow whatever path he chose. He was inclined to flit from subject to subject and to court publicity; but he made many contributions to his science and to his university without achieving the eminence of contemporaries such as Bayliss and Starling.

The discovery of the ECG

Waller's discovery of the ECG, in 1887, is his most enduring achievement but not one that is widely acknowledged in the history of medicine.

He had been working on the electrical activity of the excised mammalian heart in conjunction with Burdon Sanderson and colleagues. He was familiar with the extensive work of du Bois Reymond who had shown that electro-myographs could be recorded in man by surface electrodes. It was thus a short step to look for similar evidence of cardiac activity. He showed quite clearly that regular movements of the capillary electrometer meniscus could be correlated with the mechanical registration of the heart beats and that he was not observing electrical artefacts. The published electrocardiograms are very poor, even by the instrumental standards of the day, but Waller recognised that it was an important finding and gave it much publicity in talks and articles during the ensuing year. In Berlin he took the ECG of a horse connected by long leads from the stable below, and then that of his host, du Bois Reymond. In 1889 at Basle he gave a demonstration at the first International Physiological Congress which Willem Einthoven attended. Einthoven always paid generous tribute to Waller as the discoverer of the ECG even though his own contributions vastly outweighed those of Waller in both science and application. With the same sluggish and insensitive capillary electrometer Einthoven was able to show in detail, and to name the PQRST complex with recordings which would stand comparison with those of today. After his first flurry of activity Waller dropped his study of the ECG and published nothing on it between 1890 and 1909, by which time Einthoven was the internationally accepted leader and Waller contributed little of any significance. It is sometimes asserted that Waller failed to recognise the clinical importance of the electrocardiograph; he certainly did not envisage the widespread use of such a cumbersome and intricate instrument except by trained hospital staff. He was not a clinician and, to his credit, he introduced the string galvanometer to the National Heart Hospital and to Thomas Lewis.

Nevertheless, even within the limitations of the day, Waller could have done more to extend our basic knowledge of the ECG, for example, by applying to the electrometer records the mathematical corrections which were then available. However, he did leave to posterity one of the enduring anecdotes of physiology. In 1909 he demonstrated the ECG on his bulldog Jimmie at a Royal Society Conversazione. This was widely reported in the press and it led to a question in the House of Commons planted by the anti-vivisection lobby. The Home Secretary, Herbert Gladstone, humorously dismissed the complaint that Waller had illegally conducted an experiment that fell under the 1876 Cruelty to Animals Act. He likened the pots of saline in which the dog was standing to paddling in sea water, to the amusement of the House. Waller, always ready to make a point, featured Jimmie in several publications, on that year's Christmas card and on the famous caricature that appeared in *Mayfair* magazine (9 October 1915).

The University of London Physiological Laboratory

By the turn of the century Waller was restless. He had achieved much but he was still only a lecturer in charge of routine teaching at one of the smaller medical schools and his applications for chairs at Oxford (1895) and London (1899) had not been successful. He saw an opportunity for advancement in the 1894 Gresham Report on the University of London which encouraged the university to conduct its own teaching and research independently of the constituent colleges. Waller therefore proposed the establishment of a university physiological laboratory for advanced teaching and research, what would now be called a centre for excellence.

This timely suggestion came with the promise of financial support from the Palmer family and with even a site marked out for it in the Imperial Institute. The University welcomed the chance to expand its activities at little cost to itself and Waller resigned from St Mary's in 1903 to become Director of the new institution and, later, Professor of Physiology, where he was free to pursue his subject as he said: 'unclogged by the duties of elementary teaching'.

In the 20 years of its existence the laboratory, under Waller, made many contributions to physiology and to teaching even if his own output was somewhat superficial. The showman in him found expression in taking the ECGs of Max and Moritz, two chimpanzees then performing at the Hippodrome Theatre, and his demonstrations of the psycho-galvanic reflex as a response to emotions featured in popular newspapers. Nevertheless, a number of beneficial consequences arose from Waller's initiative. The University went on to found more Senate Institutes in arts and science where scholars and advanced students could promote their subjects. Inter-collegiate lectures, first organised by Waller, spread to other disciplines. The laboratory provided facilities for visiting scientists from abroad and for some London men whose own institutions had shortcomings. One such was the biochemist J A Gardner who devised methods for estimating chloroform in blood. Financial stringency after the war led to the withdrawal of a maintenance grant by the London County Council. The absence of undergraduate teaching was now seen as a disadvantage by not spreading costs and the success of King's College and University College in combining teaching and research brought into question the relevance of Waller's small laboratory. Closure seemed imminent. He put up a spirited defence and obtained a brief reprieve but his untimely death a year later (1922) was followed, within weeks, by final and irrevocable closure.

Waller was a man of ambition, not for power or position, but for academic excellence and scholarly recognition. In pursuit of these he brought many benefits to his family, to his science and to his university: not a bad achievement.

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AUGUSTUS DESIRÉ WALLER AND THE SECOND DOSIMETRIC MOVEMENT

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Past President, History of Anaesthesia Society

The first dosimetric movement dates from the beginnings of anaesthesia in England. Within one month, John Snow had pointed out the importance of knowing the dose being administered, and had published a table of ether-in-air concentrations at various temperatures - in effect of saturated vapour pressure. He went on to design a vaporizer which would allow him to control the maximum concentration being delivered, and he experimented also with the preparation of a vapour of known concentration to be inhaled from a balloon, a method which Joseph Clover elaborated into a practical apparatus. But Snow's early death, the introduction of nitrous oxide and the reintroduction of ether, resulted in a waning of interest in the idea that the anaesthetist should know what concentration the patient was getting. The second dosimetric movement, which began fifty years after the introduction of chloroform into anaesthesia, owes its origin to the efforts of the physiologist, A D Waller.

Waller and electro-physiology

Waller's interest in the action of anaesthetics stemmed indirectly from his interest in bio-electricity, which seems to date from 1881, when he was appointed to the Physiology Department of University College, London, under Burdon-Sanderson. Here he worked on muscle fatigue, and the developing specialty of electro-physiology. Burdon-Sanderson had already recorded the electrocardiogram of a frog. This had required the direct application of electrodes to the heart, but Waller, apparently reasoning that the limbs could be regarded as extensions of the electrodes, in 1887 succeeded in making the first recordings of the human electrocardiogram.[1] He continued with a study of the conductivity of nerves and other tissues, then moved on to investigate the effects on them of anaesthetics.

Waller appears to have first brought this work to public notice in his presidential address to the Section of Anatomy and Physiology at the sixty-fifth annual meeting of the *British Medical Association*.[2] This was held in Montreal, at the end of August 1897. Waller began by saying that the subject of the relative efficacy of various anaesthetics had occupied him for some years, and he believed he could offer a new viewpoint. He had developed a method which allowed the various members of a group of anaesthetics to be tested in quick succession, and their relative power to be demonstrated (Fig 1). The method involved electrically stimulating one end of a nerve exposed to the vapour being tested, and detecting the transmitted current at the other end by means of a sensitive galvanometer. He displayed recordings which demonstrated that both ether and chloroform 'at full strength' completely interrupted transmission, but whereas the etherised nerve soon recovered, the chloroformed one did not (Fig 2).

The ability to conduct impulses he called 'electro-mobility', and the effect of the anaesthetic vapours, 'immobilisation'. He also showed matched recordings of the effects of nitrous oxide, carbon dioxide, ether and chloroform on nerve conduction and on the heart, and demonstrated

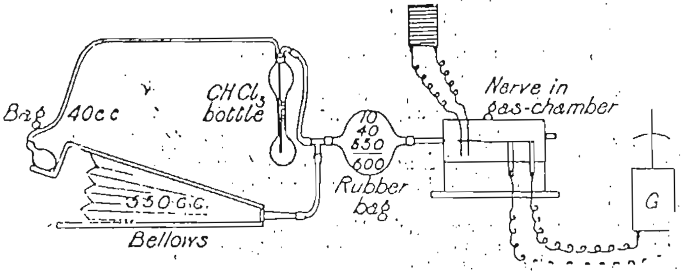

Fig.1 Waller's nerve conduction apparatus - later version[4]

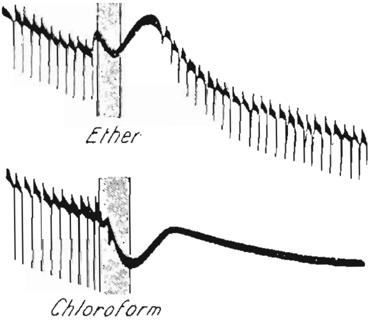

Fig.2 The effect of 'strong' ether and chloroform vapour on nerve conduction - the shaded area indicates the duration of exposure to the vapour - no recovery after chloroform - the stimuli are at one minute intervals[2]

that the effects were very similar, neither nerve nor the heart recovering from strong chloroform vapour. He produced tracings also of the effects of the ascending halides of methane, and of certain ethylene compounds, including 'dutch liquid' (ethylene chloride), and of successive strengths of ether and chloroform. From these he drew the conclusion that chloroform is seven times as powerful as ether in 'immobilising' nerves, and that in A C E mixture, where the proportion of the ingredients is 1:2:3, virtually all the effect is due to the chloroform. After considering the effects of equipotent mixtures, which generally were additive, he turned to the clinical implications of his findings.

Clinical implications

Obviously a whole patient was more complicated than an isolated nerve, and the information derived from the latter could only provide a guide, but, he thought, a peculiarly cogent one, when it has been dispassionately understood and weighed. In recent years the practical issue had been whether chloroform kills by asphyxia following arrested respiration, or by syncope through arrested circulation. This was important, and had been the purpose of the last Hyderabad Chloroform Commission, though in his view it was not central to the main issues, which were the following:

Firstly, ether, chloroform and all allied general anaesthetics have 'immobilising power' over all living tissues. Secondly, the order of extinction was brain, bulb (medulla), heart. Thirdly, the two most clinically effective agents were ether and chloroform, but if used in very high concentrations the nerve has nearly always been anaesthetised (temporarily immobilised) by 40% ether, and killed (permanently immobilised) by 10% chloroform. Chloroform is seven times as powerful as ether, and their effects are additive. John Snow had shown that the lethal quantity of chloroform in the body was twice the anaesthetic quantity. Regarding the body as a reservoir, in which the anaesthetist had to keep a balance of the volumes flowing in and out, there was a much wider tolerance with ether, whereas a few deep breaths of strong chloroform vapour could suffice to tip the balance.

As regards obstructed respiration during chloroform anaesthesia, his researches had shown that the danger was not from accumulated carbon dioxide, as Lauder Brunton had claimed, but from asphyxia. In conclusion, it seemed to him that there was no escape from the two horns of a dilemma. Either chloroform was dangerous in all circumstances, or it was dangerous when unskilfully administered. In either case, a death under chloroform should be considered a criminal offence. Certainly chloroform should never be used for minor operations.

Waller repeated the substance of this paper in a talk to the Society of Anaesthetists on 17 February 1898, with the President, Dr Dudley Buxton, in the chair.[3] He emphasised the increasing number of chloroform deaths, and produced a chart which he updated in subsequent years. Ten years ago it had averaged 20 per annum, now it was almost into three figures. He attributed this to the fearless use of the open, or what he would call the slap-dash, method: 'Everything seemed to point to the necessity of coming back to *quantity*, that was the essence of the whole matter'. He spent some time justifying his assertion that the maximum inhaled concentration should be 2%, and he thought that of the apparatuses available the Junker was the safest.

During the ensuing discussion Buxton pointed out the difference between an isolated nerve in controlled conditions in a laboratory, and a whole patient, of unpredictable behaviour, in a clinical situation. Patients varied in size, weight, and vital powers, circulation and respiration, and these were difficult to estimate. Dr J Rose Bradford, speaking as a physiologist and pharmacologist, thought that the effects of a gradual overdose and the sudden administration of a strong concentration were different. In the former, the heart continued to beat, and the effects could be reversed by artificial respiration. In the latter there was sudden, irrecoverable cardiac arrest. Dr Cook said that: 'he felt like that operator who, while he knew no anatomy, was a most successful operator on cases of stone; but when he began to study anatomy he gave up in despair, and did no more operations'. He had used Rendle's mask successfully for many years. Ought he now to abandon the open method and resort only to Junker's inhaler? Buxton replied that he could not sit in judgement upon the methods which others had seen fit to employ: 'Who made thee a judge over Israel?'. It was a deplorable circumstance that some people died under chloroform on the table, but it could not be helped. People also died in their beds after ether. Personally he thought the indictment of chloroform was: 'a cuckoo cry, based upon imperfect knowledge and insufficient data ...'. Waller's concluding remark was that clinical decisions must be left to practical anaesthetists. If he or any of his family had to take an anaesthetic, he would take or recommend chloroform, but he would be unwilling that a greater percentage than 2% should be used.

The *Transactions* account of this meeting is an indirect and summarised report. Waller published a fuller account of his talk some months later, and this should be regarded as the more authentic record.[4] It included recordings, presumably shown to the Society of Anaesthetists, of the effect of increasing percentages of chloroform vapour on nerve conduction (Fig 3).

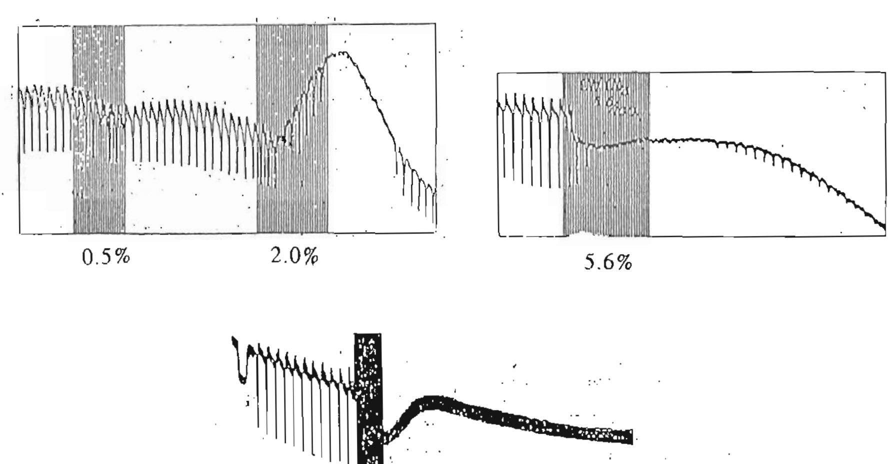

Fig.3 The effect of increasing concentrations of chloroform vapour in air on nerve conduction - the stimuli are at one minute intervals[4]

Another chloroform committee; quantification methods

During 1898 and 1899 the BMA, at Waller's suggestion, agreed to fund research into methods of estimating the chloroform content of tissues, and this work was begun under his supervision in the physiology laboratory at St Mary's Hospital Medical College. Towards the end of 1900 the Chloroform Committee that had been set up by the Section on Therapeutics of the BMA in 1891 issued its report. Waller wrote a review critical of the inadequacy of its findings, and persuaded the BMA, in July 1901, to set up another Chloroform Committee with himself in the chair.[5] The other members were Drs Barr, Buxton, Sherrington, and Victor Horsley. They co-opted A G Vernon Harcourt, a physical chemist of some distinction, of Christ Church, Oxford, who had devised a combustion method of estimating the concentration of chloroform in a gaseous mixture by passage over an electrically heated platinum wire. Within a short time Harcourt also produced his 'regulating apparatus', a draw-over vaporizer designed to deliver low percentages of chloroform, with a maximum of 2%.

The Committee was initially very active, and published reports in 1902 and 1903.[6,7] These included a review of existing methods and an account of several new ones, for estimating the chloroform content in various tissues. Harcourt described his combustion method, and Waller his new technique for estimating the chloroform content of gaseous mixtures, whereby chloroform was absorbed by olive oil in a sealed container, and the quantity estimated by measuring the fall of pressure in the container (Fig 4). The second report included a review of chloroform inhalers and a description of the Vernon Harcourt Regulator and of its clinical use.

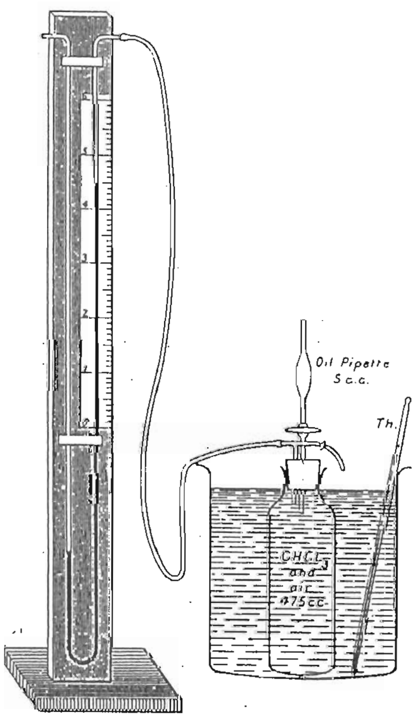

Fig.4 Waller's olive oil absorption method for determining the chloroform concentration in air.[6]

...oil, having been dropped from the pippette into the bottle has absorbed the chloroform vapour, and the pressure has been accordingly diminished.

In 1903 Waller also published his 'densitometry' method for estimating the chloroform vapour concentration. This was calculated from the difference in weight of a 500 cc glass flask filled first with air then with the vapour. The term 'densitometry' is misleading, since nowadays this refers to optical methods, and the reference for this paper has been consistently wrongly cited for the later description of the much better known 'chloroform balance'.[8]

In the same year, Waller delivered a public lecture-demonstration on the administration of chloroform, in the physiological laboratory of the University of London.[9] He began with an attack on 'two intelligent young ladies', obviously antivivisectionists, who had obtained permission to attend his course, and had then published 'a horrified condemnation of physiology and physiologists'. He continued that: 'in this laboratory animals are anaesthetised with as great certainty and accuracy as are the patients in any hospital in the United Kingdom'. He demonstrated three cats. 'Cat No.1 ... has during the last three hours been maintained in profound anaesthesia in a mixture of between 1 and 1.5%. I now pass it round the class so that you may all assure yourselves of its state, and when it returns to the lecture table it will be left to recover. Its recovery ... will be complete within an hour. By complete recovery I mean that state in which the cat will drink milk and purr, and a saucer of milk is therefore placed by the cat as its normal test.' Cat 2, presumably a family pet, had 'been borrowed for the purpose of this lecture on the understanding that it shall be returned intact', and was used to demonstrate how anaesthesia was induced; and cat 3, lacking the influence of cat 2, 'now upon the operation board, is dead, having just served for an experiment in which we measured the amounts of chloroform inspired and expired ...'while recording the blood pressure and respiration. Cat 2 was placed under a bell jar and chloroform vapour pumped in: 'The pump is one originally devised by Professor R Dubois of Lyons for the anaesthetisation of the human subject.... The only objection to its use is.... its price - £20; but .... as a laboratory instrument it is commercially economical. We have never lost an animal by chloroform since it has been in use.' (Fig 5).

