THE HISTORY OF ANAESTHESIA SOCIETY PROCEEDINGS

Volume 53
SHREWSBURY
2021

Honorary Editor
Rajinder K Mirakhur
THE HISTORY OF
ANAESTHESIA SOCIETY
PROCEEDINGS

VOLUME 53
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Acknowledgements

I would like to acknowledge the help of all the authors whose presentations at the meeting and whose manuscripts have made this publication possible.

I would like to acknowledge the help of Dr Alistair McKenzie, the past President, Dr Adrian Kuipers, the President and all past and present members of the Council.

My thanks to Dr John Pring for getting the Proceedings to see the light of the day by reviewing the manuscripts, and arranging its printing and distribution.
Papers and Abstracts from the Shrewsbury Meeting 2021

Thursday 2 September 2021

Session 1: Blessed Chloroform Lecture

From test tube to TIVA: milestones in the development of propofol.
*Dr John B (Iain) Glen*

Session 2:

Max von Pettenkofer (1818-1901) and his works on respiration.
*Dr Adrian Kuipers*

The first anaesthetic in the geographic centre of Africa.
*Dr Alistair McKenzie*

Session 3: Some British achievements in anaesthesia and intensive care.

Hidden gems in anaesthesia.
*Dr Elizabeth Bradshaw*

Early use of anaesthesia in Oxford’s Radcliffe Infirmary.
*Dr Michael Ward and Dr David Shlugman*

*Prof Katherine Venables*

Early Intensive Care Units in England.
*Dr A Anthony Gilbertson* (Read by Dr Alistair McKenzie)

Session 4: Trainees.

The ABCs of anaesthetic history – alcohol, beer and cocktails.
*Dr John H. Thompson*
Much Ado about Numbing: a history of regional anaesthesia.
*Dr Laura Naumann*

A brief history of ECMO.
*Dr Olivia Baker*

**Friday 3 September**

Session 5: Anaesthetic and ventilation techniques.

History of epidural anaesthesia and analgesia.
*Dr Robert Palmer*

Some of the history of circle systems in anaesthesia.
*Dr Patrick Magee*

Cape Engineering.
*Dr Adrian Padfield*

Session 6: International Events.

Dr Steevens’ Hospital (Dublin), Dr Percy Kirkpatrick and a year 1900 Register of Anaesthetics.
*Dr Declan Warde*

The European elucidation of respiratory physiology 1872-1922.
*Dr Alistair McKenzie*

**Session 7: Guest Lecture.**

*Dr Henry Connor*
HISTORY OF ANAESTHESIA SOCIETY

Scientific Meeting, Prince Rupert Hotel, Shrewsbury
2\textsuperscript{nd}-3\textsuperscript{rd} September 2021

Organiser: Dr Adrian Kuipers

Scientific Organiser: Dr Alistair McKenzie

FUTURE MEETINGS

UK History of Anaesthesia Society
Information will be available about the 2022 meeting at
www.histansoc.org.uk

10\textsuperscript{th} International Symposium on the History of Anesthesia
Kobe, Japan
16-18 June 2022
https://isha2022.com/

The History of Anaesthesia Society Proceedings
Honorary Editor

Professor Rajinder Mirakhur
Belfast, Northern Ireland
Email: r.mirakhur@btinternet.com
HISTORY OF ANAESTHESIA SOCIETY

Council and Officers – September 2021

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David Zuck Memorial Prize 2021

Adjudication committee

Professor Rajinder Mirakhur (Chair)
Brigadier Ivan Houghton
Dr Elizabeth Bradshaw

There were six excellent entries for this prize.

The winner of the David Zuck Memorial Prize 2021 was the following publication:

From cholera to COVID-19: How pandemics have shaped the development of anaesthesia and intensive care medicine

Adam B Levin¹, Christine M Ball²,³ and Peter J Featherstone⁴

¹Department of Anaesthesia and Pain Medicine, Western Health, Melbourne, Australia; ²Department of Anaesthesia and Perioperative Medicine, Alfred Hospital, Melbourne, Australia; ³Department of Anaesthesia and Perioperative Medicine, Monash University, Melbourne, Australia; ⁴John V Farman Intensive Care Unit, Addenbrooke’s Hospital, Cambridge, UK

Anaesthesia and Intensive Care 2020, Vol. 48(3S) 28–38

The Committee and the Council extend their congratulations to Dr Levin and his colleagues.
Deaths of Members 2019-2021

Dr Jean Horton             Cambridge
Prof Hirosato Kikuchi      Japan
Dr Colin McLaren           Wiltshire
Dr D. 'Tony' Nightingale   Liverpool
Prof John W. Severinghaus  USA
Prof Sir M. Keith Sykes    Oxford
Dr Trevor Thomas           Bristol
Dr David Walmsley          Chelmsford
Dr Gerald Zeitlin.         USA
Shrewsbury Meeting: Speakers’ photographs

Dr Adrian Kuipers
President

Dr Alistair McKenzie
Immediate Past President

Dr John (Iain) Glen
Dr Elizabeth Bradshaw
Professor Katherine Venables

Dr Michael Ward
Dr David Shlugman
LIST OF DELEGATES

History of Anaesthesia Meeting, Shrewsbury, 2-3 September 2021

Dr Olivia Baker  Dr Robert Palmer
Dr Moyna Barton  Dr James Pittaway
Dr Colin Birt    Dr Yash Pole
Dr Liz Bradshaw  Dr John Pring
Dr Ian Brett     Dr Anna-Maria Rollin
Dr Alistair Brown Dr David Shlugman
Dr Fabrizio Casale Dr Meinolfus Strätling
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Dr Adrian Kuipers
Dr Sumitra Lahiri
Dr Ronald Lo
Dr Ken MacLeod
Dr Patrick Magee
Dr Alistair McKenzie
Dr Duncan Mitchell
Dr John Moyle
Dr James Mulvein
Dr Laura Naumann
Dr Adrian Padfield

*John Snow Society
EDITORIAL

This issue of the Proceedings of the History of Anaesthesia Society Meeting would normally have been published last year following the meeting which would normally have taken place in Shrewsbury in 2020. However, as we all are aware almost all activities involving gathering of people came to a halt due to the Covid-19 pandemic. The pandemic has resulted in more than 225 million deaths worldwide and resulted in all normal medical activity coming to almost a halt to facilitate management of Covid-19 patients. Our sympathies go to the friends and families of those who unfortunately died and our best wishes go to those who are still suffering from the after effects of the disease.

Because of the restrictions in meeting indoors and the need for social distancing, many scientific meetings over the last year have been held remotely via Zoom or Microsoft Teams. It was however not possible for a relatively smaller society such as the History of Anaesthesia Society to meet like that. Also, with these remotely online held meetings the interaction which the attendees enjoy with fellow members would not be there.

The lockdowns, and the use of face coverings and social distancing has helped to control the spread of the disease. The availability of rapidly developed vaccines from the end of last year has however been the important measure helping to protect the people and has allowed gradual relaxation of restrictions. It was at this stage that the Society, like many other Societies was able to hold the last year’s postponed 53rd meeting in Shrewsbury this year on 2nd and 3rd September.

The meeting was possible with the great commitment and personal efforts of our new President Dr Adrian Kuipers. Dr Kuipers has had to organise the meeting three times including the meeting
having to be arranged and cancelled last year due to the Covid19 pandemic. We thank him sincerely for all his hard work and dedication to the Society.

The scientific programme was organised by the outgoing President Dr Alistair McKenzie and he, as he has been doing for the last four years, organised a varied and interesting programme. Dr McKenzie has been a President who has led the Society from the front and has steered it through the difficult times when the Council meetings were held remotely. He has actively organised the scientific programmes of recent meetings. We look forward to Dr Adrian Kuipers’ term as President with anticipation.

An interesting part of this meeting was the ‘Blessed Chloroform Lecture’ by Dr John (Iain) Glen not on inhalational anaesthesia but on the development of propofol, an agent almost all of us have used and continue to use.

Last but not the least, the Society and I personally, would like to thank Brig Ivan Houghton who has been the Hon Editor for the last seven years. It would have been only six years but he had to carry on for another year due to the handover not being possible during the pandemic. He has been responsible for upholding and improving the quality of the Proceedings both for scientific accuracy and its appearance.

Rajinder Mirakhur
Hon Editor
From test tube to TIVA
Some milestones in the development of Total Intravenous Anaesthesia.
Blessed Chloroform Lecture

John B (Iain) Glen
Former employee of ICI Pharmaceuticals Division/Astra Zeneca
Former owner of Glen Pharma Consultancy
E-mail: iglen2@compuserve.com

This manuscript describes my personal journey from the discovery and development of propofol and the infusion technology and techniques and may therefore appear somewhat autobiographical.

Having qualified in veterinary medicine and surgery at Glasgow University in 1963, I took the opportunity to study for a Diploma in veterinary anaesthesia, the first speciality Diploma to be introduced in veterinary medicine, and became responsible for clinical anaesthesia of both large and small animals at the veterinary school. Around this time a number of new agents had been introduced for medical use and I began to explore their use in animals. These included ketamine, neuroleptanalgesic combinations of fentanyl with droperidol or fluanisone, and the combination of anaesthetic steroids alphaxalone and alphadolone (‘Althesin’, Glaxo). This interest in research prompted me in 1971 to apply to join a multi-disciplinary team of chemists and biologists at ICI Pharmaceuticals Division laboratories in Cheshire concerned with the evaluation of potential new volatile and intravenous anaesthetic agents. I moved south in 1972 as a biologist leading a small group in the evaluation of new compounds provided by project team chemists.

Our target included both potential new inhalational and intravenous anaesthetics. In relation to the latter, we sought a drug which would reproduce the quality of thiopentone in the provision of rapid, smooth induction without excitatory effects but would also be more rapidly metabolised such that anaesthesia could be maintained by repeated injection or continuous infusion. None of the water soluble analogues of etomidate or ketamine synthesised by project team chemists proved to be of interest. Roger James, another of our team, then decided to select from the ICI compound collection a number of lipophilic compounds that could now be
prepared in aqueous solution with the aid of Cremophor EL as used in the commercial presentation of propanidid (‘Epontol’; Bayer). Interesting activity was seen in 2,6–diethylphenol, one of the first compounds tested and led to a systematic evaluation of related alkylphenols with the activity of 2,6-diisopropylphenol first observed on May 23, 1973. By October 1974, sufficient work had been done in mice, rats, cats, rabbits and pigs for me to recommend ICI 35,868 as a candidate for development as an agent for induction and maintenance of anaesthesia with the following features:

- rapid, excitement free induction;
- repeated doses or infusions given without prolonging recovery;
- recovery rapid and excitement free with animals bright and alert and often keen to eat shortly after regaining consciousness.

Formal development began in November 1974 with toxicology, teratology, pharmacokinetic, disposition and metabolism studies conducted by experts in our Safety of Medicines Department. Instead of initial studies in patients, Brian Kay and colleagues at Derby took part in a study with subanaesthetic doses of radiolabelled drug which confirmed that metabolism in man replicated that seen in animals. Following this study Dr Kay moved to Ghent in 1977 where, with the approval of Professor Rolly, he was able to begin a clinical trial with propofol 2% in 16% Cremophor EL and 8% ethanol. A few days later Dr Kay called to say he had given propofol to 22 unpremedicated patients and it was more potent than I had anticipated with a mean induction dose of 0.94 mg.kg⁻¹, and pain on injection was seen in some patients. In view of this result, the concentration of propofol was reduced to 1% and the need for ethanol avoided.

Once the Committee on Safety of Medicines (CSM) approval for UK studies had been obtained, double blind studies with propofol at a dose of 1 mg.kg⁻¹ and ‘Althesin’ were set up. It quickly became apparent that 1 mg.kg⁻¹ of propofol was an inadequate dose in unpremedicated patients and the studies were replaced with dose finding studies which suggested that 2 mg.kg⁻¹ would be a more suitable induction dose for future studies. After this result was obtained an internal team meeting discussed the viability of the project and decided by five votes to four to continue studies with the Cremophor formulation while work on an alternative surfactant formulation was developed. Some years later Professor Rolly provided me with a copy of the
anaesthetic record of the first patient to receive propofol and it became apparent that the patients studied by Brian Kay had been premedicated with 2 ml ‘Thalamonal’ (fentanyl and droperidol) thus explaining the lower than expected propofol induction dose in Dr Kay’s initial study.

Because of the sensitivity of the dog to Cremophor EL, minipigs were selected for the comparative evaluation of the haemodynamic effects of propofol with those of thiopentone and ‘Althesin’. The observation of a suspected anaphylactoid reaction on the second injection of ‘Althesin’ led to a comparative study of the effects of repeated injections of thiopentone and the Cremophor containing agents ‘Althesin’ and ‘Epontol (propanidid)’. No adverse effect accompanied the repeated administration of thiopentone whereas a second administration of Cremophor or the two Cremophor containing agents, given two weeks after an uneventful first exposure, led to a high proportion of anaphylactoid reactions, with a marked but transient reduction in polymorphonuclear leucocytes suggestive of complement activation.4

With this model we were now able to examine possible alternative formulations and another ICI surfactant, Synperonic PE 39/70 was effective in solubilising propofol and was well tolerated in our pig model. The desirable properties of propofol were retained when formulated in Synperonic PE 39/70. All pharmacological studies were repeated with satisfactory results, but unexplained histological changes in liver halted work with this formulation in 1980.

Earlier work with a potential emulsion formulation of propofol had been unsatisfactory but, as emulsion technology had improved, my group worked closely with our Pharmaceutical Department to identify suitable constituents for an emulsion formulation of propofol. This work eventually led to the current soybean oil emulsion formulation. Once a final formulation had been developed, all pharmacology studies were repeated and confirmed that the desirable properties of propofol were retained.5 Toxicology, teratology, pharmacokinetic, metabolic and disposition studies were also repeated with satisfactory results, demonstrating the safety of the new formulation.