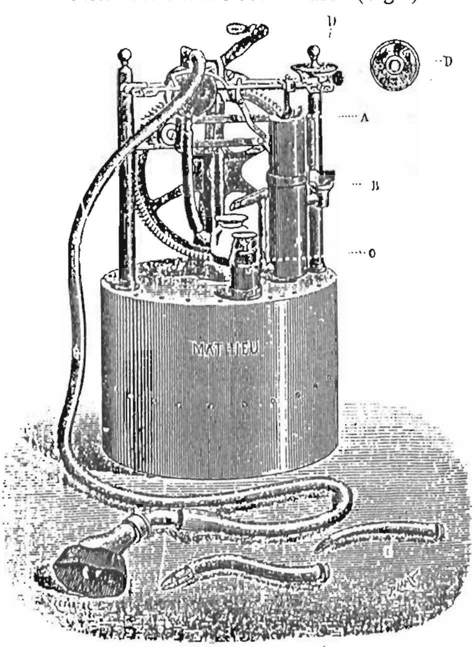

Fig.5 The Dubois chloroform vaporizer

With Cat 3 the input and output concentrations of chloroform vapour were measured by densitometers, and the total uptake in mg per minute was calculated. The cat was first anaesthetised with 2.7% chloroform vapour, and sustained normal respiration and blood pressure. The percentage was then increased to 14.2, and it died in three minutes. Densitometry measurements showed that during the first phase the chloroform uptake had been 27 mg per minute, and during the second, 210 mg per minute.

Waller continued with another demonstration in which chloroform was dripped onto the cloth of a wire frame mask, and the air beneath aspirated into a densitometer. He found that by varying the tightness with which the edges of the cloth were applied to the sides of the face, the concentration ranged from 2.5 to 11.2%. With very loose application a percentage as low as 0.8 could be obtained. He produced an updated chart showing how the annual number of 'deaths from anaesthetics' had risen during the previous ten years. He concluded by stressing again that safety depended on the control of dosage, and referred to two series of cases that he had anaesthetised using the Dubois pump, at Herefordshire General Hospital, and, by the courtesy of Dr F W Hewitt, at St George's.

In 1904 Waller published, in the *Lancet*, significantly, a paper in which he reported on the examination of apparatuses currently available for the quantitative administration of chloroform.[12] He began with the statement that it was based on a laboratory report of work performed by his co-author J H Wells and himself, which had been submitted to the Special Chloroform Committee of the British Medical Association in July 1903. It was important 'that the facts and conclusions obtained by independent investigation relating to the question of safe and unsafe methods of effecting anaesthesia should not remain unpublished'. He continued with an analysis of the capability of contemporary methods of administration to deliver a controlled quantity of chloroform, pointing out that the French and German 'drop' was different in volume from the English. He had examined Snow's, Junker's, Harcourt's, and Dubois's apparatuses, and had concluded that draw-over vaporizers were inherently less safe than plenum, because with shallow breathing a higher concentration of vapour tended to build up, although the absolute quantity being inhaled might be lower than with deep breathing. Contemporary theory had it that a high concentration of vapour, even from only one breath, could travel as a bolus to the heart, and cause 'relative' overdose, syncope, and sudden death. With a plenum vaporizer, Waller argued, the concentration could be fixed and independent of the depth of respiration. While in expert hands the towel method would only supply between one and two percent, he had shown that if the towel were crammed on to the face it could rise to ten. Of the three apparatuses that he considered in detail, he regarded the Dubois pump as the safest, followed by the Junker. He listed a number of problems with the Harcourt, which he placed a rather poor third. The mask had to be kept tightly applied, shallow breathing raised the nominal concentration, and shaking the bottle raised it to as much as ten times the indicated percentage. His opinion differed from that of the Special Chloroform Committee. He regarded all apparatuses such as Snow's and Harcourt's, where the chloroform intake depended on the patient's own respirations, as liable to deliver an overdose. If the Dubois was too costly and heavy, then an apparatus composed of a three wick lamp would answer all its purposes. Although this paper purported to be of joint authorship, all the opinions are expressed in the first person.

The wick-vaporizer; criticism of the Harcourt Inhaler

Waller's 'wick-vaporizer' resulted from his enthusiasm as a motorist, and knowledge of the wick carburettor used in certain makes of car. This was capable of vaporizing liquid petrol in sufficient quantity 'to drive a heavy car at high speed'. In comparison, 'it should be an easy matter to find a wick surface capable of supplying 1 to 2% chloroform vapour to, say, 10 to 15 litres of air per minute, i.e. in liberal excess of the volume of air normally breathed, which may be reckoned as being 6 litres per minute'. The 'wick-vaporizer' (Fig 6) was based on a three-wick paraffin or kerosine lamp, the evaporating surface being alterable by winding the wicks up or down. Each wick was 66 mm wide, so a length of 75 mm provided a surface of 50 sq cm. At ordinary room temperature, with a continuous flow of 8 to 12 litres of air per minute, this supplied rather more than 1 per cent chloroform vapour. Bringing the second and third wicks into action raised the concentration to 2% and to nearly 3%. A foot bellows was used to provide the continuous stream of air.[11] Waller reported that the vaporizer had proved extremely convenient for laboratory use, and he used it clinically in two cases at St George's Hospital under the supervision of Dr Hewitt. With two wicks in action induction was completed in five minutes, and anaesthesia had been maintained with one wick and half the second. Waller described this apparatus at a special meeting of the Royal Medical and Chirurgical Society held on 22 November 1904, at which the problems of chloroform anaesthesia were discussed.[12] He subsequently published this paper as a separate pamphlet - there is a copy in the library of the Association of Anaesthetists - but the apparatus does not appear to have been manufactured commercially, and has remained virtually unknown; but it does appear to offer advantages over many of the vaporizers then in use.[13] In particular, it overcame Waller's objection to the draw-over apparatuses, that a high concentration could build up if there was breath-holding.

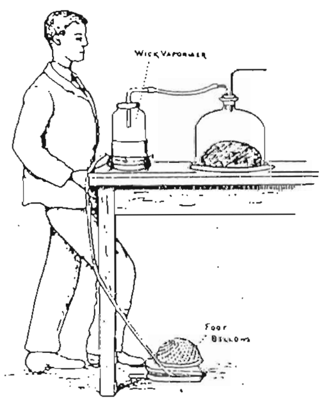

Fig.6 Waller's wick vaporizer[11]

Shortly after publishing his attack on the Harcourt vaporizer, Waller had to defend it against a rebuttal by Harcourt. The occasion was the Annual Meeting of the British Medical Association, held at Oxford, where the Section of Physiology opened its proceedings with a discussion on chloroform anaesthesia.[14] In the absence of the Chairman of the BMA's Special Chloroform Committee, Dr Radcliffe Crocker, Sir Victor Horsley took the chair. He summarized the history of the Committee, its researches and findings. It had been shown that a large part of the chloroform in the blood was held in the corpuscles, and it could not be said that chloroform accumulated in the heart. Apart from this academic work the search for an accurate anaesthetic apparatus continued, and his experience, and that accumulated by others, was that Mr Harcourt's apparatus furnished all the requirements. He proceeded to introduce some dozen speakers including the notable scientists Professors Moore, MacWilliam, and Sherrington. Harcourt demonstrated his vaporizer, and was critical of certain of the experimental methods used by the previous speakers. Waller again criticised the Harcourt apparatus, and the draw-over principle in general, expressing his preference for the Dubois vaporizer. Buxton described the causes of death under chloroform, and gave a lengthy account of his clinical experience with the Harcourt vaporizer. The work of the Committee had 'confirmed the truth that in low-percentage vapours of chloroform lies safety. We have had the great advantage of testing the matter by means of Mr Harcourt's inhaler, and have found that a chloroform vapour as low as 2% will produce anaesthesia'. He continued with the confusing statement: 'I do not mean to say that 2% is sufficient in all cases. I have found it ample in most, and regard it as adequate in all. In the larger number of patients 2% suffices for the induction of anaesthesia, and 1%, or even less, is enough to maintain an adequate degree of narcosis. It is often asserted that light narcosis involves insufficient relaxation and frequent alarming interference with respiration when viscera are handled. I suggest, as I have pointed out elsewhere, that these phenomena are not necessary, nor are they the result of light narcosis. They really belong to the domain of incomplete anaesthesia. The patient under these circumstances has never been carried into the third degree of narcosis, anaesthesia proper, but is kept oscillating between overdosage and underdosage through irregularities in the supply of anaesthetic or in the rhythm of respiration.' He concluded by emphasising yet again the dangers of a high percentage of chloroform.

Dr McCardie of Birmingham thought that the main drawback of the Harcourt vaporizer was the length of the induction period, sixteen and a half minutes with 1%. In some cases he had had to change over to ether, or ethyl chloride. The advantages of Harcourt's apparatus were the quiet, smooth induction, the perfect control of narcosis, the speedy recovery, and absence of after-effects. He suggested some modification: an unbreakable bottle would be advantageous, as would the ability to wear the vaporizer round the neck, as with the Junker, leaving one hand quite free.

A report on the use of the Dubois apparatus at Herefordshire General Hospital followed. With experience certain technical snags had been overcome, and it was now possible to induce anaesthesia in about four minutes. A number of cases were reported, together with the comment of a dental surgeon, who said that: 'I have never extracted teeth under such favourable conditions. There was absolute quietude on the part of each patient, and the fact that the anaesthetic could continue to be given through one or other nostril made the operation considerably more expeditious. There was no necessity at any time to stop even for a moment, the mouth being left to me, and never covered up, as frequently occurs in any other method of anaesthetising.' The speaker concluded by differing from the physiologists. After prolonged administration the patients were longer in coming round. This, he thought, pointed to some accumulation.

Dr Crouch, anaesthetist at St Thomas's, spoke of his own experiences with the Harcourt inhaler. When he first saw it in use he concluded that the amount of shaking that took place completely stultified the intentions of the inventor, so he gave it up. However, seeing that this discussion was to take place, he had fixed the apparatus to a stand, and arranged a longer connection to the face-piece. Furthermore, to avoid the derision of a scientific audience he had always had a fellow anaesthetist at his side to check his technique. But he regretted that he could report on only nine cases, because he found it impossible to use this method on more than the first case in the afternoon. Even the most good-natured surgeon declined to wait the necessary time between cases. He was sure that in more speedy inductions the patients were having 'a very much larger quantity than the 2% which they were supposed to be getting'. It seemed obvious to him that the success of the apparatus depended on the amount of unconscious shaking of the bottle, which could not be measured. Then there was the tendency for the attention of the administrator to be rivetted on the apparatus rather than on the patient. It could be objected that the apparatus was not in experienced hands. But that was its whole *raison d'être*, that it should give a satisfactory and safe anaesthetic in the hands of an inexperienced practitioner.

Dr A G Levy, anaesthetist to Guy's Hospital, brought the formal part of the discussion to a close, with a report on the failings of the Harcourt inhaler, which he had tested under various conditions with the use of an adjustable motor-driven suction bellows. The bottle had been kept steady, the volume of chloroform constant, and the temperature regulated by the momentary application of a flame. Levy concluded that the index was faultily graduated, and in a second series of tests during which the bottle was shaken to an extent that kept the inside wetted to a constant height above the normal level of the chloroform, he showed that only moderate shaking would raise the level from a nominal 2 to 5%. Quoting from a leading article in a recent issue of the *British Medical Journal,* which required that a chloroform inhaler should tell to a nicety what strength of vapour the patient is inhaling, he said: 'I think it can hardly be claimed that the Vernon Harcourt inhaler fulfils such a condition'. In conclusion he had to state that: 'it was Sir Victor Horsley who urged me to follow up these investigations, and that he and Mr Vernon Harcourt have kindly placed every facility at my disposal'.

Horsley, winding up the meeting, asserted that the shaking that had affected Levy's findings was quite different from the occasional agitation that might occur in clinical practice, and that the difficulties Mr Crouch had met with were exactly those that would be met by anyone trying out an unfamiliar method for the first time. His own experience of the inhaler was very favourable.

Unusually, addenda were attached to this report. There was one from Waller, which was an update of his joint paper with Wells, and made the same points again. The second was a refutation by Harcourt, strongly critical of Waller's experimental techniques and his mathematics, which concluded: 'What can be thought of experimental work which is undertaken with the object of examining a non-existent cause, and which shows it to produce an immense effect' The third was an account of the mechanics of the Dubois apparatus, by Dr Paul Chapman. Waller reacted strongly to Harcourt's addendum. In a letter to the Editor he argued against Harcourt's criticisms, and again stressed the danger of 'rising chloroform percentage with falling respiration'. This had been the purpose of the paper he had submitted to the Special Chloroform Committee of the British Medical Association in July 1903 and published in the *Lancet* in July 1904. He concluded: 'I have thought proper to deal with all the items of Mr Harcourt's criticism, which conveys the first indication I have received of the cause of the suppression of that report. I think that the suppression indicates a very defective procedure on the part of a scientific committee and of the Council of the British Medical Association.'[15]

It seems that after a further dispute with Harcourt in the correspondence columns of the *British Medical Journal*, Waller virtually withdrew from the BMA Chloroform Committee, and persuaded the British Association for the Advancement of Science to set up almost a rival body, under his chairmanship. He was able to provide laboratory facilities and staff from his own department,[16] and the succession of publications by Waller and his assistants gives the impression that a large part of its activities were concerned with the investigation of chloroform anaesthesia. Also resulting from Waller's enthusiasm were several vaporizers designed by members of his staff, or by close collaborators. These included Collingwood and Alcock.[17] Another was that of Levy, to whom Alcock ascribed the idea of the splitting ratio.[18] Both Alcock's and Levy's apparatuses had an arrangement for temperature compensation. Alcock's was a plenum, Levy's a draw-over. Levy, as appears from his subsequent publications, did not believe in the concept of relative overdose. As a counterbalance to the influence of Buxton, Waller managed to attract the support and collaboration of Hewitt, with whom he published some papers.

In 1904 Sherrington gave an account of experiments in which the isolated heart was perfused with very dilute chloroform in a saline solution, and reported that the depressant effect, which reached its maximum in one minute, very rapidly disappeared when chloroform-free saline was substituted.[19] Hence chloroform in ordinary concentrations did not accumulate in the heart muscle, and it was postulated that the effect was due to 'the formation of some easily dissociable compound between the chloroform and some active constituent of the tissues'. Moore and Roaf had recently urged that this constituent was a proteid. It had also been found that chloroform in blood was barely one-twelfth as active as the same concentration in saline. This was explained by the tension of chloroform in blood being much less than in saline: 'some constituent of the blood taking up and holding, in a relatively inactive form, a considerable fraction of the chloroform added to it'. Later work by Buckmaster and Gardner in Waller's department concluded that 97% of the chloroform was taken up by the red cells.[20]

From 1904 on, we come up against the problem of multiple publication, which was not then regarded as reprehensible, the same or very similar information being reported at a number of meetings and in different publications. Thus in the following years Waller spoke repeatedly on chloroform, with a validation of his densimetric method of estimating the chloroform content of gas mixtures.[21] In the same way, several of Waller's illustrations, for example the tracings demonstrating the effect of chloroform vapour on nerve conduction, were published in slightly different versions. In 1907, as President of the Section of Physiology of the British Association for the Advancement of Science, he delivered a lengthy address on the pharmacology and safe administration of chloroform. He had compared it with a considerable number of other agents, which he listed, and had concluded that 'chloroform is the most powerful, the most certain, the most convenient, and the most trustworthy'.[22] It is not clear how recent this work was, since from 1906 Waller's communications to the Physiological Society had concerned only the action of certain alkaloids, a mysterious bio-electric optical effect which he called the 'blaze current', and the injury current that resulted from damage in plants. In this last he was following up work begun by Burden-Sanderson.

First descriptions of the Chloroform Balance

The following year he reported on the comparison of the effects on isolated muscle preparations of ether, chloroform, and alcohol, and concluded that one molecule of chloroform was as toxic as one hundred molecules of ethyl alcohol.[23]

It was also during 1908 that he had, as he described it, the brainwave that resulted in the first apparatus allowing the concentration of anaesthetic agent going to the patient to be instantaneously and continuously monitored. This was his Chloroform Balance, and the idea was to turn his densitometer inside out, so that instead of weighing the chloroform vapour, he used its greater density to increase the buoyancy of a large sealed globe full of air. Any disturbance of the balance was indicated by a pointer moving across a scale calibrated in percentages of chloroform (Fig 7). One version was even arranged to provide a written record. He demonstrated the balance clinically, again at St George's, under Hewitt's supervision, with another plenum vaporizer of his own design, which appears to have anticipated some of the features of the Boyle's bottle.

The chloroform balance was described in the *Proceedings of the Physiological Society*,[24] and also, in April 1908, in *Science Progress*, a quarterly edited by Alcock.[25] This published mainly review articles on a broad range of scientific topics, to make recent advances known to those working in other disciplines and to the intelligent layman. Here Waller was obviously appealing to the public rather than to the medical profession, for support in his campaign for safer anaesthetic techniques, and doing it with his usual flair. The chloroform balance does not appear to have been written up in any of the clinical medical journals. It may be that Waller first regarded it as a laboratory instrument and only later began to stress its value for hospital use.

Final contributions

The next year, 1909, brought the interim report of the British Association's Chloroform Committee.[26] Here, apart from one paper by Hewitt and Blumfeld on the use of ether-chloroform mixture on the Skinner mask, one meets duplicate publication, and begins to get the feeling that Waller was running out of steam. There is another description of the chloroform balance, further reports on comparative toxicity and on the blood levels of chloroform under various conditions of anaesthesia, further support for the use of plenum rather than draw-over vaporizers, the suggestion that the Rendle and similar semi-open inhalers should be discarded, and, cutting the ground from beneath the Committee's own feet, the conclusion that: 'As regards the use of apparatus for clinical use we prefer not to express any collective opinion at present'. This meeting of the British Association for the Advancement of Science was held in Winnipeg. Accompanying Waller was his friend and successor at St Mary's, N H Alcock, who gave a demonstration of his own chloroform vaporizer.[27] After the meeting the two continued to the University of California, Berkeley, where Waller delivered the Hitchcock Lectures, in which he summarised his many years work on chloroform.[28]

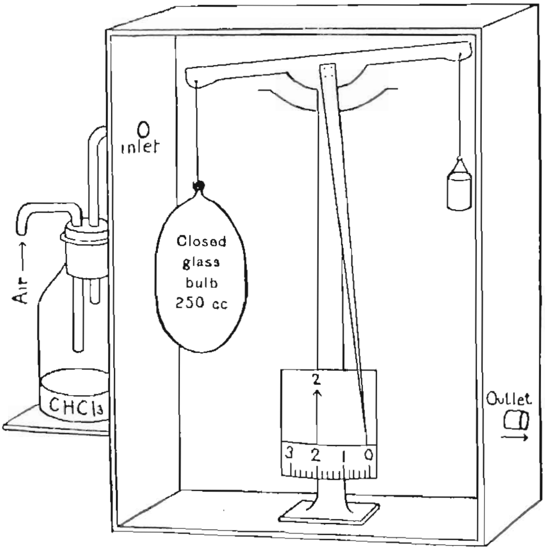

Fig.7 The chloroform balance[24]

The following year, 1910, brought the second interim report of the British Association's Committee.[29] This time it came out strongly in favour of the routine use of the chloroform balance in hospitals, and hoped that one would shortly be in operation at St George's. It also supported the General Medical Council and the British Medical Association in their request to the Home Office for better regulation of the administration of general anaesthetics. That year saw the publication also of the final and very comprehensive report of the BMA's Special Chloroform Committee.[30] At the annual meeting of the BMA at which it was discussed, Waller contributed briefly, endorsing all that Buxton had said in his introductory summary, although he still expressed distrust of the Harcourt inhaler. This appears to have been his last public pronouncement on anaesthesia.

Waller had entitled his Hitchcock Lectures *Physiology the Servant of Màn*, and this was an expression of his creed: 'while it is essential that scientific enquiry should be pursued for its own sake without regard to immediate utility, its ultimate justification consists in its practical application to the service of mankind'. So physiology was to be useful, to be applied.

Summing up, Waller, having shown by his earliest experiments on nerve the danger of chloroform overdose, spent the next fifteen years establishing the safe dose, and designing ways of measuring and controlling the strength of the inhaled vapour. To these ends he devoted a large part of the resources of his department, the physiologists Alcock and Collingwood, and the chemists Buckmaster and Gardner. Also he obtained help from Sherrington and his Department in Liverpool, and from the clinicians Hewitt, Blumfeld, and Sir Frederick Treves. He devised a reliable vaporizer, and the first and only means available for many years of actually monitoring continuously the strength of vapour the patient was getting. But because of the circumstances of anaesthetic practice, the lack of any departmental organisation in hospitals, and the peripatetic nature of private work, which made the transport of bulky equipment impractical, his apparatus did not come into wide use.

Also notable was Waller's single-mindedness. At a time when Hill was demonstrating the vasodilator and hypotensive action of chloroform on the peripheral circulation, and Embley the possibility of vagal inhibition of the heart's action, Waller managed to disregard all that was going on around him, and with a remarkable demonstration of tunnel vision, kept his eyes focused only on what seemed to be the light at the end of it. Strangely, for a physiologist, he was happy to regard the anaesthetised patient as a black box. He didn't want very much to know what was happening inside it, but only what was going in and out. Looking at the *Journal of Physiology* for the first decade of this century, one sees that the foundations of modern physiology were being laid, yet Waller was taking no part in any of this. Reluctantly, one comes to the conclusion that while he may have been a great entrepreneur and communicator, and a great stimulus to others, he was not in the first rank of physiologists. However, had his contributions to anaesthesia been widely adopted, the specialty would have taken a substantial step forward. Instead, it had to wait another thirty years for the next accurately calibrated apparatus, the Oxford vaporizer, nearly fifty for the Fluotec, and longer still for the present day monitoring equivalent of the chloroform balance.

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ETHER INHALATION IN FRANCE: EARLY EXPERIENCES

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In a paper mailed on 1 February, and published in the *Boston Medical & Surgical Journal*, on 10 March 1847, F Willis Fisher[1] reported with a lot of interesting detail the first experiences of ether inhalation in France.

Fisher, the Parisian correspondent of William Green Morton, wrote that in November 1846 a medical friend had sent him a letter in which he was informed of the discovery made by Charles T Jackson, and of the two operations performed without pain at the Massachusetts hospital on patients under the influence of the inhalation of sulphuric ether. This meant that the information had come to Europe more than two weeks earlier than the well-known date of 16 December when the passenger paddle steamer *Acadia* docked at Liverpool. Willis Fisher's medical friend was his former medical instructor, whom I have not yet definitely identified.

First use in Paris

One or two days after receiving the letter, Willis Fisher took it to Alfred Velpeau (1795-1867), at the Hospital de la Charité in Paris. Velpeau was interested, but incredulous of the newly announced virtues of sulphuric ether, and he politely declined Fisher's offer to make an experiment on one of his patients As Fisher reports, the reason for this refusal was: 'more influenced ... by a disbelief in the efficacy of the ether in destroying sensibility, than by the fear he entertained of any injurious effect the inhalation of it might have on the health of his patient'. This assertion is at variance with the later affirmations of Velpeau,[2] that the American doctor had not wished to explain to him the way to proceed.

Not having convinced Velpeau to make an experiment with ether, but feeling that it was important to bring the discovery to the notice of the profession in Paris, Willis Fisher decided to breathe the vapour himself. Suffering at that time from toothache, he determined to have the offending tooth extracted. He went to the office of a dentist, accompanied by his friend Dr Mason and other professional men. I think that Dr Mason might be Jonathan Mason Warren (1811-1867), the son of John Collins Warren (1778-1856). The experiment was made with a crude apparatus Fisher had constructed himself. Unfortunately the inhalation of ether was only continued for about a minute. Ether produced such instinctive fear and peculiar or apparently alarming effects, that the friends, on observing the excitement produced, rapidly removed the mask from Fisher's mouth. A few months later, Henry J Bigelow[3] (?-1890), wrote in the American Medical Association's transactions that sulphuric ether 'possessed the minds of the profession' and 'prevented many prudent practitioners from pushing the practice to a point at which its full effects was attained. This caution gave rise to many apparent failures, and discouraged experimenters from further trials'. This confirms the attitude of Fisher's friends.

Despite that failure, he did not lose his faith in the procedure, and he urged the French doctors to make experiments. On 15 December Jobert (de Lamballe)[4] (1799-1867) of the Hospital Saint-Louis, invited Fisher to give ether to Pierre Dihet, a patient suffering from a cancer of the lower lip. Fisher commented : 'in consequence of the morbid condition and tenderness of the organ', the patient 'experienced a difficulty in applying his mouth to the opening of the glass globe, and found it quite impossible to inhale the vapour with the requisite facility and rapidity. After inhaling the ether for a few minutes he became partially affected by it, but not sufficiently to produce insensibility, or to satisfy the surgeon, whose faith in the success of this new application of ether was not very strong'. The experiment was made without a specific purpose, without a proper apparatus. Would the result not have been different if the operation chosen had been a minor one? The extraction of a tooth with normal anatomical roots by a well trained professional man needs only from a half to one minute. A dental extraction certainly would have given more faith in the success of the new technique. Fisher called attention to the fact that unfortunately 'most of the experiments have been made by those who were unprepared to investigate so important a subject, and who were ambitious of notoriety'. The different stages of etherization were not yet recognized or explained.

After that operation no further experiments were made in France, until Malgaigne (1806-1865), curious of the reports[5] by English and American surgeons, decided to make trials in the Hospital Saint-Louis. A careful study of the reports of his five experiments reveals that in only one case did the patient completely lose consciousness. In two cases the patients were aware of the operation, feeling the scratching of the knife, but with no memory of pain. On 12 January 1847 Malgaigne advised the Academy of Medicine of his results, but after Nicolas Jean-Baptiste Guibourt (1790-1867) and Jean-Baptiste Alphonse Chevallier's (1793-1879) observations[6] on the ineffective results of prolonged inhalation of ether-laden air, further experiments were required to convince the Academy.

Between 12 and 18 January, etherization was performed during various surgical operations in different Parisian hospitals (Hôpital Saint-Louis, Hôtel-Dieu, Hôpital du Midi, Hôpital de la Charité, Hôpital des Enfants Malades, Hôpital Beaujon, Hospice des Enfants Trouvés, Hôpital Bicêtre, Hôpital des Cliniques, Hôpital du Val-de-Grâce, Hôpital de Versailles). The majority of the experiments were failures, or were only partially successful, owing to imperfection of the devices used, or the impurity of the sulphuric ether.

At the meeting of the Academy of Medicine on 19 January the members discussed the subject again. In remembering that period Willis Fisher wrote: 'It so happened that, at this moment of anxiety, one of the Boston inhalers, complete with sponge and valves, reached me. It was sent by a friend, and was an unexpected present, for which I beg to render to the kind donor my warmest thanks.' The arrival in Paris of Morton's inhaler can thus be dated about 18 January 1847. Universally admired, the Boston inhaler served as a model for all those used in Paris, added Willis Fisher. On 23 January, by invitation of Philibert Joseph Roux (1780-1854) at the Hôtel-Dieu and of Alfred Velpeau, at the Hospital de la Charité, Willis Fisher achieved perfect anaesthesia by means of the Boston inhaler: 'The patient came under the influence of the vapor in the space of three minutes, and was rendered perfectly insensible'.

Willis Fisher was very proud of the discovery made in his native city. He placed all the honour of the discovery with Charles T Jackson (1805-1880), 'whose honorable attainments and character were familiar to him'.

Experience in other centres

In other French towns surgeons now hurried to try the new technique. On 19 and 29 January, Charles Emmanuel Sedillot[7] (1804-1883) in Strasbourg, performed five experiments on dogs of different sizes. His colleague Gabriel T Tourdes (1810-1900) undertook some experiments on rabbits and had the same results: inhalation of ether vapour mixed with atmospheric air produced insensibility and a state of prostration after two or three minutes, accompanied by respiratory discomfort, profuse salivation, moans, contractions and finally muscular paralysis. In the first experiments, Sedillot used a globe of 1.5 litre capacity with two apertures. Inspiration was made through the mouth and expiration through the nose. This was Malgaigne's technique. Sedillot was immediately convinced that this method of ventilation would be too difficult a procedure for a patient. He decided to wait in order to get a better device from a surgical instrument maker in Strasbourg, J Elser. The diameter of the respiratory conduit of this new device was 3 cm, the capacity of the balloon 1.5 litres, and 200 grams of ether was poured onto the sponges. Sedillot used it for the first time on 5 February in the presence of Drs Schneiter and Marmy, for a successful operation on an anal fistula.

On 20 January, H Landouzy[8] of Reims extracted a first molar after 45 minutes inhalation of an ethereal vapour heated to 32°. The woman patient did not completely lose consciousness, but she suffered less than during the extraction performed by the same dentist on the other side of her mouth. A second trial, for the removal of a tumour in the mastoid process, was followed half an hour after the operation by bleeding. Immediately, Landouzy called attention to the haemorrhage which could occur long after the operation if performed on vascular tissues.

Michel Serre[9] (1799-1849), on 25 January in Montpellier performed an operation for nasal polyps on a door-to-door salesman. This first experiment was made without a real knowledge of the technique; he used a glass flask with two glass tubes; for 8 minutes the patient inhaled through the mouth, then Serre diverted the vapours through one nostril. This case and both of the following were failures. Four days later, A E Lazowski,[10] who had seen Serre's technique, suggested using a lead hosepipe and a modified mouthpiece of his invention, covering the patient's mouth and nose. Trials made at the Hôtel Dieu St Eloi, on the house physician Lacroix, on a medical student Marius, on a soldier, and on a woman were all successful. On 31 January Lazowski added two valves to the mouthpiece. Serre used this new device for lithotrity - the first French operation of that kind performed under ether anaesthesia. He was aware that the patient might pass from a state of complete insensibility to wild excitement, when uncoordinated movements could have caused the lithotrite to perforate the bladder. Serre used this device until 11 February after which he used Lüer's inhaler.

Lyon, the second surgical centre of the country, followed the Parisian methods. In the first weeks of January 1847, the surgeons[11] of Lyon used the ordinary inhalers of the pharmacists, thin glass pipes, or had the vapour inspired through one nostril from a hermetically closed ether flask. On 20 January Amédée Bonnet (1808-1858) was half-successful in performing two castrations, anaesthesia having not been complete for the full time necessary for the operation. In a second series of experiments after 27 January, Antoine Jean Bouchacourt (1812-1898) used a flask containing etherized sponges and closed by a cork pierced by three apertures. One tube was open to the atmosphere and the others carried the vapour to both nostrils..

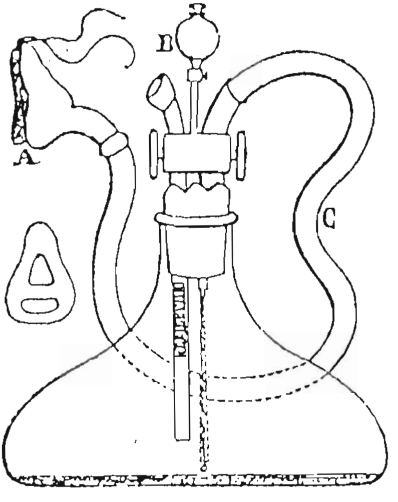

Figure 1
Bonnet and Ferrand's modification of Joseph Charrière's Inhaler

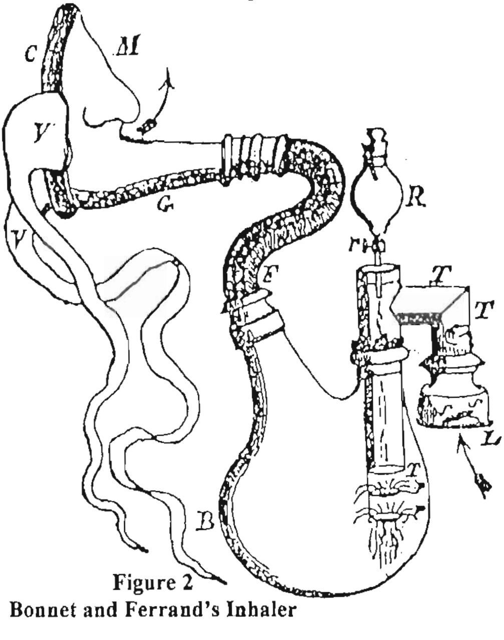

Figure 2
Bonnet and Ferrand's Inhaler

Bonnet thought that nature should be copied; he was of the opinion that it would be easier for the patient to breathe through both mouth and nose. Between 25 January and 5 February this led Bonnet and the pharmacist Ferrand[12] to make a modification to Joseph Charrière's inhaler.[13] The metallic mouthpiece (Figure 1) they devised was a mask exactly covering the nose, cheeks and chin. To allow fitting on different faces, they used a flat rubber cushion 5 or 6 mm thick between the skin and the mask. The description of this model is given in Joseph Charrière's notices;[14] it indicates that the cushion was formed by two rubber plates containing air and pierced by two apertures for the nostrils and the mouth (Figure 1). Charrière wrote that the first apparatus of Bonnet and Ferrand was not equipped with a valve which allowed the introduction of air into the container. Paul D Diday (?-1894) found that this very complicated device could move and anyway did not allow operations on the nose, maxillae or mouth.

About 1 February, Théodore Joseph E Pétrequin (1810-1876) modified the device by fitting the inhaling tube with a bifurcation, the ends of which were applied to the nostrils and the mouth; either could be removed according to the site of operation.

Diday conceived a rubber mouthpiece, fitted on the enlarged aperture of a container which could be inserted between the teeth and the lips like the cannula in the form of a double tube that Dupuytren had used for operating on a benign tumor under the tongue.

In Charrière's inhaler the ether flask was always in communication with atmospheric air. The physician of the Hôtel-Dieu of Lyon, Charles Pommiès[15] (1820-1880), understanding that this was a defect, added a valve to the end of the air conduit (Figure 2). In the same way, Amédée Bonnet substituted for the ether sponges by having a small reservoir of 6 centiliters (R in Figure 2), containing 60 grams of sulphuric ether; when a ground-glass stopper was raised by a piece of cardboard, the ether dripped into the flask. The drop rate was controlled by a tap(r) and the drops fell on to perforated plates to speed evaporation. The third modification that Bonnet and Doyère made on Charrière's inhaler was to change the 12 mm wide pipe tube to one of 2 cm.

By the first week of March, Emile Gromier,[16] a physician of the Hôtel-Dieu in Lyon, had also abandoned the ether sponges. He poured tepid water into the flask, adding the ether to form a film of 2 or 3 mm thickness on the water. He believed that as well as improved vaporisation there was less respiratory irritation, since any sulphuric acid contaminating the ether was dissolved in the water. The first operation using ether for removal of a growth, performed by Leblanc[17] a surgeon of the Hospital de Fontainebleau on 21 January was unsuccessful, but anaesthesia was effective on 30 January for amputation of the right leg of Warrant Officer Malkaine of the 1st Regiment of Hussars.

In Bordeaux, the surgeon of the Hospital Saint-André, J J D Puydebat,[18] decided on 2 February to perform, even with an imperfect ether inhaler, an amputation through the thigh on a sixteen year old whose fracture from two years previously had been badly managed by a surgeon of La Teste. The patient presented with a hectic fever. Nevertheless, after 6 minutes of inhalation he was anaesthetized for 7 minutes, and felt no pain during the operation. The second and the third attempts by Puydebat, on 4 and 9 February respectively were failures; but the fourth case, performed with a Charrière's modified inhaler on 12 February for an anal fistula, was successful.