Meanwhile, clinical trials with the Cremophor formulation had continued in patients without previous exposure to Cremophor and, very much against my
advice, a commercial plan to proceed to market the Cremophor formulation was approved by senior management. Almost 1000 patients had received this formulation in clinical trials. The first adverse reaction to the Cremophor formulation was reported from Belfast in 1980 when about 500 patients had been studied at that centre. By mid-1981 a total of four possible reactions had been encountered and management agreed that the Cremophor formulation was not a satisfactory product.

The physician Ron Stark became responsible for the further clinical evaluation of propofol and he and his clinical research associate Sue Binks created a detailed plan for a UK clinical programme in 1200 patients to support use for both induction and maintenance of anaesthesia with the emulsion formulation. On July 19th 1983 the emulsion formulation was administered for the first time to a patient in Oxford and was approved in the UK for induction and short-term maintenance in early 1986. By this time, I had moved to our Medical Department to deal with the coordination of European and other overseas clinical trials and clinical pharmacology studies.

An early study on maintenance of anaesthesia by infusion of ‘Latherin’ had been published in 1975 by Tim Savage and colleagues at the London Hospital but a mean recovery time of 18 min after a mean surgery time of 33 min was not particularly rapid. An important study by Fred Roberts and colleagues at Bristol used computer simulation to derive a stepped infusion scheme of propofol to achieve a target blood propofol concentration of 3 \(\mu g\cdot ml^{-1}\) and provided a good starting point for many other studies for maintenance of anaesthesia. I was concerned that the delivery range of syringe pumps available at that time was generally limited to a maximum rate of 99 ml.h\(^{-1}\) and in 1986 I contacted a number of manufactures to alert them to an emerging opportunity as I felt that there would be a benefit in delivering the induction dose by infusion. The response I received from BOC Healthcare proposed a prototype device with the ability to deliver bolus infusion rates of 300, 600, or 1200 ml.h\(^{-1}\) with a 50 ml syringe and continuous infusion rates up to 200 ml.h\(^{-1}\). After clinical evaluation and a few minor modifications, the Homed 900, the first of a new generation of syringe pumps, which could be controlled manually or interfaced with a computer, became available. This was followed by the development of similar devices by other syringe pump manufacturers and a number of
academic groups began to follow the pioneering work of Helmut Schwedler in Bonn who used a computer programmed with a pharmacokinetic model for propofol to determine an appropriate infusion profile to rapidly achieve and maintain a desired drug concentration.9 Other similar systems were being developed by other research groups and after ICI hosted a workshop on this topic in 1990 and I was convinced of the merit of this approach, but it was not until after a further international workshop held in The Hague in 1992 that the Commercial Section at ICI was convinced to embark on a commercial development. I was concerned that terms such as CATIA (computer assisted total intravenous anaesthesia), TIAC (titration of intravenous agents by computer), CACI (computer assisted continuous infusion) and CCIP (computer-controlled infusion pump) generally inferred control of anaesthesia by a computer, rather than an anaesthetist, and gained agreement from the principal groups working in this area to use the term ‘target controlled infusion, (TCI)’ as a more appropriate alternative.10 To standardize drug delivery it was important to select a preferred pharmacokinetic model for propofol and on the basis of computer simulation studies and a prospective clinical study, the model described by Marsh et al was chosen and was incorporated in a ‘Detrusor’ electronics module.11-14 This could be supplied to syringe pump manufacturers to ensure standardized drug delivery over time at any particular target setting and body weight. A pre-filled syringe presentation of propofol for use in a TCI pump also incorporated an electronic tag to confirm the presence and concentration of propofol.

Over the period that propofol has held a dominant position in anaesthesia a number of potential competitor agents have been evaluated and discarded. Minaxolone citrate, a water soluble neuroactive steroid agent from Glaxo proved to be an effective anaesthetic but was withdrawn from development because of toxicity seen on long term administration in rats.15 Organon 21465, a water-soluble neuroactive steroid was found to be unsatisfactory because of involuntary movements and slow equilibration with the biophase.16 Fospropofol (Lusedra), a water soluble pro-drug was approved by the FDA in 2008 on condition that it was to be used by those with anaesthetic competencies. This and an unfavourable adverse events profile limited its use and it is no longer marketed.17 AZD-3043, an esterase metabolised modulator of GABA-A produced by Theravance was found to be an effective anaesthetic in clinical studies by AstraZeneca but side effects
including erythema, chest discomfort, dyspnoea and episodes of involuntary movement halted development.\textsuperscript{18} Eltanolone (Kabi-Pharmacea), an isomer of pregnanolone formulated in Intralipid had a slower onset of effect than propofol, and involuntary muscle movements, urticarial reactions and four reported cases of convulsions in clinical trials.\textsuperscript{19} ABP-700 a short acting ester derivative of etomidate showed dose related excitatory effects. This and the finding of seizures in dog studies halted further development.\textsuperscript{17} PF 0713, (R,R)-2,6-di-sec-butylphenol, closely related to propofol had similar efficacy and safety, but trials discontinued because of slower onset and longer duration of action.\textsuperscript{20}

A recently approved potential competitor to propofol is remimazolam, structurally similar to midazolam with an added ester linkage such that its action is terminated by esterase hydrolysis.\textsuperscript{21} It has been approved primarily for procedural sedation for short procedures but may deserve consideration as the hypnotic component of general anaesthesia. Alphaxalone, one of the neuroactive steroids in ‘Athesin’ formulated previously in Cremophor EL has been reformulated in 7-sulphobutyl-ether-\(\beta\)-cyclodextrin (‘Phaxan’) by Drawbridge Pharmaceuticals in Australia. In a comparative clinical trial Phaxan provided fast onset, short duration anaesthesia with fast cognitive recovery similar to propofol, but with less cardiovascular depression and no pain on injection.\textsuperscript{22} A further promising candidate to challenge propofol is a closely related alkylphenol with the incorporation of a cyclopropyl group (HSK3486, Ciprofol) from Sichuan Haisco Pharmaceutical group in China.\textsuperscript{23} Clinical trials with an emulsion formulation found that Ciprofol was safe and well tolerated at doses from 0.1-0.5 mg.kg\(^{-1}\). Ciprofol 0.4-0.5 mg.kg\(^{-1}\) induced equivalent sedation/anaesthesia and had a similar safety profile to propofol 2.0 mg.kg\(^{-1}\) used for colonoscopy.\textsuperscript{24} Time will tell if further experience with any of these agents will allow them to compete with generic propofol.

References


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17. Sneyd JR. Thiopentone to desflurane- an anaesthetic journey. Where are we going next? *British Journal of Anaesthesia*, 2017; **119** (S1) i44-i52.


Max von Pettenkofer (1818-1901) and
his work on respiration

Adrian J Kuipers
Retired Consultant Anaesthetist, Shrewsbury

Early life

I doubt that many us who live outside mainland Europe have ever heard of
this great German and or of his even more famous mentor Justus von Liebig.
Pettenkofer was born from a humble background in 1818. Fortunately for
him, he had a wealthy uncle, a pharmacist, who paid his schooling and his
university fees in the hope that Pettenkofer would also become a pharmacist.
Pettenkofer left his school in Munich to study sciences at the local university
and at the same time became an apprentice to the Royal Court Pharmacy.