On 5 February, Mathieu Louis M Mayor[19] (1775-1847?) of Lausanne, reduced a hernia under ether. He used a wide-necked vase and a waterproof cloth with which he covered the patient's head without any fuss. To have a view of the patient's face, a glass window was made in the cloth.[20]

On 6 February, Jean Gaspard Blaise Goyrand[21] (1803-1866) from Aix, amputated the breast of a woman in the town of Tretz. Despite the imperfect device used, muscular relaxation was achieved after three and a half minutes. Two days later in Marseille, Reymonet[22] was successful in an amputation of the thigh, Rigal,[23] from Gaillac (Tarn), extracted molars and painlessly inserted seton drains in the neck. Blanche[24] in Rouen succeeded in an operation on the tibio-tarsal joint. In Dole (Jura), Armand Jobert,[25] the Director of the Maison de Santé des Capucins, used ether inhalation in a case of insanity, performing at the same time a blood-letting on the arm and application of cupping glasses on the thigh. He related his treatment, which included Unani remedies, on 13 February.

In the hospital of Senlis (Oise) on Monday 1 March, Léon Clément V Voillemier[26] (1809-1878), in front of his colleagues Jules Leclercq and Bellenger, and ten residents of the town, amputated the forefinger of the right hand of Jean-Baptiste Arsène Dargent from Villevert. On 3 March in Besançon, Martin[27] amputated the middle finger of an alcoholic patient; after 20 minutes of ether inhalation insensibility was not complete. A purer quality of ether was necessary. In the hospital Saint-Jacques, Corbet gave ether for a hernia operation using Lüer's inhaler; hysterical reactions occurred.

Conclusion

Thanks to Willis Fisher's tenacity the first European trial of anaesthesia was performed in Paris. Early experiments with ether inhalation provided many failures; although different patients responded in different ways, the French surgeons and instrument makers did not lose faith in a promising new technique.

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FREDERICK WILLIAM COCK (1858-1943)
A NEGLECTED HISTORIAN OF ANAESTHESIA

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On the occasion of the centenary of ether in 1946 Massey Dawkins delivered a superb lecture at University College Hospital (UCH) on the introduction of anaesthesia into England. This was subsequently published[1] and Dawkins acknowledged that he was grateful to Dr F W Cock for information derived from his collection of letters now lodged in the Royal Society of Medicine (RSM). When I came to study these I realised at once what an important collection they are.[2] In all there are 202 items of which 119 refer to the introduction of ether, the remainder are reminiscences of Robert Liston as a surgeon. This paper refers only to the 119 items concerning anaesthesia. Many of the others were published by Cock under the heading *Anecdota Listoniensia*.

I could not recall having seen these important letters published in full. Searching the literature I found an earlier and similar acknowledgment was made in 1930 by Lord Dawson of Penn when he was President of the RSM.[3] He had addressed a meeting of the Section of Anaesthetics about Henry Hill Hickman, the centenary of whose death it was, but he referred also to the introduction of ether six years after Hickman's death. He, too, says he is indebted to Dr F W Cock of Ashford for further facts. Next, I found that Ellis had included references to two articles by Cock in his own much-quoted paper in *Anaesthesia* in 1976.[4] One was to an article in the *UCH Magazine* in 1911[5] and the other to the *American Journal of Surgery* in 1915.[6] Ellis makes no comment at all on these papers in his text, he seems merely to have included them for completeness. He does not mention the collection of letters at the RSM so presumably he did not consult them.

During 1911 brief annotations in both the *Lancet* and the *British Medical Journal* (*BMJ*) drew attention to Cock's *UCH Magazine* article but apart from these I have found no other references to his work. I would be interested to hear of any others.

The introduction of ether anaesthesia was followed by numerous reports in medical journals of the day, but all are short, factual and give little detail of the events. It was not until the 50th anniversary of ether in 1896 that greater detail was supplied in a series of contributions to a *BMJ* symposium celebrating this jubilee.[7] Here are listed a number of those believed to have been present at Liston's operation at UCH and, of these, Cadge and Squire added their recollections to the symposium. Cadge, a surgeon, prefaced his account by saying: 'I write from memory as I have no notes of the occasion'. William Squire, the anaesthetist, starts his account: 'my own share .... seems to me greater now than it did at one time'. Both are surprising statements suggesting that neither realised the significance of the occasion.

Dr William Cock's collection of letters

Dr Frederick William Cock appears fourteen years later when, on 22 October 1910, letters from him appeared in both the *Lancet* and the *BMJ*. These stated he was collecting material for a description of the first operation under ether in Europe, that performed by Robert Liston on 21 December 1846, and would like to hear from any surviving witnesses. In response he received 11 letters, some from the 2 surviving witnesses, the remainder from the family or pupils of those who had been present and were now deceased.

The survivors were Dr H Montague Duncan and Dr Edward Buckell, both of course now old men. Their letters do not add much to what is already known, but their significance is that they were clearly an important part of the source material used by Dawson in 1930 and by Dawkins in 1946. Whilst these authors also used material previously published in the *Lancet* and the *BMJ*, much of their inside story must have come from these letters written by Duncan and Buckell to Cock. Because Dawson and Dawkins paraphrased them it is worth quoting directly from the original letters.

Dr Duncan, by now 88, wrote claiming he was the first in Great Britain to inhale ether vapour:

> 'In 1846 ..... I gained admission to the meeting of the Medico-Chirugl Socy to hear Geo Johnson's lecture on the kidney. After the lecture Dr Morton of Boston (or his assistant from America) exhibited his inhaling apparatus. A patient from the UC Hospital who had promised to appear to be tested failed to do so and as no one else wanted to submit to the trial, I offered myself - for during the enforced 5 years apprenticeship of the time I had made and studied the effects of nitrous oxide after the method of Sir H Davy and practised its effects on my young acquaintances so safely that I boldly and fully inspired the ether vapour - becoming unconscious and awoke in full health and in presence of many anxious faces. The only inconvenience being an itching and stinging of my wrists which showed that needles had been inserted (without my feeling their punctures at the time) and noticed a little bleeding.'

There is a discrepancy here. Duncan links his experience to a lecture by Johnson on the kidney. However, the *Transactions of the Medical and Chirurgical Society* show that this lecture was given not in November 1846 but a year earlier in November 1845. Surely Duncan did not fabricate the story, more likely that his 88-year-old memory was at fault. Indeed, when pressed by Cocks for dates he confessed he could not remember exactly. The *Transactions* do not help further because their practice was to record only the main lecture of the evening and not any informal events which followed. Perhaps on this occasion they missed a journalistic scoop!

Duncan's letter goes on to say how he had often wished to communicate his knowledge to Dr Morton, the founder of painless operations, but did not know how to contact him. He also describes how Liston invoked the help of William Squire, the medical student on his firm, how together they watched James Robinson in Gower Street administering ether for tooth extraction, and then sought the help of William's father, Peter, the pharmacist who over the weekend devised the inhaler they used during Liston's amputation.

Dr Edward Buckell's letter recalled:

> 'I was standing close to Liston .... when he took out his watch and challenged us to mark the time he occupied in the removal of the thigh. My memory is, and always has been, that it was 27" ...... I am satisfied that Mr Peter Squire was closely engaged in the actual

administration of the ether and that William Squire was acting in concert with him and it cannot be said that one or the other was solely responsible.'

Among other letters are three referring to Robinson. The first came from one of his pupils, John Wood, who wrote:

'I was a pupil of Mr James Robinson of Gower Sreet from 1853 to 1861. I always understood he was the first to use ether in England and I believe Mr Liston took it up immediately after witnessing some tooth extractions at Mr Robinson's.'

Wood then refers Cock to Robinson's nephew, Mr Ridley Manning Webster, who in his turn wrote:

'My uncle by marriage Mr James Robinson died in 1862. ... He called my attention to Dr Boott's house in Gower Street and said that this was where the first administration of Ether for general anaesthesia took place in England.'

Cock's collection includes letters from several relatives of those who had been present recounting what they had been told. Cock incorporated all this material in his paper entitled: 'The first operation under ether in Europe - the story of three days' in the first issue of the *UCH Magazine* in 1911.[5] It seems surprising that this article has so seldom been quoted subsequently in comparison with the very well-known one by Dawkins of 1947.[1] It was the latter's brief mention of : 'a collection of documents given by Dr Cock to the RSM' that brought them to my attention. Today, therefore, we learn little new except that all the facts were recorded as early as 1911. The value of the collection lies in its being the primary source for much of this information and it is important that it should be recognised as such.

William Cock - the man

We may, of course, learn much more from these documents than mere facts. Cock's article is not just a record of events. It is an historical account, carefully researched and well-written in an entertaining style, a combination of erudition and lightness of touch. He starts off, as a good writer so often does, by catching his reader's attention with something apparently entirely irrelevant, quoting R S Surtees, the 19th century author of many humorous books about fox hunting. In *Hawbuck Grange*, written in 1847, Surtees wrote that 19 December 1846 was: 'one of the worst days of the worst hunting season on record'. He not only refers to the vile weather but goes on to mention the newly introduced ether and its effects in producing unconsciousness. Surtees says:

'I wish someone would send instructions for indicting the weather. Talk about ether for cutting folk's heads off when they're asleep without hurting of them, I wish they'd etherize me and let me sleep during a frost.'

Cock says casually that he thinks this may be the first reference to ether in the general literature. However, not content merely to quote Surtees, he checks up with the Greenwich Magnetical and Meteorological Observations where two-hourly recordings of the weather are recorded. A scribbled note in his own handwriting on a scrap of paper quotes the Greenwich weather records for December 1846:

December 1846:

16 Snow 6/7pm
17 Fine
18 Raining
19 Foggy and raining
20 Raining and blowing
21 Cloudy, frosty night
SW wind F49.5-33.8 Temp at 2pm 49.5

Surtees, it seems, was not exaggerating. As a good historian, Dr Cock ends his article with an extensive and accurate bibliography, unusual at a time when writers were not as careful about quoting their sources as today.

Next we can learn that William Cock was an imaginative man. When the old operating theatre used by Liston was demolished prior to new ones being opened in 1900, Cock rescued the iron railings separating the audience from the operating area and had them installed at his own residence, the Well House in Appledore, Kent.

In 1922 he had another original idea, namely, to present mementoes of the discovery of anaesthesia to both University College Hospital, London and the Massachusetts General Hospital, Boston. He had two bells made, both cast from the same ingot as the then new Westminster Abbey bells. These he had inscribed: *Nolae pulsatio amoris ratio'* which may be translated as: 'when I do sound let joy abound'. The UCH bell was presented at the annual dinner in October 1922.[8] The other arrived safely in Boston and was acknowledged with gratitude by the surgeon J C Warren. Unfortunately, UCH has not taken good care of their bell as they have today (August 1997) no knowledge of the bell or its whereabouts.

William Cock, physician and historian

Frederick William was the son of Frederick Cock, also a doctor. The Cocks were an old family from Romney Marsh in Kent who could trace their ancestry from William Cock, a smith, who in 1432 had made some of the ironwork for Lydd Church. Frederick Cock senior began to study medicine in France and Germany, then returned to England and qualified MRCS in 1851 from UCH and MD Edinburgh two years later. He married and settled into practice in London in Westbourne Park Terrace as physician and anaesthetist.

It was here that Frederick William was born in December 1858. Like his father, he travelled though not as far afield, studying medicine both at UCH and at Durham University, where he qualified with first-class honours in 1884, and MD two years later. He followed his father as physician and anaesthetist in Westbourne Park Terrace. He was anaesthetist to the Guy's Hospital Dental School and during the First World War was Honorary Anaesthetist at King George Hospital. He seems to have had academic inclinations and maintained his connection with UCH as a demonstrator in anatomy, physiology and chemistry at various times.

In 1898 at the age of 40 he married Frances, daughter of Alfred Evans of Exeter. She died in 1937 and they had one son.

Cock's historical interests were wide and in 1902 he was elected a Fellow of the Society of Antiquaries, to serve on its Council in 1923-24. His citation read: 'He is a man engaged in the collection of materials for the history of Romney Marsh'. He was a liveryman of the Worshipful Society of Apothecaries, admitted by an unusual route. In the 1890s the Society was short of members and for a brief period opened its freedom to all those qualified as licentiates. Not one to miss a chance, Cock joined and was promoted to the Livery in 1908.

Cock followed his father as both a member and President of the Harveian Society. We know nothing about his father's year of office as the Society's Minutes for the 1870s are lost. William presided over the Society's 75th session. His Presidential address, given on 10 January 1907, is summarised in the Minutes. It was not about anaesthesia but the story of William Waylett, an 18th century man-midwife of Lydd, Kent. It was based on a casebook of Waylett's which Cock found in the care of an old lady, a Miss Buss, resident in the Almshouses at Lydd and clearly he had meticulously researched it. The Minutes describe it as having been published as a monograph the following year.

During his year of office the Society held, amongst other topics, a discussion on the mortality in lying-in hospitals. During this, Dr Adams had objected to the use of chloroform in labour because he considered it diminished the pains so much that it often necessitated the use of instruments, which in turn increased the incidence of sepsis. Dr Handfield-Jones, however, thought it was particularly useful in private cases in neurotic subjects and if used carefully did not interfere with labour and may save rupture of the perineum. Arguments about obstetrical anaesthesia have barely changed over the years since then.

Cock joined the British Medical Association in 1889 and was a regular contributor to the journal over the period from 1910 to 1940. I have traced 29 communications on a wide variety of topics, always written in a delightfully light witty style. These usually, but not always, have some medical and/or historical connection and a few recall his own experiences as an anaesthetist. One of these, a case report entitled: 'Herniotomy in old age'[9] reads:

> 'An old lady who in her youth had been the playmate of Queen Victoria at Kensington Palace. Corpulent with pendulous abdomen and bilaterial herniae. I was sent for early one morning and found the right side had strangulated. Charles Stonham of the Westminster Hospital operated. The patient was in a small iron bedstead in a very narrow room with hardly space to move in, so much so that I had to lie down beside her with her head over my left arm and my thumb in her mouth to make an airway whilst I dropped chloroform with the other hand on a mask. All went well .... she was up in a fortnight. I sat her up in bed that night for 2-3 hours. The sequel a year later the other hernia strangulated. We went through the same drill successfully. Again the old lady recovered .... though she had a stitch abscess. She was 89 the first time, 90 the second and she lived five more years.'

In addition, he contributed regularly to the *UCH Magazine* and to *Archeologica Cantiana*, the journal of the Kent Archeological Society, which includes seven scholarly articles from his pen.

In 1923, when he was 65, Cock moved from his London residence to his country home at the Well House, Appledore, where he had earlier installed the UCH theatre railings. He had joined the Kent Archeological Society in 1898 and served on its Council and as a Trustee. He wrote a history of Appledore Church which, with his friend, the stained glass artist Godfrey Wood Humphry, he had embellished by installing new windows during the 1920s. His library of books and manuscripts on Kent antiquities was described as one of the most complete and famous in the county. He served for many years as a Justice of the Peace.

William Cock died just short of his 85th birthday on 9 October 1943 and was buried in the churchyard at Appledore. His library was sent to be auctioned by Sothebys. Their catalogue shows that it was sold in 391 lots over two days in May 1944 and fetched £3,967.10s.0d. Sadly, it was dispersed amongst numerous buyers.

Several obituaries record his life. The *BMJ*[10] describes him as: 'an old friend of the journal with his learned little notes on out-of-the-way subjects'. A longer obituary appeared in *Archeologica Cantiana.*[11] Here, Cock was described as probably the greatest living authority on Romney Marsh and its history, always generous of his time in helping students and enquirers:

> 'We shall all miss his cheerfulness and kindness and goodness: we shall treasure the memory of his industry in research, his desire to share with others what he had learnt, and his unfailing charity. He never said an unkind or harsh word.'

Perhaps now, the world of anaesthesia will come to appreciate these qualities and at last give him an honoured place in our history.

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MANAGING CHANGE IN CLINICAL PRACTICE - THE EARLY DAYS OF INHALATION ANAESTHESIA

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(Abstract)

Inhalation anaesthesia was the first medical and scientific technique to become established as a legitimate means of pain relief. Fitting the new technique into routine medical practice and popular culture involved the development of a framework of ethics, judgement and expectations, a process which generated intense conflict between individual practitioners and between the medical world and the public.

The recent publication of John Snow's anaesthetic case-books has renewed interest in the early years of anaesthesia,[1] and reviewers have called for the records to be analysed to explore how new powers, roles and responsibilities were negotiated.[2]

This paper presented preliminary findings of new research which uses the case-books to explore the importance of class, race and gender in medical science and medicine. It focused on Snow's interpretations of his patients' reaction to the new technique and the types of patient he thought appropriate for various kinds of anaesthesia.

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OMBRÉDANNE'S INHALER

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The paper in which Louis Ombrédanne[1] introduced his ether inhaler has recently been published in the *Cahiers d'Anesthésiologie*, with an introduction by Professor Jean Lassner.[2] Although it has been well summarised by Bryn Thomas[3], the original paper is of particular interest to anaesthetists, because it gives an account of the reasons for producing another apparatus, and of the early efforts to construct an efficient inhaler before the final apparatus was designed. The paper gives an interesting insight into the condition of anaesthesia in France ninety years ago.

Professor Lassner briefly describes the early inhalers of Morton and Snow, and also of Ormsby and Clover, with which Ombrédanne compares his own apparatus. He then concludes his introduction as follows:

> 'It is well-known that the practice of anaesthesia was very rapidly adopted on the continent of Europe, but unlike in England, where it had been the province of doctors, it was left to every kind of assistant. It is not by chance that for the first operations performed under ether on the Continent, the names of the surgeons who performed the operations are retained, but not of those who administered the ether. It is in this context that one must consider the remarks concerning the anaesthetist which one finds in Ombrédanne's article of 1908 which is reproduced below.
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> 'Ombrédanne (1871-1956) specialised in paediatric surgery and occupied the chair of that specialty in Paris from 1925. We owe to him improvements in various operative techniques - in orchidopexy and the correction of hypospadias and hare lip. His interpretation of the radiological appearances of congenital dislocation of the hip has kept its importance. Ombrédanne's interest in anaesthesia led to work which lasted for several years, culminating in the 1908 publication. The quality of simplicity of its use which this first article stressed was confirmed by the long-lasting popularity of his apparatus. It dominated anaesthetic practice for more than 50 years and was widely used in other countries, for example Belgium and Germany.
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> 'In the large anaesthetic textbook by H Killian and H Weese published in 1954, the authors report gas analyses of the contents of Ombrédanne's rebreathing bag at the half-open position carried out by Fohl and Mittel (pp 477-478). They found an oxygen content of 15.67% and a carbon dioxide content of 4.3%. The stertorous respiration of those being operated upon is explained by these levels of CO_2 and also the risk of cyanosis. The fixed proportion of the entry of air and the level of ether meant that in increasing the latter one diminished the percentage of oxygen. The surgeons were so used to hearing the noisy respiration of their patients that they expressed anxiety at the introduction of the modern techniques after the second world war. Thus the qualities of the apparatus contributed to the delay of modern anaesthesia in France.'