In 1840 following a row with his uncle he packed it all in and for a while
became an actor, which he unfortunately was not very good at. Although he
had no intention ever to practice, he decided to study medicine and returned
to Munich for his studies. Once qualified and having been inspired by
Liebig, he became a research chemist. This was followed by a period of
working for the Royal Mint. Whilst there, he continued his researches and
made many discoveries, such as Poporino Antico an ancient dye. He
improved the manufacture of the coinage, the quality of building cement, as
well as an improved amalgam for filling teeth. As an aside, he saved the
Paintings of the Munich Art Galleries by discovering a way of restoring their
varnish. These are just a few of his contributions to science. It is not
surprising that it was not long (1847) before he was appointed Professor of
Medical Chemistry at Munchen (Munich)University.

The health of the city of Munich (population 170,000) was appalling at that
time, with frequent outbreaks of cholera; much worse than in London, a far
bigger city. In fact, it was one of the worst in Europe. London, having had
some terrible outbreaks of cholera, was far ahead in public health matters
compared with the rest of Europe. Convinced that something could and
should be done he gave two open lectures to the good ‘burghers’ (socially
higher class citizens) of Munich. Despite deliberately understating his case,
he managed to convince them, that it made good economic as well as
humanitarian sense to invest in public health and a great deal of money was raised for a new water supply and sewerage system. Pettenkofer believed in Public Welfare in the broadest sense and encouraged the building of parks and the planting of trees. As he predicted, the death rate fell following his measures from 33/1000/annum to the UK level of 22/1000/annum with a concomitant large drop in illness. Munich soon became one of the most desirable cities of Europe to live in. Von Pettenkofer became internationally famous and received amongst many other decorations, The Gold Harlem Medal from the British Institute of public health. He was so revered, that he was addressed as ‘Your Excellency’.

However, even a man of Pettenkofer’s calibre could not always be right. He steadfastly insisted that it was not the Cholera bacillus, which caused the disease, but the ground water it was in. To prove his point, he drank an ampoule of water heavily contaminated with cholera and to everyone’s complete amazement and to the delight of his followers, he was no worse for the ordeal. There was no arguing with that!

Despite his fame and increasing age he always remained an approachable man and retained his interest in local issues and in the world around him. Unfortunately, in 1901, at the age of 83, severely depressed, after many a sleepless night from an extremely sore throat, and becoming increasingly worried at the thought of senility, he shot himself.

**Justus von Liebig**

It is just worth spending a few words on Von Liebig as he played such an important role in Pettenkofer's life. He was born in Darmstadt, Germany, in May 1803. His education was a disaster and he left school without qualification. Soon afterwards he was apprenticed to an apothecary. In 1822, having received a grant, he studied in Paris under the great Gay Lussac.

Justus von Liebig was appointed Assistant Professor at the University of Giessen at the age of twenty-one. There he soon established himself as one of the best teachers in Europe and became one of the most academically and financially successful biochemists in the world. There seemed no limit to his interests from explosives to artificial fertiliser; the latter a discovery which has done much to feed the world. Later he also discovered chloral hydrate in
1832. Liebig was also concerned with human metabolism. He was of the opinion that body heat was formed by the metabolism of carbohydrates and fat. Muscular energy however was obtained by the metabolism of muscle itself. It was therefore vitally important to consume vast amounts of meat to keep increasing one’s work output and to build up musculature. He invented, with more than a little help from Pettenkofer, Liebig's Extract of meat for which he made outrages claims. He opened a factory in London called The Liebig Extract of Meat Co (LEMCCO).\(^3\) This led to the manufacture of the OXO cube.

Max von Liebig registered Fray Bentos trade mark for his corned beef in 1881. The factory employed four thousand employees and slaughtered up to six thousand animals a day. The Argentine beef industry was mainly setup to satisfy the vast amounts of meat this extract of meat required. The meat was mostly slaughtered and exported via Fray Bentos in Uruguay, a country which had then and still has close financial ties with the UK.

Pettenkofer and his researches on respiration

Pettenkofer must have been a very busy man and I was therefore extremely surprised to find an article written by Pettenkofer in English in The Lancet.\(^4\) Here he describes, with clear diagrams, a machine for collecting expired carbon dioxide (CO\(_2\)), water vapour and marsh gas from an animal or human without hindering their normal activity. The whole apparatus had the disadvantage of being the size of a small house and was powered by a two horse power steam engine which needed half an hour to stabilise after having been stoked up. His article can be divided into four parts namely the construction of the apparatus, its calibration, its use and finally the results. This is only a very brief resume and for those interested I would heartily advise reading the original article.

Construction

The principle of his apparatus is straightforward, namely one places an animal in a container and a pump continuously samples the air out of the container. It should be possible to determine the consistency and quantity of gases produced by the animal, if one knows the consistency of the air outside the container. The King of Bavaria gave him a grant of 7000 (£600) gulden.
He used it to construct an eight-foot cubed cast iron chamber but unfortunately, with a wooden floor which later gave problems. This was attached to two huge bellows, driven by a steam engine, which sucked the air out of the chamber. "A very ingenious device" which ran with a clockwork which regulated the speed of the bellows. Slots in the walls of the chamber allowed fresh air entry to avoid a vacuum being created in the chamber. In between the bellows and the chamber was a large water gasometer. The exact amount of air passing through the chamber could be measured. We are dealing here with a fresh air flow of 20,000 litres an hour and it was impossible to analyse all the air passing through the chamber. A very small proportion of that air was sampled with the aid of a much smaller pump (which was also driven by the steam engine). The amount of air sampled was again accurately measured using a much smaller gasometer. By comparing the readings given by the small and large gasometers the proportion of air sampled to that actually passing through the chamber could be accurately worked out. The outside air was sampled using a very similar pump arrangement.

*Determination of the Gases*\(^5\)

Carbonic acid was analysed with Baryta Ba(OH)\(_2\), water vapour being absorbed by strong sulphuric acid and hydrogen (H\(_2\)) and marsh gas using a red-hot platinum rod which converted H\(_2\) to water and marsh gas to carbonic acid.

*Calibration*\(^6\)

Pettenkofer describes burning a stearine candle the composition of which had been accurately determined to calibrate the carbonic acid analyser. He took great care to assure that the flow of air was sufficient that it went one way but not so strong as to blow the candle out. A nasty smelling gas was injected into the chamber and when it couldn’t be smelt outside the chamber, he was satisfied that the gas flow was one way and that the air did not escape through the door and slots. The calibration of the water vapour analyser by boiling a given amount of water proved to be difficult. The problem was solved by sealing the wooden floor which was absorbing the steam.
A volunteer spent 24 hours in the chamber. He did this on two occasions whilst being denied food. The amount of carbonic acid produced by this volunteer during the two spells was nearly the same. This was accepted as proof enough that the equipment was reliable.

The Experiment

A specially trained dog was placed in the chamber and fed various diets of which some were all fat, some all meat and some all carbohydrate. The urine, faeces and expired air were all collected and the results tabulated.