The failure of Ombrédanne's inhaler to obtain popularity in Britain was probably partly because Hewitt's modification of Clover's inhaler overcame some of its disadvantages and partly because it was nearly half the weight.

The Hon Editor suggested that having presented, with Professor Lassner's approval, an abridged version of this paper to the meeting, I should provide for the *Proceedings* a full translation of Ombrédanne's original article, which now follows.

It is important to remember that Ombrédanne was dealing with untrained personnel and therefore had to lay down a rigid sequence for inducing and maintaining anaesthesia. With this in mind, one must admit that his apparatus was ingenious. Ombrédanne criticised Clover's inhaler for having too narrow tubes but, as Bryn Thomas points out, the ports in his own apparatus were not very wide - the chimneys were 17 mm square, the bag outlet 19 mm wide, the facepiece outlet 25 mm and the 'stepped' air inlet 112 sq mm in all.

As a final note, Professor Lassner informs me that Ombrédanne changed his name from the family name of Ombredane, as he did not like being a 'donkey's shadow' (ombre d'âne)!

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UN APPAREIL

POUR

L'ANESTHÉSIE PAR L'ÉTHER

Par M. le docteur OMBRÉDANNE,
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We have no intention of comparing the respective advantages and disadvantages of ether and chloroform in general anaesthesia. We consider chloroform to be a very dangerous agent, for we are aware of the considerable number of accidents it produces each year, without being able to give accurate figures.

The danger of chloroform consists in the 'white syncope', which cannot be foreseen or avoided, and for which there is no effective treatment. The danger of ether consists in the pulmonary complications which on the contrary can be nearly completely avoided, for:

1. Ether has relative contraindications: advanced age and pleuropulmonary disease. In hospital practice where ether is employed as a general rule, but where old men and patients with pleuropulmonary disease are anaesthetised with chloroform, more pulmonary complications occur with chloroform than with ether. Moreover, those contraindications

are not absolute, and perhaps we will no longer admit them if a very long experience of the apparatus we describe below confirms the first 300 results.

2. The pulmonary complications of ether are largely *avoidable*: they occur in subjects who have been *cyanosed* during anaesthesia or who have salivated abundantly; now, these phenomena usually follow the use of *massive doses*.

There is therefore much progress to be made in the administration of ether by striving to reduce the doses given.

We have sought to achieve this progress by using an apparatus which allows one to maintain the patient on the threshold of anaesthesia, and therefore without cyanosis, permitting on the other hand induction to take place slowly and progressively, without a massive initial dose, which is agonizing for the patient and where danger from the point of view of pulmonary complications seems to us obvious.

For five years now we have been looking for the solution to this problem, and in the last year we have found it. In the course of our research, we have noted a certain number of interesting facts concerning ether anaesthesia.

First proposition: *One cannot anaesthetise a patient with a fresh mixture of air and ether vapour; at the very most, one can maintain anaesthesia in this way induced by another method.*

We have in fact, used for operations on the face[1], an ether vaporiser constructed from a sort of teapot filled with sponges soaked in ether (figure 1). From the spout of the vessel a rubber tube goes to the patient's mouth: this device allows anaesthesia to be maintained, but not to be induced.

Figure 1

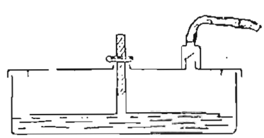

Figure 2

Later, when Ricard made his excellent chloroform apparatus, we constructed an identical apparatus, but much bigger, in which the glass vase was replaced by a crystalliser 12 centimetres in diameter (figure 2). The disc was plunged into the ether, forcing the air to bubble through the liquid: the result was the same as with the former device.

These two experiments repeated time and again left no doubt about the validity of the first proposition.

Second proposition: *Ether anaesthesia functions well only if the patient breathes in a more or less confined space.*

This notion could already be suspected from the results obtained by the old masks of Julliard and Landau.

Julliard's mask gave better results the greater its capacity. To obtain induction it was necessary to raise it no more than once after it was applied to the face; in other words, to make the patient breathe in a confined space.

Having accepted the principle of breathing in a confined space, we constructed an apparatus placed like a cork on a jar full of ether; this cork held two tubes, one leading to a bag of goldbeater's skin [cow's intestine], the other ending in an inhalation mask; in the course of this last an opening allowed the regulation of the entry of supplementary fresh air (figure 3).

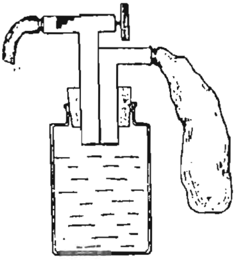

Figure 3

Already this apparatus was better; nevertheless, in men it did not always allow us to achieve induction, even when giving its maximum action.

We blamed the too small diameter of our tubes and the distance which separated the ether vaporiser from the facemask, thinking that perhaps these factors favoured the condensation of the ether vapour.

Third proposition: *The ether vaporiser must be near the facemask; the tubes must have a wide diameter.*

We wanted to ensure that these two conditions did not interfere with the necessity of the confined space. Filling a half litre reservoir with tow, we poured 250 grams of ether into it. This reservoir lay directly over the mask, from which it was separated by a metal diaphragm; below was a means of admitting a variable amount of fresh air. In spite of the huge dose of ether this supplied, the patient did not become unconscious.

Fourth proposition: *An addition of fresh air is necessary, whatever the duration of anaesthesia; the necessary proportion of fresh air is not very great.*

The first part of this proposition resulted from the operation of the English inhalers of the Clover type. We should say at once that, as regards the operation of Clover's and similar English inhalers, we did not want to found our criticisms on the too small numbers of anaesthetics we saw practised in London: we base them only on what we found in the very recent work of Dudley Wilmot Buxton.[2]

These inhalers, we say, not being furnished with the means of introducing fresh air, give rise very quickly to cyanosis if one does not frequently raise the mask above the patient's face. It is the chief inconvenience of the English inhalers that they continually produce either apnoea or cyanosis, through lack of fresh air.

The second part resulted from our statements about our earlier apparatus. One knows, on the other hand, that the sole fact of raising Julliard's mask renders further anaesthesia practically impossible: a good ether anaesthetic, therefore, needs the addition of fresh air, but fresh air prevents the onset of sleep. There is an amount to be determined which lies between these very narrow limits.

Fifth proposition: *The surface available for the evaporation of the ether must be very considerable.*

It is a fact that we have established with our previous models of apparatus in stating that, in putting ether freely into them, anaesthesia was difficult to establish, while one easily obtained this result by soaking the sponges with the same quantity of ether. We have therefore accepted as proved the preceding propositions, which can be summarised thus:

> *To obtain good anaesthesia with ether, there must be an ether vaporiser near the facemask, and only having tubes of very wide section; the patient must breathe in a confined space, but there must be an addition of fresh air. The surface of ether available for evaporation must be considerable.*

From the theoretical point of view, these propositions are easily explained on physical grounds: the density of ether vapour and its easy evaporation depend on the use of tubes of wide diameter and on a vaporiser near the mask. The necessity for fresh air arises from the same principle of respiration which cannot exist in an absolutely confined space without rapid anoxaemia and asphyxia.

It is more difficult to explain the need for this respiration in a relatively confined space. Does the existence of the skin bag allow the *concentration* of ether vapour or does a certain quantity of inhaled *carbon dioxide* favour narcosis? The concentration of ether vapour did not suffice for a good anaesthetic, since our apparatus (figure 4) did not give good results.

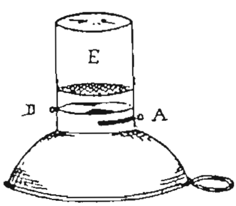

Figure 4

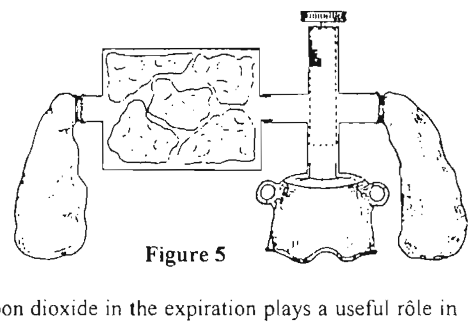

Figure 5

Therefore, it must be admitted that the carbon dioxide in the expiration plays a useful rôle in anaesthesia.

Recently, Langlois has recalled attention to the non-toxicity of carbon dioxide, which Gréhant has already revealed, and has cited experiments which show the rôle of carbon dioxide in the regulation of the heart and respiration.

But if carbon dioxide in low dosage is a useful adjuvant, that dose must be kept very low, never to result in accidents.

From this practical point of view, we have achieved the conditions of which we believe we have proved the necessity in the apparatus of which we are now going to speak.

This apparatus can be considered as a tap with three openings leading:

1. the first to the atmosphere;

2. the second into a bag, a reservoir of *confined air*;

3. the third into a reservoir filled with sponges soaked with ether, this reservoir being prolonged equally by a similar bag, augmenting its capacity, the whole constituting the *generator*. A trial apparatus of this type was constructed with two separate bags (figure 5). It functioned perfectly. It remained only to establish a practical device, with only one bag: this is the one we use today (figure 6).

A sphere is filled with sponges soaked in ether: this sphere is the *generator*. It is traversed transversely by a diametrical tube ending at one extremity in a bag, and at the other in the outer air, where it opens by windows arranged in steps (*K*) (figure 7).

In this diametrical tube there open laterally:

1. Two chimneys *G* and G^1, one at the entrance, the other at the exit of the respired air. A half partition baffle *R* forces the air to expand into the sphere, instead of passing directly from one chimney to the other;

2. A tube *H*, which leads to the facepiece;

3. A bypass tube *J* leaves the previous tube and ends in the diametrical tube.

The existence of this bypass tube, absolutely independent of the way opening into the vaporiser, is an important characteristic of our apparatus.

In the diametrical tube, there rotates a hollow pipe, closed at *N*, and pierced by windows *O*, O^1, O^2, opening progressively; the window O^2 is always open. The movements of this pipe are activated by the rotation of *an indicator* on a graduated scale marked from 0 to 8.

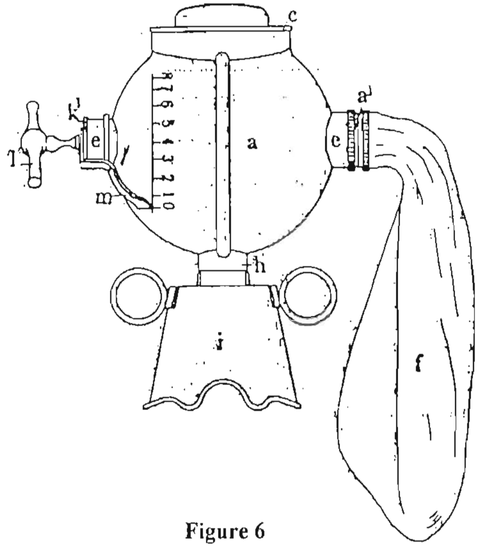

Figure 6

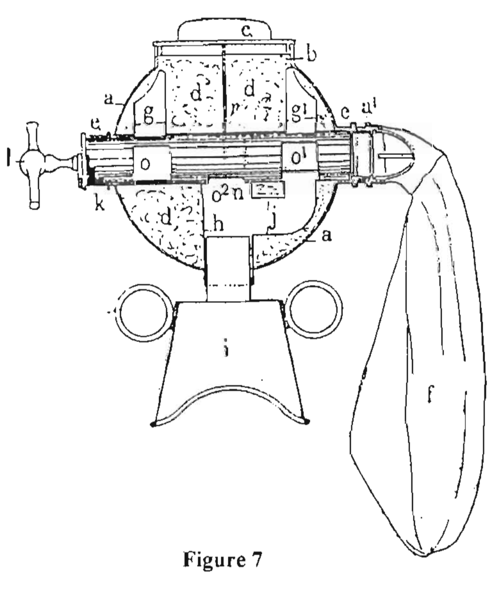

Figure 7

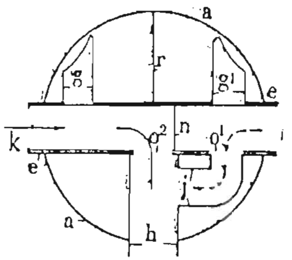

Figure 8

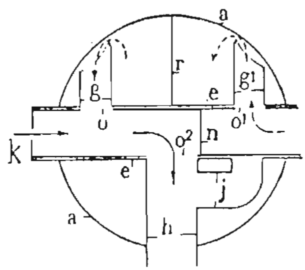

Figure 9

In position *O* (figure 8), the windows *G* and G^I are closed; *K* and O^I are fully open. A lot of fresh air enters the facemask, and a little confined air.

The only ether which gets in is that which filters through the closed windows *G* and G^I.

In position 4, the median position: the window *K* is semi-closed, *G* and G^I are semi-open; O^I is semi-open.

Into the facemask there enter: (1) fresh air; (2) ether vapour from the bag, saturated by passing through the sphere; (3) confined air containing ether vapour, but coming via the by-pass pipe O^IJ without being saturated in the sphere.

In position 8 (figure 9): the window *K* is open at the minimum; *G* and G^I are fully open; *J* is closed.

Into the facemask there enter: (1) a little fresh air; (2) ether vapour saturated by passage through the sphere from the bag.

The respective dimensions of the windows were determined by trial and error.

Such is the internal mechanism of our apparatus.

Constructed in this way, it has given us excellent results. We wanted to verify yet once again the accuracy of certain of our propositions. In particular, we sought to separate the vaporiser from the facemask.

In those conditions we were not able to render our patients unconscious; but once induction was achieved with the ordinary manoeuvre, we were able to maintain anaesthesia with the separated apparatus.

In the second place, we sought to substitute liquid ether for the sponges soaked in ether; the functioning was much less good. We observed a tendency to apnoea and coughing; some men did not become unconscious at all even when the apparatus was fully open. Therefore, the sponges, by giving an enormous surface for evaporation are indispensable, moreover they avoid all chance of seeing liquid ether run into the bag or escape through the opening *H*.

So much for the internal mechanism and the interior functioning of the apparatus; here is its method of use.

The facemask was sterilised, its rubber cuff boiled. At the bottom of the skin bag one could, if desired, add some drops of any perfume, which is allowed to dry. One ensures that the bag is not punctured.

The indicator being set at 0, the upper orifice is opened and 150 grams of ether is poured on to the sponges. The sphere is turned in all directions, then inverted; ether must not run out, but be all absorbed by the sponges. The upper orifice is closed again.

The mask is attached, using slight pressure. It is applied to the face, the indicator being at 0.

It is left in this position for *two minutes*, the patient being told to breathe deeply. Then, minute by minute, the indicator is advanced by *one degree*, or better, from half-minute to half-minute, the indicator is advanced by half a degree.

One rises thus to 5 or 6 for men, to 4 or 5 for women; one waits one or two minutes for induction to be complete, then goes back, in the same way, to the maintenance number, which for men is about 4 and about 3 for women.

It should be understood that these maintenance numbers are only averages; they are the result of observations of anaesthetics given by students of the department and in particular from numerous graphs made by our externs and our friend M Tison. Some women remain perfectly anaesthetised at 2½, others need 3½. Some men need only 3; old alcoholic men must be maintained at 5 or even 6.

It is only exceptionally that we use the higher numbers 7 and 8 to anaesthetise confirmed alcoholics. It is a rough average which should be avoided and we consider dangerous the manoeuvre of the English inhalers which normally use the degree *f (full ether)* at the end of a minute or a minute and a half. Moreover, the result according to Buxton is the frequent presence of cyanosis and of spasms requiring the administration of oxygen(!). There is nothing astonishing in that with Clover's apparatus, which does not admit fresh air. The apnoea which it also produces appears to be the consequence of the lack of fresh air and of a large dose of ether. For us it is a major failing of an apparatus not to be able to produce anaesthesia except by this violent process. Moreover, most of the English surgeons are so used to it that they begin by attaching the inhaler to a source of nitrous oxide at the beginning of the anaesthetic.

The most perfect inhalers derived from Clover's do not escape this criticism: the Probyn Williams inhaler also had equally three degrees and a 'full ether' and functions with liquid ether without sponges. The description given by Buxton makes no mention of a source of fresh air. The improvements of which this author speaks would be only the increase in diameter of the tubes and the suppression of the warm water chamber, which is in fact a perfectly useless element in Clover's apparatus.

Once the patient has his maintenance concentration, anaesthesia continues without any interruption for an hour and a half. The 150 ccs at the beginning always suffice. After that time, another 50 ccs of ether must be put into the apparatus: we have had to do it twice. The English inhalers with liquid ether only receive 2 ounces of ether, giving half an hour of anaesthesia. Recharging the apparatus every half hour only causes interruption of the anaesthesia.
The apparatus is not heavy: two rings attached to the side of the mask permit the thumbs to hold it and the other fingers to raise the angles of the jaw. If need be, an elastic rubber band maintains the apparatus in place without the anaesthetist having to hold it.

In the Trendelenburg position or in the lateral position, the functioning is the same; the position of the patient is unimportant, since the ether is not liquid in the sphere. To operate on the face, one anaesthetises the patient at first as described above; when anaesthesia is obtained, the mask is detached from the sphere, one places it on its support and attaches to it a rubber connection ending in our buccal obturator. A plug of gauze in each nostril prevents the entry of air into the nose. At this point, the indicator must be raised one division to continue a good anaesthesia.

When one wants to anaesthetise another patient after the first, it is sufficient to open the apparatus, pour in another 150 ccs of ether, then allow the excess to run out by inverting the sphere; the amount of sponge is calculated to absorb about 150 ccs and no more.

From time to time it is useful to remove the sponges and squeeze them to remove the water of condensation which has accumulated in them.

So much for the technique. Here, in summary, are the considerable advantages we find in using this apparatus:

1. It releases very little ether vapour into the room; it does not incommode the anaesthetist, for it is directed straight downwards. This vapour in minimal quantity and mixed with carbon dioxide and water vapour probably avoids the danger of inflammability; we have often used our apparatus in rooms heated by open fires.

2. The face mask, with its very small dimensions, allows one at any time to examine the patient's appearance and the state of the corneal reflex, without needing to raise it.

3. The induction of the anaesthetic is *not at all upsetting* for the patient, who is insensibly accustomed to the ether; he has not the horrible sensation of suffocating which other methods give.

4. The state of excitement is often completely absent, especially in women. When it occurs in men, it is of very short duration.

5. One observes neither the apnoea nor the persistent coughing which one sometimes has at the beginning of the anaesthetic with Julliard's mask or Clover's inhaler. If the patient coughs, one must move back one degree - *there is too much ether*; one increases it again more slowly. Complete anaesthesia is obtained in six to seven minutes in men, and five to six minutes in women. This relatively slow progress is necessary for anaesthesia to supervene without distress for the patient, without agitation and without cyanosis. We disapprove of the anaesthesia in ninety seconds advocated by Buxton.

6. One always achieves anaesthesia, even in alcoholic men. It supervenes slowly and progressively. There is evident superiority over the English inhalers, which maintain anaesthesia well, but induce it with difficulty. The proof is in the fact that everyone is disposed to begin the anaesthetic with nitrous oxide.

It seems to us that the inferiority of the Clover type of inhaler arises from two causes: first, they use liquid ether, from which the surface for evaporation is too small; then because the interior arrangement of the apparatus, very different from ours, has narrowing in the tubes. Free ether has the added inconvenience of not allowing the operation of the apparatus in every position.

7. The action of the mixture of anaesthetic gases is produced *absolutely continuously for one and a half hours*. This continuity is an important factor in the smoothness of the anaesthetic. In the English inhalers which receive only the necessary dose of ether for half an hour's anaesthesia, the level of the indicator must be advanced a short time before this time limit, then moved back again when one adds another dose: leading to interruption in the narcosis.

8. Never any cyanosis. The patient can and *must remain pink*. It is the business of the anaesthetist who regulates the indicator; often half a degree suffices to make the slightest cyanotic tinge disappear. It is obvious that, in some patients, the angles of the jaw must be raised and pushed forward to favour free respiration.

In the conduct of the anaesthetic the state of the pupil is unimportant and is not reliable. The *abolition of the corneal reflex* must be obtained, proof that the anaesthesia is adequate, there must *never be any cyanosis* which, as we have said, is easy and proves that the anaesthetic has not been pushed too far. As soon as one has achieved for the patient these two essential conditions, all goes without any modification for the whole period of the anaesthetic, for an average of one and a half hours, without having to touch the apparatus.

The sensitivity of the apparatus is such that the observations made by our extern and friend M Tison have shown that an average of one degree higher is needed for men than for women.

It does not seem to be the same with the English inhalers, which appear less sensitive, for Buxton gives only one figure for both sexes.

9. Vomiting during the operation and excessive salivation are less common with this apparatus than with Julliard's mask. We do not know why. If there is salivation, one must obviously raise the mask to wipe the mouth very quickly; apart from this, *one should never*

remove the mask, as opposed to the Clover inhaler, where this manoeuvre is the only means of giving the patient a little fresh air from time to time.

10. About five minutes before the end of the operation, at the moment when the operator begins his sutures, the indicator is progressively moved back to *0*.

Awakening is extremely rapid, which is explained by the fact that the patient has always been maintained at the level of sufficient anaesthesia. We have seen only one patient *strain* during a laparotomy when an untrained anaesthetist stopped keeping the mask on the face, which causes rapid recovery owing to the penetration of fresh air.

11. At the moment of waking, there are none of those cries which stir up a whole ward, or rouse a nursing home, no more of that restlessness which would throw the patient out of his bed if one did not watch him closely; the recovery is as calm as that after chloroform. Vomiting after recovery is also rarer than with the older methods: we do not know why. These are advantages particularly appreciated by our hospital's chief nurses and have a certain effect on the morale of all around.

12. The frequency of pulmonary complications *will certainly be greatly diminished.* For the ten months in which M Nélaton and we have used this apparatus several times a day, we have anaesthetised or seen anaesthetised more than 300 patients.

The report of M Nélaton to the Société de Chirurgie has given these results: two cases of bronchitis lasting twenty-four hours and one more serious lasting four or five days, but cured without incident. The discussion which followed this report showed that some patients anaesthetised with this apparatus still remained cyanosed and had stertorous respiration. That is true, but it is rare and we do not hesitate to say that, in the majority of cases, the fault lies with the anaesthetist.

An anaesthetic apparatus is not an automatic machine for putting patients to sleep; it is a device which allows one to give, in a continuous fashion, the appropriate, necessary and sufficient dose of anaesthetic agent. Badly managed, the apparatus gives more than it should and cyanosis appears.

In general, this is what occurs. The assistant charged with giving the anaesthetic begins to put the patient to sleep. After several minutes, he looks elsewhere, only occupying himself absent-mindedly with his patient; the mask, badly applied to the face, gapes at some point and the patient, inspiring fresh air through the hole, wakes up.

The anaesthetist turns the indicator and increases the dose of ether. Then soon, by chance, the mask falls back into place; the patient then takes too much ether and becomes cyanosed; the anaesthetist moves the indicator back, often too quickly; nevertheless, the anaesthesia would continue if the mask were not raised again; the patient wakes again, another large dose is given, and so on.

It is in this way that we have seen a certain number of poor anaesthetics, recalling those we used to see in the past. The principal cause of these poor anaesthetics is the defective application of the mask.

Yet another cause is the carelessness of the anaesthetist who does not trouble to find the minimum figure for each patient. We know of those undergoing surgery who have been left at 7 from the beginning of the anaesthetic; it is not surprising that they become cyanosed and bronchitic, since we know of no-one needing more than 4 after a quarter of an hour's anaesthesia, if the mask is well applied.

Lastly, the matter of death has been mentioned; it concerned a patient having a gastro-enterostomy who, the evening of the operation had a temperature of 3_7 [3.7? or 37?] degrees, and died the following morning; at autopsy, the lungs were very congested. Is the speed of onset of the pulmonary congestion really due to the ether? Are there not a number of other causes which one could incriminate with as much reason as the anaesthetic agent? On the other hand, this is not the place to discuss the rôle of anaesthetic agents in the genesis of postoperative pulmonary complications; the question has been well ventilated by Professor Le Dentu[3] and would involve us much further than we wish to discuss here.

The fact is undeniable that ether is more harmful to the bronchi than chloroform.

We maintain that we have considerably diminished this harm by lowering the doses of ether needed for anaesthesia, by allowing the patient to receive just sufficient to obtain complete anaesthesia and by substituting continuous for interrupted anaesthesia. And as one sees neither syncope nor even a warning of it in the course of ether anaesthesia, we conclude that the use of our ether apparatus, which lessens by a considerable amount the inconveniences of etherisation, but which gives, on the other hand, in the great majority of cases, an anaesthetic presenting all the advantages of chloroform narcosis without having its dangers, brings a new development capable of countering the severe judgement which too many surgeons have about ether anaesthesia.

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THE EARLY DEVELOPMENT OF FLUORINATED ANAESTHETICS

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The story of fluorinated anaesthetics lies within the past 75 years; this paper briefly discusses their experimental development during the early part of this period, from the 1920s to the launch of halothane in 1956.

After the First World War it must have been evident that if progress in anaesthesia was to be made, a non-flammable, non-irritant ether, or a less toxic chloroform would have to be found. Trial and error with a variety of vapours and gases suggested that halogenation might be the key to improvement but the toxicity and flammability of chlorinated compounds prevented any advance in that direction.

While elemental fluorine is the most reactive substance known to chemists, many fluorine-substituted compounds are, paradoxically, remarkably stable. Progress in their synthesis took place after World War I and, because stability can mean non-flammability, fluorinated compounds at first attracted the attention of British and American mining safety experts working on co-operative projects concerned with the prevention and control of underground fires and explosions. They were also of interest to industrialists trying to find more acceptable refrigerants.

The danger of leakage of ammonia had, until this time, prevented the development of domestic refrigerators, and an American chemist and entrepreneur, Thomas Midgley jr. recognised the possibilities of the new fluorinated hydrocarbons in the search for a non-flammable, non-toxic, non-odorous refrigerant. By 1928 it was clear that he was on the right track and Midgley ensured that the animal toxicity of these substances was closely studied and that the least toxic of the non-flammable 'Freons', as they came to be known, were developed for domestic and commercial refrigeration.

Pharmaceutical industry interest was stimulated by this commercial development of non-flammable compounds of low toxicity, and a two-year fellowship for 'pure science research in anesthetic gases' was created in the USA by the Ohio Chemical Company. The holder of the Fellowship between 1929 and 1931 was E May Bixby who worked at the Western Reserve University, Cleveland, Ohio with Harold S Booth. In the introduction to their 1932 paper discussing flammability data for 166 gases derived from the mining safety work, they proposed that 'the best possibility of finding a new noncombustible anesthetic gas lay in the field of organic fluoride compounds' and that 'it was logical to study those organic fluorides which are derivatives of the best of the known anesthetics'.[1] How right they were!

Bixby and Booth were unable to prepare fluoroform, the trifluoro derivative directly comparable to chloroform and their papers dealt with mono and difluoro derivatives, neither of which produced anaesthesia. However, these substances were found to be non-flammable and the substitution of fluorine atoms for chlorine decreased toxicity and increased stability. Five years later fluoroform was prepared but again did not prove to be a satisfactory anaesthetic, however this work confirmed that increasing fluoridation increased stability, lessening flammability.[2]

Further work on the anaesthetic potential, flammability and pharmacology of the Freons and other saturated fluorocarbons was carried out in America between 1937 and 1940 but without success; all the substances tested in several animal species were found to be toxic and non-anaesthetic.[3,4]

Fluorine technology during the 2nd World War

Soon after the entry of the USA into the war in 1941, the potentially overwhelming power of atomic fission was realised, and we must turn to the rapid advances in fluorine technology which resulted from the demand for high octane aviation fuel and the development of the atomic bomb.

While there is plenty of natural metallic uranium in the world, 99% of it in the stable ^{238}U form, there is very little of its contaminant, the highly fissionable ^{235}U. The problem facing the US Administration and its scientists, was how to separate the isotopes to get sufficient ^{235}U isotope to make the weapon. The only practical method was to transform uranium metal into its sole gaseous compound, uranium hexafluoride (UF_6), by reacting it with elemental fluorine, and then to partition the resulting gas mixture into fractions rich in each isotope. Several ways of carrying out this most difficult separation process were proposed; centrifugation, differential diffusion through a barrier membrane and super-mass-spectrography. Membrane diffusion proved to be the least difficult.

Elemental fluorine in large quantities was required and, because of their existing expertise - partly gained from work on refrigerants, British workers from Birmingham University and ICI joined Americans in carrying out the fundamental research leading to industrial-scale production of the highly reactive element. After many technical difficulties, the American and British research prepared the way for the manufacture of the bombs and the abrupt end of the war in 1945. It also meant that there was a substantial body of experience and knowledge of fluorine chemistry both in the UK and the USA.

Between 1943 and 1945, well before the bombs were actually dropped, Benjamin H Robbins (a pharmacologist and Chairman of the Anesthetic Department) and colleagues of Vanderbilt University in Nashville, Tennessee looked at the anaesthetic activity of 46 fluorinated compounds, newly produced by Earl T McBee and his associates at Purdue University, Lafayette, Indiana. We can be reasonably sure that many, if not all of these substances were by-products of nuclear fission research.[5] Robbins' work was published in 1946, a few months after the end of the war. Compounds containing chlorine and bromine in addition to fluorine were included. The introduction of a second halogen atom - either chlorine, bromine or iodine - into a fluoro-hydrocarbon was found to markedly increase potency, and bromine substitution increased potency 2-4 times more than chlorine.[6]

The American workers found that anaesthesia could be induced with reasonable safety in dogs with several of these compounds, but with hypotension, arrhythmias and convulsions in some cases. Four compounds were thought to be worthy of further study, and this group looked at $CF_3CHBr_2$and several other halothane-like substances (Figure 1). How near Robbins was to giving us halothane 10 years earlier! I do not know why this promising work was not followed up at the time but it is likely to have been due to economic commercial factors.[7]

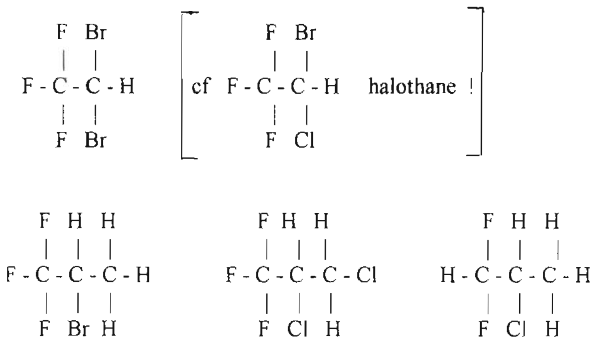
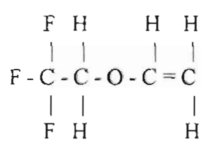


Figure 1
Compounds considered to have anaesthetic potential by Robbins (1946)[6]

Fluroxene

From 1950, advances were occurring on both sides of the Atlantic. Firstly, in the USA, the pharmacologist John C Krantz's group at the University of Maryland examined a number of fluorinated hydrocarbons and ethers for anaesthetic properties, but at first with little success. The summary of their 1953 paper, proposing further work on a fluorinated ether, said that (contrary to Robbins' earlier findings): 'mixed halogenated and fluorinated hydrocarbons ... offer little promise as volatile anesthetics.'[8] Fortunately this view went unheeded by ICI, who were at this time, well-advanced with their own fluorinated compound studies.

The Baltimore group proposed that fluorinated ethers in general offered the greatest potential as practical anaesthetics and this view, of course, has ultimately proved to be correct. Their most favoured agent was synthesised in 1951 by J G Shukys of the Air Reduction Co, New Jersey; it was trifluoroethyl vinyl ether, the first clinically useful fluorinated anaesthetic, later to be named fluroxene or Fluoromar ('mar' after Maryland). (Figure 2).


fluroxene (Fluoromar)

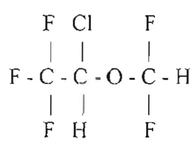

for comparison
isoflurane

Figure 2

The pharmacology of fluroxene was originally established using 6 frogs, 20 white rats, 10 dogs and one monkey. It was found to be as potent an anaesthetic as di-ethyl ether, and compared favourably with other ethers in these species. It was apparently non-toxic to liver and kidney, did not produce cardiac irregularities in dog and monkey, and, though flammable, (its lower limit of flammability was 3%), it was thought to present 'less of a fire and explosion hazard than similar non-fluorinated ethers'.

Krantz and his co-workers wrote that: '... the properties of [fluroxene] warranted its trial in man as an anesthetic' and on 10 April 1953, only a month after submission of their pharmacology paper, Krantz (the pharmacologist) used it to anaesthetise his physician-anaesthetist colleague in Chicago, Dr Max Sadove. Induction took only 32 seconds and light anaesthesia by the open drop method continued for 6 minutes without ill effect. Recovery was reported to be 'rapid and uneventful', and this must have been so because, only 30 minutes after emerging from anaesthesia himself, Dr Sadove successfully anaesthetised a middle aged woman with fluroxene for a rectal operation! He found that 'the relaxation was good; blood pressure and pulse were essentially unaltered'. This, then is the brief report of the very first clinical anaesthetic with a fluorinated agent.[9]

Surprisingly, two years elapsed before even an interim paper on 40 clinical anaesthetics with fluroxene appeared.[10] A further year later, in 1956, two groups (one headed by Dr Sadove) could only produce data from a total of 169 administrations. Fluroxene was not an overnight success.[11,12]

The original - rather limited - toxicity studies had appeared satisfactory but because the hepatotoxicity of the non-halogenated analogue, divinyl ether, then became known, further toxicity studies were carried out on fluroxene in 1956. Six dogs were deeply anaesthetised for one hour a week for eight weeks. No histological evidence of organ pathology was found. Armed with these data a New Drug Application for fluroxene was filed with the US Food and Drugs Administration on 2 December 1957.

By this time, of course, non-flammable halothane had appeared. Not surprisingly, halothane was generally preferred to fluroxene though the latter remained in clinical use, in the USA mainly, for over 15 years. It was not until 1973 that Eger's group showed, contrary to previous assessments of fluroxene toxicity, that frequent repeated 1.5 MAC exposures were lethal to dogs, cats and rabbits, though not to man. Marketing of fluroxene was discontinued in 1975.[13]

It will be clear that fluroxene, though in limited clinical use before the introduction of halothane in 1956, really only became generally available at about the same time as the British drug.

Development of halothane

The empirical approach to the development of fluorinated anaesthetics which took place between 1930 and the early 1950s has been emphasised. Spasmodic progress in chemical synthesis and halogen substitution meant that a mainly uncoordinated assessment of new compounds took place during this period.

More fundamental work, however, had been going on. In 1938, Dr John Ferguson working for ICI in Runcorn, Cheshire put forward an explanation of the apparent paradox that a wide range of dissimilar agents can produce anaesthesia, and an extension of the Meyer-Overton lipid solubility theory. As I understand it, one of Ferguson's proposals was that although anaesthetics (and other agents) have comparable effects on living organisms at greatly differing applied concentrations, this is related to their varying thermodynamic characteristics: their vapour pressure, tissue solubility and partition relationships.[14] The importance of Ferguson's postulates, I think, lies in their predictive value.

As a result of earlier work on halogen substitution and the company's war-time experience it is not surprising that further fundamental studies of fluorine compounds were undertaken at ICI. Under Ferguson's direction, a direct approach was made: 'What, if any, are the special properties of fluorine compounds which might be exploited commercially?'.[15]

While the ICI studies were in progress, L J Mullins at Purdue, Indiana, put together, in a 1954 paper, the accumulated physico-chemical data on narcotics, and extended the Ferguson hypotheses to produce both general proposals on the mechanism of anaesthesia and a prediction that a fluoro-chloro-paraffin might be an ideal anaesthetic.[16] Mullins was presumably unaware that he was setting out the ideas which the British group had been using in commercial research for two or three years.

Chemical stability was the factor of greatest interest to the British group at ICI, and the need for a better, more stable, non-flammable inhalant anaesthetic was discussed at a meeting of the General Chemicals and Pharmaceuticals Divisions of the Company in the late autumn of 1950. I have no doubt that this initiative stemmed from Ferguson's background in both narcotic theory and fluorine technology, added to knowledge of Robbins' unexploited 1946 data on the potential for fluorinated alkanes as anaesthetics.