Conclusion

The dog did not lose and could actually gain muscle despite being deprived of meat and was capable of exercise without it.

Aftermath

Despite Pettenkofer’s findings, the public continued to believe in the strengthening properties of the von Liebig Extract of Meat and remained firmly embedded in the public mind and bouillon is still described as Krafts Brühe in many German speaking restaurants today. Fray Bentos continued to boom, supplying armies of the world with bully beef (Corned Beef). However, following a massive outbreak of typhoid in Aberdeen in 1964 which was traced to Argentinian Corned beef, the latter lost credibility and the huge slaughter houses are now closed down.³

There is still a Max von Pettenkofer Institute in Munich today.⁷ Fray Bentos which closed in 1976 has become a world heritage site, and Liebig’s laboratories in Giessen now house the Liebig Museum. There is a “von Liebig Center for Science” in Pennsylvania USA,⁸ and of course, Oxo cubes and his extract of meat (Figure 1) are available to buy this very day.
Figure 1. Jars of Liebig meat extract (photograph by Adrian Kuipers)

References

5. Pettenkofer M. Researches on respiration. The Lancet 1862; 80: 500-1.
The first recorded anaesthetic in the geographic centre of Africa

Alistair G McKenzie
President, History of Anaesthesia Society 2017-21
Honorary Clinical Senior Lecturer, University of Edinburgh

It has been claimed that the first anaesthetic in Central Africa was by the missionary, Dr Robert Laws at Cape Maclear on the southern tip of Lake Nyasa (now Malawi) in 1876.\(^1\) A glance at the map of Africa reveals that this point is far from the geographical centre of Africa in the northern Congo, which at that time was still unexplored.

The first recorded anaesthetic in the geographic centre of Africa took place 11 years later. It was supervised by Surgeon Major Thomas H Parke in the Congo Free State during the Emin Pasha Relief Expedition (EPRE) of 1887-89, led by Henry Morton Stanley. Sangfroid to say the least, Parke endured considerable hardships during the expedition and his clinical acumen was severely tested. He brought knowledge of pygmies’ arrow poison to Britain, published his medical experiences based on his diary\(^2\) and later published a guide to health in Africa.

The EPRE ravaged the health of Stanley and most of the nine officers he recruited. Half-way through the expedition, one was discharged home because of an ulcerating wound, one withdrawn home and two died. Of the remaining five officers who completed the expedition, three were dead just four years afterwards, including Parke who died from a brain tumour at only 35 years of age in 1893. As Parke was a graduate of the Royal College of Surgeons in Ireland, it was in Dublin that he was honoured by a bronze statue, to the cost of which Stanley was the largest contributor. Stanley lived until 1904.

References


Frances May Dickinson Berry (MDB)

The first woman anaesthetist to give a “substantive” paper at the newly founded Section of Anaesthesia at the Royal Society of Medicine (RSM) was Mrs May Dickinson Berry (Figure 1) on the 9th of April 1920.¹

Figure 1. Frances May (née Dickinson), Lady Berry. National Portrait Gallery

Henry Connor explains:

“The Society of Anaesthetists was founded in 1893. Dickinson Berry met the requirements to join it as she was on the staff of a London Teaching Hospital. It was when the Society of Anaesthetists was amalgamated with the Anaesthetic Section of the RSM that she gave her paper”. She was the Honorary Secretary to the Section from 1910 to 1912.”¹
One would think that her professional experience would have been mentioned in her obituary in the BMJ but it instead stresses her mountaineering and cycling skills. Her obituary includes a really unflattering photograph and begins by saying that women medical students gained academic distinction “only at the cost of wearing odd clothing of a masculine character” and the “cultivation of an aggressive manner which often gave offence”. Happily, MDB, because of her “personal charm and good taste in dress” caught the “discerning eye” of an anatomy demonstrator, John Berry, who gave her “a sound knowledge of anatomy and won her heart”. They were often seen riding horses in Hyde Park as respite from her work at the Elizabeth Garrett Anderson Hospital (EGA). The writer of her obituary also worked with her during the First World War when she established a hospital in Serbia. The Berrys later founded a scholarship to enable Yugoslavian women to come to London and train in medicine at The Royal Free Hospital (RFH).

Katharine G Lloyd-Williams (KL-W)

Katharine Lloyd-Williams (Figure 2) became the first woman President of the Section of Anaesthetics from 1956 to 1963, 63 years after the section was founded. I remember how she let me draw up drugs in the anaesthetic room while teaching me the basics of anaesthesia. Little did I know that her Presidential address to the RSM had been on ‘the Anaesthetist’s role in Undergraduate Training.’ In the second paragraph, she says “it is not difficult to get enthusiasm from students” for the specialty of anaesthesia. For myself, this was very true.

It is sad to note from her obituary in the BMJ that “Students have forgotten her only ten years after her retirement and her portrait no longer hangs in the junior common room”. This is a disgrace as KL-W was first woman Dean of the RFH from 1945-62, represented Medical Schools in the Senate from 1954-60 and was the Dean of the Faculty of Medicine, University of London between 1956 and 1960. She also served on the General Medical Council.

Katherine Lloyd-Williams who was born in Nantcwnlle near Lampeter began her studies as a physiotherapist and practised in London but heard a lecture by Dame Mary Scharlieb and thanks to her godmother’s legacy she was admitted to the London School of Medicine in 1921. “Kitty” was
appointed as consultant anaesthetist to the now RFH and EGA Hospital and elected FFARCS in 1948. Her special interest was obstetric anaesthesia and she published a book on the subject in 1964 but a major achievement was saving the RFH group after the loss of beds due to the bombing of Grays Inn Road. During World War II KL-W was the only consultant anaesthetist in RFH helped by a registrar and two juniors with a weekly visit by Stanley Rowbotham, a fellow consultant anaesthetist, then stationed at Aldershot.

Figure 2. Dr Katharine Georgina Lloyd-Williams (From the RCoA website; accessed 29 October 2021)

In 1948, as Dean of the RFH she oversaw the introduction of men to the London Medical School for Women (LMSW) with 2 men, and the move of the RFH from the Grays Inn Road to its present position in Hampstead.

There is an editorial in the British Journal of Anaesthesia detailing her work and outstanding achievements.4 Katharine Lloyd-Williams was awarded the CBE in 1956 and died in 1973.
Edith Gilchrist (EG, figure 3)

Edith Gilchrist (EG) was a Consultant Anaesthetist I remember as a student. I remember her for the tactful manner in which she dealt with George Qvist (RFH general surgeon), who had put his fist through the operating lights during a tantrum while I was scrubbed up with him. She also worked with Cecil Joll, (thyroid surgeon) and Dick Dawson (plastic surgeon). Being so busy clinically, it is no wonder that she published little. However, she loved the history of anaesthesia. EG was the first lady president of the Harveian Society, a member of the Hunterian Society and a founder of the History of Anaesthesia Society and a Council member of it. EG was the Curator of the RFH Archives which now reside at the National Archives at Kew.