The proposed specification for the target ICI anaesthetic was that it should be a liquid boiling about 60°C, non-flammable, active as an anaesthetic at low concentrations and with a good safety margin. Rapid and quiet induction and recovery and freedom from severe cardiovascular effects were desirable characteristics. It was reasoned that fluoroalkanes were likely to fulfill these criteria.

Those selected for the anaesthetic research possessed CF_3 or CF_2 groupings, not only due to their inherent stability but because their presence in the molecule was known both to reduce the reactivity of nearby chlorine or bromine atoms and lower the boiling point. From existing company data, it was possible to predict approximate boiling points prior to synthesis, and by keeping the hydrogen content low it was fairly certain that the compound would be non-flammable. A further important factor was the availability of more advanced methods of analysis and purification as it is likely that much of the earlier work in the field had been confused by the presence of impurities - rather like the situation in the early days of chloroform.

The chemist, Dr C W Suckling, joined ICI in 1942, and started by making highly fluorinated compounds for reasons which only became clear to him with the advent of atomic warfare in 1945. His experience was vital in the synthesis, during the early 1950s, of a small number - about a dozen - of novel likely candidates for the new agent which Raventós and colleagues screened in mice and rabbits. Of this first small set of compounds, only halothane appeared likely to be a satisfactory anaesthetic and a more extensive pharmacological work-up by Raventós in rats, dogs and monkeys indicated that clinical trials would be justified.[17] Raventos died at the age of 77 in 1982 but Suckling - now aged 77 - is still alive. (Figure 3)

Figure 3 - Drs J Raventós and C W Suckling

The first human application of halothane was on 20 January 1956 in Manchester, by Dr Michael Johnstone; his work belongs to the next chapter in the history of fluorinated agent:.

The story of the development of halothane is an excellent example of 'target research'; the use of soundly based prediction to produce a new substance with specified characteristics. Further extensive studies of alkane compounds like halothane failed to produce a better anaesthetic and its day has mainly passed. After a bumpy start - neither fluroxene nor methoxyflurane were very satisfactory agents - Krantz's 1953 prediction, that fluorinated ethers would become the agents of the future has proved to be correct, with agents of this type dominating inhalational anaesthesia world-wide for the past 20 years.

Acknowledgements

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THE EVOLUTION OF THE ANAESTHETIC RESEARCH SOCIETY

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At the end of the Second World War, the return of a Labour Government, perhaps not unlike today, brought the promise of better housing, better health care and better education. Certainly, the National Health Service Act of 1946 sought to honour the commitment of the war-time coalition government that health care would be provided free at the point of delivery for all the people of the United Kingdom. When the Act came into effect in July 1948 there can be little doubt that it was widely welcomed by the great majority of people even though the medical profession was less enthusiastic. But even if some of the senior members of the profession were implacably opposed, the younger doctors, particularly those who had served in the Armed Forces, were prepared to co-operate and there was a general air of optimism. Salaried appointments, either full-time or part-time, were created in the hospitals which were no longer dependent on charity to maintain them. In addition, formal training programmes for junior doctors were instituted with an established career ladder. Nevertheless, the situation was still far from perfect and some specialties, such as general surgery, became so overcrowded that many surgeons were in their 40s before they reached consultant status.

Anaesthesia was the exception. The specialty had expanded rapidly and the introduction of new drugs and new techniques offered young doctors the opportunity to build careers for themselves based not so much on the art of anaesthesia but on scientific practice. In the immediate post-war years, ether, chloroform and cyclopropane lost their popularity, as curare and similar drugs were developed which made the control of anaesthesia more rational. Techniques of controlled hypotension based on total spinal block, deliberate arterial bleeding and the discovery of ganglion blocking drugs made the management of anaesthesia more specific. Surgical techniques, too, had changed and the evolution of heart-lung machines made open heart surgery possible. As surgery expanded so did the need for better postoperative care with dedicated beds and specialised nursing. The intensive care unit was a natural development and anaesthetists with their newly learned expertise in ventilation became the obvious choice to run such units.

With the extension of their responsibilities beyond the operating room it was clear that anaesthetists had a bigger role to play in hospital systems. The National Health Service administrators learned that to be able to staff their hospitals it would prove necessary to support academic development in anaesthesia which had received a substantial fillip with the establishment of a Research Department of Anaesthetics within the Royal College of Surgeons. Joint appointments were created between the hospitals and the universities and substantial funding was made available to ensure that research was encouraged. For example, under the leadership of Professor Ian Aird, the Professor of Surgery at the Postgraduate Medical School, new academic appointments were made in anaesthesia and, although not without difficulty, both space and technical assistance were eventually provided. One interesting and slightly bizarre suggestion successfully resisted by Professor Aird was that a Professorship in Anaesthetics should be created in the Postgraduate Medical School to be occupied by a physician who would be attached to the Department of Medicine. It apparently was not considered that an independent Department of Anaesthetics was needed despite the fact that one had been created prewar in Oxford, and later in Cardiff. The next chair to be created was that founded by the British Oxygen Company in the Royal College of Surgeons in 1959 and more recently transferred to the London Hospital Medical College.

A forum for anaesthetic research

With the expansion of anaesthetic research, it soon became apparent that research workers needed a forum of their own in which to exchange and develop ideas. Some were members of the Physiological or Pharmacological Societies or the Medical Research Society, all of which provided an opportunity for anaesthetists to present their work but, not surprisingly, these bodies lacked the expertise needed to explore the work presented so that criticism tended to be superficial. By the summer of 1958 some of us had decided that something needed to be done and as John Nunn has described in his paper on the first meeting of the Anaesthetic Research Society (*British Journal of Anaesthesia* 1988; **61**: 639-641) three of us, Dr Nunn himself who was then a Leverhulme Research Fellow in the Research Department of Anaesthetics in the Royal College of Surgeons, Dr R P Harbord, the Reader in Anaesthetics in the University of Leeds and this author who at that time was a Lecturer in Anaesthetics in the Postgraduate Medical School, met in the Fellows' bar in the Nuffield College to discuss informally what steps could be taken to resolve the problem. It is not necessary to describe the details since that has been done by Dr Nunn but in essence it was decided to circulate those individuals known to us who were actively involved in anaesthetic research regardless of discipline, which explains why from the very beginning pharmacologists, physiologists, physicists and chemists were associated with the anaesthetic research group, as it came to be known.

All of those to whom we wrote responded positively and we were greatly heartened by their enthusiasm although some more senior anaesthetists were, to say the least, lukewarm and in one instance openly hostile. We were perhaps fortunate in that among those from whom we sought advice, John Gillies and Ronald Woolmer were strongly supportive and urged us to go ahead with our plans. As John Gillies pointed out: 'Get it going and they will all be there'.

The Anaesthetic Research Group

The first meeting was held in the Research Department of Anaesthetists in the Royal College of Surgeons on Friday 24 October 1958. Six papers were presented and it is perhaps significant that the first was presented by a physiologist, Dr G A Graham who was also the deputy director of the Research Department. The meeting ended with a general discussion that was not recorded but it would seem that the title of the 'Anaesthetic Research Group' must have evolved either then or during the course of the dinner that followed. The dinner has always been regarded as a most important part of the proceedings in that it allowed informal discussion in a friendly atmosphere without the need to score points. In addition, as the numbers grew, it provided the opportunity for younger members to meet and discuss their plans informally with more senior colleagues.

The purpose of the group was to provide a forum for the presentation and discussion of original research in anaesthesia. To facilitate discussion, attendance at meetings was limited to those with a major interest in anaesthetic research as already indicated. But membership was open to anyone with such an involvement regardless of discipline and, undoubtedly, this multidisciplinary approach became one of the group's strengths. There were no permanent officers. Membership and policy were decided by the members at a business meeting. A chairman, usually the next host, was appointed at each business meeting for the forthcoming meeting. Between meetings, necessary decisions were taken by the appointed chairman. Three meetings were to be held each year - one in each academic term. The summer meeting was normally held on a Saturday, the autumn and spring meetings on a Friday. Initially, the meetings consisted of six papers of 15 minutes duration with a further 15 minutes allowed for discussion. The pattern of the meetings followed that adopted by the more established biological societies. Papers were presented and not read and presentation times were rigidly enforced. Discussions were vigorous. The need for constructive criticism was widely accepted so that, although often forthright, they were rarely acrimonious and differences were as often as not sorted out in the bar at the end of the day!

The early meetings were essentially those of a peer group. Attendance was limited to 45 although the host had discretion to invite visitors. These fell into two main groups; the first consisted of young research workers who had been invited to present papers sponsored by individual members; the second were distinguished senior scientists such as Sir Henry Dale and Sir William Paton, to name but two, who had taken a direct interest in anaesthetic research and who added greatly to the quality of our discussions. In addition, it became established practice to invite visiting scientists from overseas who were currently working in the UK. Such invitations were almost invariably taken up and some went on, not only to become members but also to provide some of our younger research workers with the opportunity to work overseas, particularly in North America.

A problem that arose early in the history of the group was the publication of abstracts. The matter was raised as early as June 1960 at the Liverpool meeting when it was proposed that a short abstract of 400 words should be offered for publication with the aim of establishing priority for the authors and perhaps also making contact with other investigators in the same field. It was agreed that both anaesthetic journals published in the United Kingdom should be approached to ascertain whether or not the editors would be interested in publishing the proceedings. However, there was a significant minority against publication and the debate continued in subsequent meetings. Opponents of publication argued that there was a serious risk that the character of the presentations would be altered. Instead of research in progress, the presentations would consist of work already completed and unlikely to be substantially altered by criticism at the meetings, however valid. Undoubtedly there was substance in the argument but the practicalities of the situation prevailed and when the matter eventually went to a postal vote a majority was obtained for publication. The first proceedings to be published, those of the 1964 June meeting in Edinburgh, appeared in the *British Journal of Anaesthesia*. Ever since, the journal has continued to publish the proceedings except in the very rare instance when individual authors were unwilling to agree to publication.

The somewhat casual approach of the founder members to organisation was no problem with small numbers but became more difficult to sustain as the membership expanded. During the early years, the reluctance to accept a formal constitution led to major difficulties, particularly in relation to the selection and acceptance of members. Business meetings came to be dominated by membership problems to the exclusion of matters that perhaps deserved more serious consideration. Eventually, in the mid sixties, a small working party was formed to try and resolve this problem and to advise the group on an improved constitution. As a result of the working party's deliberations, Professor Gordon Robson, in his capacity as chairman of the 1967 autumn meeting, wrote to the members in October of that year to seek their support for the working party's proposals. He pointed out that the membership rules were ambiguous and that, in particular, as the rules of the group stood, the constitution, such as it was, could be radically changed at each meeting and that what was needed was a period of stability. Of immediate importance was the need for an Honorary Secretary whose task would be to rationalise the affairs of the group. Moreover, to do that, since the overall membership was then approaching 200, it would be necessary to establish a small annual subscription to meet the costs of running the group. It had become unreasonable to expect the host departments to underwrite the group's activities.

New rules and a new name

At the meeting held in November 1967 at the Royal Postgraduate Medical School, the new rules, with some minor amendments, were approved and Dr John Norman was elected Honorary Secretary and Treasurer. A subscription of £1 per annum was also agreed and those arrangements were accepted for one year in the first instance. With the continued increase in membership and the more rational approach to organisation, it was inevitable that further changes would be proposed and they were not long in coming. Within the next year it was proposed that the name of the group should be changed and at the 1968 autumn meeting in the Royal College of Surgeons in November it became The Anaesthetic Research Society with effect from the first meeting in 1969. The change in title had obvious advantages. The immediate benefit was that it became easier for members to obtain financial support to attend meetings from the hospital managers in the various Health Authorities who were reluctant to support groups, but were enabled through the National Health Service Act to grant leave and expenses to doctors to attend scientific meetings as part of the continuing education process. Moreover, the new title made it easier to become a registered society for tax purposes. For younger members of the Society still in the training grades, membership offered the opportunity to embellish a curriculum vitae and to meet potential employers, particularly in the academic field. It provided status at a time when it was needed most.

During the next few years, the wrangles about the different grades of membership continued and there were few meetings at which the problem was not raised. Eventually, at the business meeting in Cardiff in November 1972, Dr John Norman who had just been re-elected Honorary Secretary and Treasurer, pointed out that the membership of the Society had reached 250 and that the current administrative arrangements were unlikely to meet the requirements of the membership. There was general agreement that a working party should be set up 'to examine the ways in which the Society could be reorganised to permit the most effective presentation and discussion of original research in anaesthesia'. It was hoped that any proposed reorganisation could be implemented at the next Annual Business Meeting in 1973.

In due course, the working party's recommendations were circulated to the members and the report was discussed in June 1973 and adopted at the Annual General Meeting held at the Royal Postgraduate Medical School in November 1973. The basic recommendations were as follows:

A new constitution based on those of other medical research societies was adopted. It was emphasised that the only purpose of the Society was the presentation and discussion of research in anaesthesia and related subjects and that it should not assume any 'political' function. Accordingly, it was accepted that only one category of membership was needed although the Society might wish to elect a few distinguished research workers as honorary members. It was also agreed to place the administration and the organisation in the hands of a small elected Committee who would appoint a chairman. Thus it was in 1974 that an Executive Committee under the chairmanship of Professor R A Miller, with Dr J Norman as Honorary Treasurer and Dr L Strunin as Honorary Secretary, effectively took over running the Society.

Today, more than 20 years later, the essentially professional approach of the committee has ensured that the Society has remained an important influence in anaesthetic research and that membership is regarded by young research workers as sufficiently prestigious to justify mention in application for grants or posts. Such status puts substantial responsibility on members of the Society and, more particularly, on the members of the elected executive committee to maintain the standards originally defined by the Anaesthetic Research Group (Payne, JP. *British Journal of Anaesthesia* 1988; **61**: 523-4). While it cannot be denied that the scientific approach has been maintained, it remains to be seen whether or not the more political approach now a feature of the Society's activities will add to the scientific development of the speciality.

ANAESTHESIA AND ANAESTHETISTS IN FICTION AND LEGAL PROCEEDINGS

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The span of this paper covers from 1846 to the present day. It is concerned with influences on the lay perception of anaesthetic agents and of anaesthetists, and the examples chosen will reveal my taste in fiction. Anaesthetists have an overall belief that their image is poor in terms of how the specialty is seen by the public, and frequent attempts are made to improve our public relations. My belief is that we are on to a losing streak, because anaesthetic agents and their use have consistently been looked upon as matters to some degree sinister.

Let me start with my first interest in anaesthesia. This was as a schoolboy. It did not come from my feeling of being aware during dental extractions under gas and air, but from reading Sir Arthur Conan Doyle's Sherlock Holmes stories. I shall mention two of them. In 'The Disappearance of Lady Carfax' from *His Last Bow*, the good lady having been abducted is found in a coffin, her head surrounded by cotton wool soaked in chloroform. The point was that she was to be buried, dying either of chloroform or of suffocation. Interestingly, Dr Watson in his successful resuscitation efforts uses artificial respiration and even injected ether. In 'The Three Gables' from *The Casebook of Sherlock Holmes*, Mrs Maberley is chloroformed during an attempted burglary, and the description obviously presumes a public knowledge of anaesthetic agents.

We know that following the introduction of ether anasthesia the attempts to patent it and the many arguments which developed over the discovery led to a public awareness of aggressive issues between participants. A century later the Hollywood film *The Great Moment* highlighted some of this unpleasant wrangling, particularly the conflicts between Morton and Jackson. Fear of this new capability to cause unconsciousness, and distrust of both the agents and their users has been fuelled in a span of press reportage and literary output from Charles Dickens to Michael Redpath's 1997 novel *Trading Reality* in which the hero and heroine are chloroformed to assist in their drowning.

Reports of legal cases in the lay press

Dickens, as editor of the magazine *Household Words*, gave the public much of interest and concern about anaesthesia. The issue of 16 April 1853 has this passage:

> 'Experience also shows that fatal results have often followed the administration of Chloroform to the persons who have exhibited decisive and unaccountable dread of it. This is a curious fact that we may account for .... we believe either by some theory or instinct or by some superstition of the forecast shadow of approaching fate.'

This you may regard as merely one point of interest, but earlier issues reported more sensational stuff. In February 1850 the magazine carried legal reports about two ladies indicted on a charge of robbing a solicitor having stupefied him with chloroform:

'He was proceeding along the Whitechapel Road when he felt someone touch his side and a rag or handkerchief was pressed over the lower part of his face. He became insensible until the following morning when he slowly revived.'

The jury returned a verdict of guilty and the prisoners were sentenced to be transported for 15 years. A similar offence occurred in Surrey and here the sentence was 10 years transportation. In the same journal on 12 February 1850 the issue of rape under the influence of chloroform was discussed. In this case the accused broke bail and prior to his trial left for the continent. On 30 April there was another report of a man charged with administering chloroform with a criminal intent because it was administered to a young lady who had accompanied him to a public house near Regent's Park:

'They walked homewards together and her brother having left them he led her down a yard and after attempting to take liberties with her poured the contents of a vial on his handkerchief which he applied to her nose and mouth. She called out and gave him into the charge of a policeman who came up. The prisoner was remanded on bail.'

The interesting thing is that in neither of these latter two cases is the word chloroform actually used in the quoted legal reports, but at the time the public would have felt it to be the agent, and Dickens certainly presented it as such.

A jump forward to the mid 1880s brings us to the trial of Adelaide Bartlett, which was widely reported. The Bartletts were shopkeepers of Dulwich and Herne Hill and were a basically unhappy couple. Mrs Adelaide Bartlett had fallen friends with the Reverend Dyson. During the latter part of 1885 Mr Bartlett became ill with possible mercury poisoning and was in a chronic phase. Following Christmas, Mrs Bartlett asked Mr Dyson to help her purchase a large amount of chloroform, which he did on Monday 28 December. Mrs Bartlett described how she would administer this drug to her husband, sprinkled on a handkerchief to control his spasms. Interestingly, on 31 December, following a large meal of oysters at noon and jugged hare at three, Mr Bartlett had a tooth successfully extracted under gas shortly after five o'clock. At about midnight on that New Year's Eve Mrs Bartlett said to the servants that her husband had died. They noticed a peculiar smell, perhaps of chloroform. It is small wonder the case was so widely reported; there was obviously enough of interest for a book to be written about it. The domestic situation was extraordinary. Mr Bartlett during his illness had encouraged his wife in her relationship with Mr Dyson. He then made advances to her and she stated she used chloroform to calm him down. The verdict could be described as a qualified not guilty. The foreman of the jury stated:

'We have well considered the evidence. Although we think grave suspicion is attached to the prisoner, we do not think there is sufficient evidence to show how or by whom the chloroform was administered.'

Again, I put in your mind the huge influence this case must have had on the image of anaesthetic agents to the general public.

20th century fiction

Returning to fictional cases, and leap-frogging over the Sherlock Holmes period, brings us to a fascinating crime thriller of the thirties. This is *The Nursing Home Murder* first published in 1935; Inspector Alleyn, the creation of the New Zealand authoress Ngaio Marsh, is the investigator. The Home Secretary, Sir Derek O'Callaghan, is operated on by Sir John Phillips, a Harley Street surgeon. The anaesthetist is Dr Roberts and the murder is accomplished by an anaesthetic-related drug. Sir Derek's death shortly after his operation is due to an overdose of hyoscine. The theatre nurse is involved, she having known the Home Secretary in her youth, a scenario almost identical to that in the film *Green for Danger.* Alleyn demonstrates that the syringe containing the extra dose of hyoscine was concealed in the anaesthetic machine. The anaesthetist turns out to be insane, with notches on his stethoscope for multiple murders. Dr Roberts also believes in eugenic sterilisation and is a fellow traveller with communism. There is a parallel here with Dr de Caux, whose extraordinary career was described by David Wilkinson at two early meetings of our Society (*HAS Proceedings* Vols 3 and 4). Inspector Alleyn featured in a major TV series of the nineties and *The Nursing Home Murder* is still in print, but by chance I recently purchased a first edition and discovered that Miss Marsh did not write it alone. A joint author was Dr H Jellet. All I can tell you about him so far is that he was registered on 24 December 1894, and by 1896 he had additional qualifications from Dublin and his address was registered as New Zealand. Obviously Dr Jellet is going to be a future project for me.

Moving on to mid-century, I mentioned the film *Green for Danger,* which highlighted the dangers of mixing up oxygen and anaesthetic gases, but there have been much more recent unfortunate depictions of anaesthesia and anaesthetists. February this year saw a re-run of the episode of the TV comedy *Porridge* which referred to laughing gas and what the dentist did to the young lady while she was under its influence, again giving the image of anaesthetic agents assisting in sinister or possibly criminal activity. We have had anaesthesia-related items unprofessionally portrayed in the *Carry On* films, in *Doctor in the House* and many of its sequels, and a host of other film and TV comedies and dramas. Again, in February this year, viewers saw a re-run of *A Touch of Frost* which described the murder of a nine year old after his finger was amputated under chloroform. An episode of *Kavanagh QC* showed an operation during which it was considered normal for the anaesthetist to leave the patient to go to another commitment before the procedure had finished. Nor is it only fiction denigrating anaesthesia. In March this year we were told by Ken Goodwin, a successful member of the *Comedians* of the 70s that: '... the surgeons could hardly operate for laughing because I was saying such funny things under the anaesthetic'. This was reported in the *Radio Times.*

Finally, let us return to the popular novel. Robin Cook's books *Coma* and *Harmful Intent* both deal in a sinister manner with anasthesia. In the latter, the local anaesthetic, Marcaine, is replaced with harmful intent by an extract from a frog. In Claire Rayner's *Fourth Attempt* the anaesthetist is an imposter and his work is described as basically easy to be carried out by any educated person. Furthermore the proposition is made: 'patients die from good anaesthetics'. What an image this author presents of anaesthesia and its administrators! In the 1983 book by Dick Francis, *The Danger,* a girl is snatched after a hood of cloth is pulled over her head: 'then it smelled sweet ... ether, chloroform, something like that'. Later the hero himself is kidnapped after an injection in the thigh renders him unconscious. This brings to mind the much reported technique used by an Israeli anaesthetist for the sedation and concealed transport out of the country of Dr Deko. Much less believable have been the more recent newspaper stories of train robberies in Eastern Europe with the sleeping compartments being filled by anaesthetic vapour.

In fiction, as we have seen, the older agents are still surprisingly popular. In Clive Egleton's *Death Throes* (1994) ether and chloroform are used to abduct the hero. Kingston Medland's 1996 thriller *Until Dawn* has ether being used by one of today's most hated villains, the serial killer.

These days the public may generally feel good about well-trained anaesthetists, but my belief is they also have a doubt, built-in by these fictional and real life events - a fear of anaesthetic agents, and thereby of anaesthesia.

SOME LIVERPOOL FIRSTS

Dr R Finn, Emeritus Consultant Physician,
Royal Liverpool University Hospital

It is not widely known that in 1812 the then Prime Minister, Spencer Percival, was shot in the House of Commons by a Liverpool madman. John Wilkes Booth who assassinated Abraham Lincoln was also born in Liverpool. Ours has always been a troublesome city. It was given its charter in 1207 by King John because he wished to use the Port as a naval base for operations against Ireland. But Chester remained the more important port until the Dee silted up. Only then did Liverpool begin to grow, and its initial growth was due to the slave trade. This was a triangular trade in which manufactured goods from industrial Lancashire were taken to Africa and exchanged for slaves, who were transported on the second leg to the plantations of the West Indies or America. They were sold for sugar, cotton and tobacco which were brought back to Liverpool.

It is probable that no slave ever came ashore in Liverpool but we must feel deeply ashamed of this aspect of our history. The Government stipulated that each ship must carry a surgeon to care for the slaves, and many of these were licensed in Liverpool. The slave trade brought great wealth to Liverpool, not least from the compensation paid following its abolition.

Major scientific advances do not occur randomly but are concentrated in areas of affluence. For a period of about 100 years from the early 19th century, Liverpool was the second largest port and commercial centre of the largest and most wealthy empire the world has ever known. The growing city was enormously vibrant, and like a powerful magnet it drew in talent. A Golden Age of Liverpool Medicine was inevitable.

Orthopaedics

Most bone injuries and diseases were originally dealt with by lay bone-setters. Their clinical material was limited and they did other work, as the only concentration of trauma occurred with battles which were few and far between. This all changed with the industrial revolution and the massive migration to the cities. The Liverpool docks provided the first major steady source of bone injuries and it was predictable that this would attract the bone-setters.

Evan Thomas, from a famous family of Anglesey bone-setters, came to Liverpool in 1830. His reputation brought patients from America and Australia and medical jealousy resulted in several legal suits against him. He therefore decided that the next generation should be qualified, and sent his five sons to obtain the MB Edinburgh. The most famous son was Hugh Owen Thomas who rapidly developed an international reputation. He was grossly eccentric. He wore a frock coat buttoned up to the neck, a glazed peak cap, gauntleted gloves, and always had a cigarette in his mouth - hardly the appearance of a medical man. He drove round in a cart of his own design with four red wheels and two black horses in tandem.

When he died in 1891 aged 57 he had worked for 30 years without a holiday and had only been away from home for six nights. He started work at 6am and finished writing in his study at midnight. On Sundays he held his famous free clinic when 200 patients might attend. He believed in fresh air for TB and nursed his young patients in soap boxes chained to the railings of their house. He was a difficult man who did not attend medical meetings even when invited, but he was a mechanical genius whose Thomas splint saved many lives in the First World War. He is now recognised as the father of modern orthopaedic surgery and his portrait hangs in the National Portrait Gallery with Darwin, Hunter and Jenner. Hugh Owen Thomas is possibly Liverpool's most famous son.

His nephew Robert Jones was, in the family tradition, apprenticed to his uncle, and he graduated in medicine from Liverpool. He was appointed supervising surgeon to the Manchester Ship Canal, which was the first organised accident service in the world. He was a technically brilliant surgeon who became Director of Military Orthopaedics in the First World War. He was appointed to the Royal Southern Hospital which became the world Mecca for orthopaedics and as Sir Robert Jones he was the leading orthopaedic surgeon of his day. The mutation from Welsh bone-setter to establishment surgeon was complete. In retrospect his main contribution was to spread Thomas' seminal ideas amongst the orthopaedic establishment, because he was as good a communicator as his uncle was a bad one.

Radiology

Very shortly after Röentgen's discovery on 8 November 1895, Robert Jones heard of it in a private letter written to a German lady in England. A little later he was consulted about a boy with a bullet in the hand, and he arranged for Sir Oliver Lodge, the distinguished Professor of Physics, to attempt an X-ray of the hand. This was successfully carried out in the Physics Department on 7 February 1896 - probably the first X-ray taken for a clinical purpose. Sir Robert persuaded Thurston Holland to become interested and the first X-ray department in the country was set up at the Royal Southern Hospital in October 1896.

Tropical medicine

Troop ships from around the Empire frequently docked in Liverpool and the War Department requested the use of some beds at the Royal Southern Hospital for sick soldiers prior to their transfer to other hospitals in the UK. Many had tropical diseases and this led to the creation of the Liverpool School of Tropical Medicine in 1899. This was the first in the world, London being second by 3 months. The first Director was Ronald Ross who had discovered malaria parasites in the stomach of the anopheles mosquito, proving its role in the transmission of the disease. His Nobel Prize was one of three associated with Liverpool at the zenith of its power, the other awards being to Sherrington the neurophysiologist, and Sir James Chadwick who discovered the neutron.

Public health

Liverpool's record in Public Health is probably unique, with a number of firsts in this field: the first full-time Medical Officer of Health, Dr William Duncan; the first home nursing service; the first horse-drawn ambulance service; the first public baths and wash-houses; the first children's ward in a general hospital (the Royal Southern). The stimulus for these advances was no doubt the combination of great wealth and extreme poverty. Many of the poor lived in unventilated cellars holding up to 30 people with no sanitation. Epidemics were common and life expectancy short. The growth of an affluent, caring liberal class led to innovations to improve the situation. A more cynical explanation might be that the unwashed poor were seen as a threat to the health of the wealthy merchant families.

Hay fever

My favourite Liverpool First highlights a causal link between a medical discovery and the socio-economic environment. John Bostock was a physician at the Royal Infirmary in Liverpool for 20 years before he moved to London, became Lecturer in Chemistry at Guy's and eventually a Vice-President of the Royal Society. In 1819 Bostock published the first description of hay fever from which he personally suffered. The aetiological link with pollen was made by Charles Blackley, a Manchester physician. But why was hay fever not described until the 19th century? The clinical picture is quite different from the common cold, and both the genes and the pollen had long been present. And why were the discoverers both from the northwest of England? The answer to both is to ask what was special in this area at the beginning of the 19th century. Surely it must be the birth of the industrial revolution. I have suggested elsewhere that industrial pollution damages the nasal mucosa, allowing the entry of pollen particles which initiate an immunological reaction leading to the symptoms of hay fever.

Rhesus disease

The prevention of rhesus disease came at the end of Liverpool's period of economic prosperity, and is a marvellous example of serendipidity or chance in scientific discovery. Cyril Clarke settled in Liverpool as a result of his war-time naval connections, but the story starts with the First World War and a rumour that Zeppelins would bomb Leicester. The Clarke children were evacuated to a village in the care of a governess whose hobby was butterflies. This led the young Clarke to a lifelong fascination with the insects. He became particularly interested in mimicry, when the butterfly's colour and pattern act as camouflage. The inheritance of butterfly colour patterns is controlled by a group of linked genes called polygenes. This led Clarke to take an interest in Rhesus blood groups, which are similarly controlled by polygenes.

At this stage I was given an MD project to study Rh disease, and in the course of the work we studied the phenomenon of transplacental haemorrhage in which foetal red cells cross the placenta into the maternal circulation. It is the mother's reaction to these cells which causes the disease in the foetus. It seemed possible that destruction of these cells by an appropriate antibody could prevent the disease. So it did, and the rest is history. It can be calculated that over 50 years this treatment will save about a million lives in Europe, which puts it in the same league as Ross's demonstration of the mosquito as the vector for malaria.

And finally

I conclude with a brief mention of three totally unrelated Firsts. Noel Chevasse who had been a House Officer at the Royal Southern Hospital was the only man to win a Victoria Cross and Bar in the First World War. As well as the first clinical X-ray of 1896, the first clinical isotope scan, which showed a retrosternal thyroid, was carried out in Liverpool. This was in 1948, by radiologist George Ansell and the atomic physicist Joseph Rotblatt, who left Liverpool for St Bartholomew's and recently received the Nobel Peace Prize for his work in trying to prevent the proliferation of nuclear weapons. In 1774 Matthew Dobson, a physician at the Liverpool Royal Infirmary, was the first to describe sugar in diabetic urine, which earned him a permanent place in the history of medicine. Nobody knows what he looked like and I cannot show you a portrait. There was one, in the mess of the Royal Infirmary until about 1874, when it was damaged beyond recognition by a House Surgeon who used it as a target for his pea shooter. I suppose the confluence of two such events could only happen in Liverpool.

Guest Lecture

SEEN AND UNSEEN ARCHITECTURAL GEMS OF LIVERPOOL

Maggi Morris, Lecturer,
Dept of Building and Environmental Health, University of Liverpool

Ms Morris, uniquely qualified as an architectural historian with an MSc in Public Health gave a guest lecture full of interest, entertainment and enthusiasm. Using double projection slides of a remarkable variety of Liverpool buildings, she made architectural concepts understandable to her medical audience, while tracing the history of the town and its docks, the changes in the population and the development of famous institutions. She brought to life the rise and fall of the maritime economy, the fight for public health, and the developments in housing and education. Her conclusion was a confident prediction for the future. Conservation projects are already bringing new life to the old buildings. With tourism and a large influx of students Liverpool is becoming a 24 hour city.

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Correspondence

The Editor

Sir,

The late Dick Ellis in the introduction to his facsimile edition of John Snow's *On Narcotism by the Inhalation of Vapours* (London, RSM Press 1991) mentioned that the only complete set that he could locate of the three pamphlets in which Snow reprinted the series from the original articles in the *London Medical Gazette* was in the library of the Royal College of Physicians of Edinburgh. A survey conducted on his behalf by the British Library failed to find a complete set 'in any of the relevant major research libraries in the English-speaking world'.

However, a recent search for one of Snow's publications in the library of the Royal College of Surgeons in Lincoln's Inn Fields inadvertently turned up two others. While looking for the reprint of his first paper on chloroform of February 1848, which had been bound into a book of tracts, the Librarian produced Snow's *On the Inhalation of the Vapour of Ether* of 1847, and a volume in which the complete set of *On Narcotism* had been bound with several of his other essays. All three are presentation copies inscribed to the College by the author.

I feel that these should be on record. I certainly regard the library of the RCS as a major research library, not only for surgery, but for the history of anaesthesia. It has complete sets of the most relevant nineteenth century journals, and also of the major anaesthetics journals of this century.

David Zuck

BOOK REVIEW

Careers in Anesthesiology. Autobiographical Memoirs. Volume 1.
Park Ridge, Il. Wood Library-Museum of Anesthesiology, 1997. ISBN 0-9614932-8-3 (Hard Cover Edition); ISBN 0-9614932-9-1 (Paperback Edition). 217 pages. Illustrated. $35.00 (Hard Cover): $25.00 (Paperback)

The Wood Library-Museum has inaugurated a series of autobiographical memoirs dealing with the second half of the twentieth century. This first volume under the editorship of Raymond Fink contains contributions from three distinguished American anesthesiologists, William Hamilton, Eli Brown and E M Papper. Each considers the development of anaesthesia in his lifetime and in so doing presents an interesting picture of the way anaesthesia has changed in the United States during the past fifty years or so, both in terms of the improvements that have occurred in clinical practice and safety of patient care and also in the changes that have resulted in the organisation of anaesthesiology. The first is largely mirrored in the changes that have been seen in Britain, but the organisation of anaesthesia departments, the development of research departments, the formation of national institutes and the influence of government have evolved along different paths. The British reader will often find this difficult to follow, especially as abbreviations such as the use of initials, sometimes without explanation, are common.

Each contributor writes of his own experience. As William Hamilton spent much time at the University of California in San Francisco, Eli Brown at Wayne State University in Detroit and E M Papper at the Columbia-Presbyterian Medical Centre in New York the reader is given information of how anaesthesia developed in centres across the United States, though all travelled extensively both at home and abroad. The British reader who has worked or travelled in the United States will recognise many of the names mentioned and he will be interested in the opinions of the contributors who have visited Britain.

William Hamilton worked with Dr Stuart Cullen in Iowa, before accepting the Chair of Anesthesia at the University of California in the 1960s. He then became one of the important figures in American anaesthesia and took a sabbatical leave at the Nuffield Department of Anaesthetics at Oxford. Eli Brown became Chair of the Anesthesiology Department of the Sinai Hospital of Detroit when the hospital had only been in existence for about a year and a half. He built the department up, began to accept students from Wayne University in 1956 and was asked to assume the chair of the Department of Anesthesiology at Wayne State University in 1975. He was active in the work of the American Society of Anesthesiologists spending one year as President.

Of the three contributions in this volume, that of E M Papper is by far the longest occupying some 140 pages out of a total of 217. Papper gives a more complete autobiography, writing about his upbringing in a Jewish family in New York with parents from central Europe, his entrance to medical school and later his development of an interest in anesthesiology ending up holding many prestigious positions. In retirement he became interested in why it took so long for anaesthetic agents which had been discovered many years ago to be used for pain relief in surgery. Now based in Miami he became a graduate student in the Department of English following which he was awarded a PhD on his seventy-fifth birthday in 1990.

The contributions are well written, though too many misprints have passed the proof reader's eye. The frontispiece to the volume, from a painting by Leroy Vandam of Boston, shows the headquarters building of the American Society of Anesthesiologists. It is planned that it will also appear in subsequent volumes. Let us hope that many more of these are to be written.

R S Atkinson

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HISTORIC ANAESTHETIC APPARATUS

Prof H Stoeckel, Emeritus Professor of Anaesthesia at the University of Bonn, Germany, is creating a museum of historic anaesthetic apparatus and would be pleased to receive information concerning historic apparatus which might be purchased to augment the collection. He would be grateful if those possessing any spare items of historic equipment could communicate with him at the following address:

Prof. Dr.med. Dr.h.c. H.O.Stoeckel FRCA,
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IS YOUR DEPARTMENT 50 YEARS OLD?

During 1998 the HAS would like to publish in its Proceedings a record of those Departments and Societies of Anaesthesia which have reached their 50th (or even longer) Anniversary. If your organisation qualifies, please send before 15 April a brief (maximum 500 words) summary of its beginnings and development to: Dr Marshall Barr, Hon Editor, Norscot, Rosebery Road, Tokers Green, Reading RG4 9EL. Tel/fax: 0118 9479346.