Figure 3. Edith Gilchrist, RCoA website (https://rcoa.ac.uk/obituary-dr-edith-gilchrist, accessed 25 October 2021)
Barbara Pleuvry (BP)

The woman who published widely and reviewed for the British Journal of Anaesthesia and many Pharmacology Journals and influenced/saved my career after specialising in anaesthesia was Dr Barbara Pleuvry (Figure 4).

Figure 4. Barbara Pleuvry with her grandchildren; Photo courtesy of her husband

I accepted a locum post in St Anthony, Northern Newfoundland, after achieving the FFARCS. Thinking I knew everything, I became the only anaesthetist during a Canadian winter. Humbled, but enjoying every minute, I resigned my registrar post and accepted another locum in St John’s, Newfoundland. Returning to England, I was lucky to be accepted as an SHO to a research position, half anaesthetics and half attached to the Pharmacology Department of the University of Manchester. Here I met Barbara and famous pharmacologists such as chain-smoking James Raventos, the investigator of halothane fame.
Trainees in Manchester hoping for a consultant post often went to Barbara who taught them that anaesthesia is applied pharmacology, and instilled some scientific rigour into their research which resulted in papers in peer reviewed journals.

Barbara encouraged and mentored me to submit my research for a successful MD thesis from the University of London.

BP born in 1944, qualified BPharm from the University of London in 1966 and obtained her MSc in 1967. She became a Research Assistant in Manchester and London. She returned to the University of Manchester with a PhD in 1969, and was first appointed as Lecturer in Anaesthesia and Pharmacology, and finally as a Senior Lecturer. Barbara was a Pharmacology examiner for the Part II FRCA (1995-1996) and President of Manchester Medical Society (1995-1996). She retired to Whaley Bridge (of bursting dam fame) in 2004 and is a proud grandmother and a good friend.

This paper recognises the important contribution these women made to anaesthesia.

**Acknowledgement**

Dr Duncan Mitchell for technical support.

**References**

2. Obituary. Lady Berry, M.D. *British Medical Journal* 1934; **1**: 780.
Further Reading
McIntyre N. How British Women became Doctors: The Story of the Royal Free Hospital and its Medical School, 2014; UK, Wenrowave Press.
Early Anaesthesia at the Radcliffe Infirmary Oxford

Dr David Shlugman & Dr Michael Ward
Retired Consultants, Oxford

The Radcliffe Infirmary (RI; Figure 1) situated within 1 mile of the centre of the medieval University City of Oxford, opened to the public on October 18th 1770. Its name is known throughout the world as a result of Dr John Radcliffe’s trustees giving the then huge sum of £4,000 (a sum probably equivalent to several million pounds in today’s terms), in 1758 towards its building some 40 years after his death.

Figure 1. the original Radcliffe Infirmary (image supplied by Oxfordshire Health Archives archives@oxfordhealth.nhs.uk)

A brief outline of Radcliffe’s story and his rise to eminence in British Medicine introduces the study of the original ‘Operation Records Register’. The records began in 1838 following an edict from the House of Commons that “required all operations of the ‘higher order’ (i.e. not carried out by junior staff) to be recorded”. Each case was meticulously described in copperplate handwriting following a decision of the RI’s Quarterly Court to follow the decree. Each case was numbered sequentially. The data collected were probably also used as a form of early ‘audit’.

39
Close study of the Register with special reference to the introduction of the use of anaesthetic agents, allowed us to discover several cases where early anaesthesia was mentioned (often it appeared in passing as a novelty!).

The first recorded use of anaesthesia in Oxford was on the 4th March 1847 approximately 3 months after the first use of ether in University College Hospital (Figure 2). There is no mention of who administered the vapour. The entry reads: “Case 117 Charlotte Launton of Yarnton; at 16, this girl was admitted under Mr Parker in February 1845 with necrosis of the right tibia……. A large part of the shaft of the tibia was removed, without anaesthesia,… the girl remained in the Infirmary for 19 months. On 10th February 1847 she returned and the leg was removed above the knee without anaesthesia…. On 4th March the operation was the Double Flap & ether was used with complete success…. Discharged June 16th 1847.”

Radcliffe Infirmary, Oxford – 4th March 1847
First Recorded Use of Anaesthesia in Oxford

Figure 2. The record of the first anaesthetic 1847 (Photograph by Dr Michael Ward)

The second use of ether was on 28th June, Case 121 (so only 4 surgical procedures between 4th of March and 28th of June). This was amputation of the right leg of a 17 year old girl again for sepsis worsening over 6 months and the record noted ‘Ether vapour was inhaled in this case, by means of Twiss apparatus with complete success. The time taken occupied in inhaling
was about 2 ½ minutes.” We have no idea who or what Twiss and his apparatus looked like? (It was suggested during the meeting in Shrewsbury that Twiss might be the name of designer of an inhaler used for administration of respiratory stimulants)

That date also saw the third use of ether for the amputation of the crushed hand of a 13 year old boy working in the University Press (which still occupies the same site behind the Radcliffe Infirmary site on Walton St). The register notes that induction took 2 minutes and was completely successful.

Fuller examination of the Register gave details of 12 cases in whom anaesthesia was used in the first 20 months, of which 4 received ether, and 8 chloroform, the latter being first used on April 24th 1848. There is no information recorded in any of the cases as to who administered the anaesthetic.

The Radcliffe Infirmary buildings ceased to be a hospital in 2007 after 237 years of being at the forefront of British Medicine. It is now home to the Faculty of Philosophy of the University of Oxford.

**Reference**

Harry Walker, 1918-1959: 
an Illustration of the Mid-Twentieth Century History of Anaesthesia.  
Middlesbrough, Edinburgh, Burma.  

Katherine M Venables  
Emeritus Fellow, St Cross College, University of Oxford

Introduction

I am writing a hybrid memoir-biography drawing on my father’s life. He, Harry Walker, was one of the earlier Fellows of the Faculty of Anaesthetists and when I contacted the College, I learned that he was unusual for his time in that he decided to become an anaesthetist while he was a medical student.¹ I thought a summary of his career might be of interest to the History of Anaesthesia Society. I am a physician and my account lacks detail about anaesthetic techniques but I hope it illustrates the extraordinary events that young anaesthetists lived through in the mid-twentieth century.

Medical School

Harry trained at the School of Medicine of the Royal Colleges in Edinburgh, one of the extra-mural schools set up in the nineteenth century to counter what was often seen as a stagnant and old-fashioned medical curriculum in the universities. Lectures were at Surgeons’ Hall and clinical work in the Royal Infirmary. Medical teachers in Edinburgh moved seamlessly between university and hospital appointments, private practice, and extra-mural teaching. The School was absorbed into the University of Edinburgh after the Second World War.²

The School was an interesting place. The Scottish Colleges resisted the General Medical Council’s proposal to restrict the intake of refugees from fascism and, as well as British students and others from the then-Dominions, the School accepted emigrés from Europe (Figure 1). There was also antisemitism in the USA and some students had been rejected by prestigious American schools despite excellent grades. Surgeons’ Hall archive contains a sequence of letters home by one of these young Americans.³ A few years later, the University set up a Polish Medical School, which further increased the diversity of the Edinburgh student population.
Figure 1: Medical students outside Surgeons’ Hall at the outset of the Second World War, September, 1939. Harry is fourth from the right wearing a trench coat and scarf.

By the time Harry joined the Royal Army Medical Corps (RAMC) in 1943, he could tell the Army that he had administered over 1,000 anaesthetics, some while he was a student. He took photographs of operations at the Royal Infirmary, carefully annotating them with the anaesthetist’s and the surgeon’s names (Figure 2).

House Jobs

The Second World War brought stratagems to increase the supply of doctors. As well as bringing medical students like Harry in to the workforce before qualifying, women doctors were deployed in military roles they had not previously occupied, and retired and overseas doctors called up. The Colleges complained that the Army did not use doctors’ expertise appropriately and as a result non-medical officers were recruited to the RAMC in administrative roles to release doctors for clinical work.⁴
Figure 2: Two photographs of operations, Royal Infirmary, Edinburgh, 1940-41. Taken by Harry.

Harry started his house jobs six months before he qualified, back home in Middlesbrough at the North Riding Infirmary (Figure 3a). His testimonials note his interest in anaesthesia. ‘I was much impressed with his skill as an anaesthetist which was markedly superior to the average shown by a young graduate.’ And, ‘he shews a special aptitude in this branch of his profession’.

Figure 3. Harry Walker: a. house surgeon in the dispensary of the North Riding Infirmary, 1942; b. consultant anaesthetist in Teesside, 1949-59.
The Army

After an induction at the RAMC Number 1 Depot in Hampshire, Harry went to 190 Field Ambulance for further training, a small mobile hospital based then in Northern Ireland. In his letters from Burma he recalls Nissen huts and the Irish rain. It is unlikely that either posting provided these new Army doctors with much clinical training. The focus was on reorientating their outlook. Much of the early timetable was devoted to military law, administration, man management and the organisation of medical services. There were physical jerks and cross-country runs. Although they were non-combatants under the Geneva Convention, doctors were expected to lead soldiers and be capable of protecting their patients, so they had lectures on such topics as reconnaissance and movement by road, learned how to operate a service rifle and the principles of camouflage, watched machine gun and other weapons demonstrations, and practised map-reading.

Before the war, civilian surgeons and anaesthetists valued their autonomy but the Army required standardisation, protocols, a restricted range of equipment, and meticulous record keeping so that patients could be handed on safely. The ethos was also different, the broad aim put starkly in *A Field Surgery Pocket Book*: ‘The main function of the medical units during battle periods is to relieve the combatant formations of the encumbrance of non-effective by clearing them from the battle area.’

190 Field Ambulance was training for the invasion of Sicily and there are photographs in the Imperial War Museum collection showing stretcher bearers lowering a simulated casualty down a vertical Irish cliff, and doctors pretending to set up a surgical procedure in a tent (Figure 4). Buttons and boots are polished, uniform is correct, surgical gowns are crisp and white. It is all very different from the few official photographs of surgical teams at the front, the sweat-stained shirts, hurricane lamps, broken buildings, and sand, dust, and mud.

India

After a course on Tropical Medicine in Liverpool, Harry travelled in a troopship in a Mediterranean convoy to the Suez Canal and then on to India, arriving in Bombay in December 1943 to join the Fourteenth Army under General William ‘Uncle Bill’ Slim. After the disastrous British defeats of
1942, with the loss of Singapore (thought to be impregnable) to the Japanese and the humiliating retreat through Burma, Slim spent time training and re-equipping his Army. Harry was posted first to 21 British General Hospital in Jhansi in Uttar Pradesh as a ‘general duties medical officer’ in charge of a medical ward. Cases of sickness, such as malaria, dysentery, and scrub typhus, far outnumbered battle casualties in the Burma Campaign, even with Slim’s insistence on meticulous hygiene and anti-malarial prophylaxis. Lord Louis Mountbatten, the Supreme Allied Commander of South-East Asia Command, wrote that ‘the terrain of the South-East Asia theatre was one of the most unhealthy in the world.’

Figure 4: RAMC personnel training in Northern Ireland, August 1943. © IWM H31669.

An ambulance train arrived at the hospital every few days and the number of beds rose from five hundred to over a thousand. 21 British General Hospital also supported the Chindits, special forces designed to operate behind Japanese lines. The hospital commander records meetings with the Chindit Senior Medical Officer about medical screening, a dedicated ophthalmological service, advice on packing mule panniers, and setting aside
one hundred beds for venereal infections caught during the Chindits’ pre-deployment leave.

At last, Harry received postgraduate training in anaesthesia. The military medical authorities decided that ‘battle casualties require a high degree of competence’ and training centres were set up in India. Harry was sent further north to a hospital in Bareilly, close to the Himalayas, for February and March 1944. He was due to join a mobile surgical unit but instead was posted hundreds of miles east to 66 Indian General Hospital in Dimapur, a major railhead on the Assamese border with Burma. The Japanese had started their ‘March on Delhi’ and surgeons and anaesthetists throughout north-east India were hastily seconded in April 1944 to deal with casualties evacuated from the siege of Kohima.

**Kohima**

In Kohima, the fighting was like the worst of the trench warfare of the First World War. Three of the fourteen doctors in Kohima were killed and one wounded. Wounded men lay on stretchers in bunkers for up to two weeks and were killed or re-wounded where they lay. By the time the casualties arrived at 66 Indian General Hospital they had mortar, grenade and bullet wounds, many infected or maggot-infested, and some with gas gangrene. As well as British, Indian and West African troops, the patients included Indian non-combatant labourers, Naga tribesmen, and a small number of Japanese prisoners of war.

**Mobile Surgical Units**

Kohima was Harry’s first experience of combat surgery. From now on he was posted to the Fifth Indian Mobile Surgical Unit (5 IMSU) as its anaesthetist and second-in-command. He joined it first in Imphal, then encircled by the Japanese, although air supplies continued. The unit was one of four MSUs on the Imphal plain. After the Japanese retreated, 5 IMSU moved through the mountainous Indo-Burmese borderland, crossed the great Manipur, Chindwin and Irrawaddy rivers, and then moved rapidly through the central Burmese plain from Mandalay to Rangoon. The unit transferred from Division to Division of the Fourteenth Army, depending on the need, usually paired with a second MSU so that they could spell each other.
MSUs had first proved their worth in the Spanish Civil War. In the Second World War, they were important in the North African desert and Italy, as well as in Burma (Figure 5). Their purpose was to stabilise battle casualties close to the fighting so that they could be safely evacuated to base hospitals. Evacuation was preferably by light plane but also by jeep or truck. Mules or stretcher-bearers were used if a section of road was muddy or otherwise non-motorable. These were small units, usually with three doctors, a surgeon, an anaesthetist, and a general duties medical officer, and about nine or ten other ranks, amongst whom the non-commissioned officers were vital, performing a variety of skilled tasks.

![Figure 5: Major Grace gives an anaesthetic under shellfire in an abandoned building, Lanciano, Italy, December 1944. © IWM NA10222.](image)

MSUs carried enough equipment for one hundred operations on two tables, but were not fully independent. They were co-located with a larger unit, such
as a Field Ambulance (a small mobile hospital), which nursed their patients and undertook support functions such as pay and rations.\textsuperscript{14-16}

There are several memoirs by surgeons who worked in mobile units but I have found none by anaesthetists. John Baty wrote about 7 IMSU, based in the Arakan coastal region of Burma (Figure 6).\textsuperscript{17} The autonomy and mobility of these units gave them a buccaneering quality and they would ‘liberate’ any useful item they found. Baty’s MSU made creative use of bamboo and he comments that they preferred to be associated with Indian than British units because their cooking was better. Harry’s MSU used part of the wing from a Japanese Zero fighter plane as the reflector for their operating lamp and there is one small photograph taken inside his operating tent showing the Zero wing and also a clock from an abandoned house (Figure 7). Harry’s corporal stands, shirtless and in shorts, by the entrance to the tent. ‘Were shelled here’ Harry notes on the photo’s back. ‘Damage – one scraped back from jumping into a trench!’

![Figure 6: Personnel of the Seventh Indian Mobile Surgical Unit, Arakan, Burma, 1945. Baty JA. Surgeon in the Jungle War. London: Kimber, 1979.](image)

Unsurprisingly, the work of these units was intermittent. One observer wrote that ‘during the brief periods when we were engaged in battle, the activity became frantic with the surgical team working flat out; wounded soldiers were treated first and then civilians [and lastly Japanese prisoners]. At other times, casualties tended to be brought in at a manageable rate.’\textsuperscript{18} A record of operations by 15 IMSU survives for the period of the ‘race to Rangoon’ and shows the wide variation in number of operations per day (Figure 8).\textsuperscript{19} When
the number of battle casualties was low, the units carried out other emergency procedures such as appendicectomies, circumcisions and dental extractions.

Figure 7: Inside the Fifth Indian Mobile Surgical Unit’s operating tent, Ngarzun, Burma, March 1945.

Figure 8: Daily operations by the Fifteenth Indian Mobile Surgical Unit during the ‘race to Rangoon’, 25 February to 27 May, 1945. Drawn from Wellcome Library GC/226/A5.
Singapore and Surabaya

The end of the war against the Japanese was a slow process with much bloody ‘mopping up’. Even after the Americans dropped atomic bombs on Hiroshima and Nagasaki on 6 and 9 August 1945, there were still large numbers of heavily armed Japanese soldiers in South-East Asia and fighting continued until the Japanese Army surrendered in September 1945. Harry’s unit rested and re-fitted in Singapore and Harry treated Allied former prisoners of the Japanese. He undertook inspection trips to prison camps for surrendered Japanese soldiers and members of the Indian National Army, who had fought with the Japanese, as well as a reconnaissance to Malaya where his unit expected to be posted.

Instead of going to Malaya, Harry went to Java and was part of the battle of Surabaya, where Allied troops supported Dutch forces against armed irregulars during the heavy fighting for Indonesian independence. The civilian casualties disgusted him and he wrote home with weary cynicism, that ‘It is quite simple, our method of “pacifying” a country – we merely blow the town to bits with bombs & shells & kill the inhabitants by thousands until they decide they have had enough.’ He had ‘200 odd Javanese civilians in here – legs blown off, arms missing, shot in the guts, head, everywhere – ranging from kids of 2 or 3 months to old men and women of 70 and 80.’ Presciently, he wrote that ‘we kill the Javanese, and the Javanese kill our lads and in the end it’s the Dutch who will take over the country, and Britain’s name will stink for years out here as the murderer of civilians.’

The National Health Service

Harry Walker returned to England in 1946 and was discharged from the Army in 1947. He gained some experience of peacetime anaesthesia in the military hospital at Catterick and spent six months of postgraduate study in the Section of Anaesthetics at the University of Edinburgh. This placement was part of a government scheme for doctors designed to ease the transition to civilian practice. He also spent a short time in general practice, much-needed experience after such highly focussed Army posts. He became a resident anaesthetist in the North Riding Infirmary in 1948 at the start of the new National Health Service, and a consultant to the Teesside group of
hospitals in 1949 (Figure 3b). Again, he had glowing testimonials in which the phrase ‘an excellent anaesthetist’ recurs again and again. Because of his knowledge and skill in the practice of all the most modern types of anaesthetics, there was a great demand for Dr Walker’s services in this area, where his abilities are now held in high regard by all his colleagues’ one reference says. ‘I have every confidence in him when he undertakes anaesthetics for me’ writes the senior surgeon. ‘He has the necessary disposition for an anaesthetist’ says another, without elaborating on the nature of this ‘disposition’, but other references include the phrases ‘interested and conscientious’, ‘very pleasant and stimulating colleague’, ‘most likeable personality’, ‘courteous and agreeable’, ‘full of enthusiasm for his work’, culminating in ‘in every way a first-class man.’

Harry was an active young consultant, chairing hospital committees and supporting the British Medical Association. He had a serious interest in his specialty and bought Barbara Duncum’s important history on its publication.20 He married and had three children, and rekindled his links with family and friends. He built a sailing dinghy and took a cottage in the North York moors. But he was not able to fulfil his potential, either professional or personal. He had only ten years as a consultant and died in 1959 at the age of forty of a myocardial infarction, one of the early casualties of smoking in the cohort studied by Doll and Hill.21

References

Early Intensive Care Units in England

Alfred Anthony Gilbertson MD FFARCS
Emeritus Consultant Anaesthetist, Royal Liverpool Hospital
Honorary Research Fellow, Institute of Translational Medicine,
University of Liverpool

Introduction

This study was conducted as a result of my reading in the publication by the Intensive Care Society of a notice of the 50th anniversary of the founding of the Society in June 1970. The notice included a note that ‘Four years after the first ever UK intensive care unit opening at St Thomas’ Hospital London. Dr Alan Gilson alongside colleagues identified the need for a specialist Society for intensive care.’ The Intensive Care Society was born in 1970; so, if that date was four years after St Thomas’s unit had opened, that unit must have been opened in 1966.

I have found little detailed literature about the founding of St Thomas’s Unit; however, the Obituary of Geoffrey Spencer confirmed that a year after he had been appointed Consultant anaesthetist at St Thomas’s he had founded the Intensive care unit in 1966.¹ But was this the first ICU in the UK?

The literature contains details of several Intensive Care Units (ICUs) which had opened before June 1966 (before St Thomas’s Unit). It is often difficult to determine when specialised units such as postoperative care or respiratory units became intensive care units but in several cases the care and facilities provided before 1966 were clearly recognisable as intensive care and intensive treatment or therapy.

Units offering early intensive care in England

The following are accounts of the earliest ICUs in England. In their paper ‘The first intensive care unit in the world: Copenhagen 1953, Berthelsen and Cronqvist had provided a definition of an Intensive Care Unit: they defined an intensive care unit “as a ward where physicians and nurses observe and
treat desperately ill patients 24 hours a day.\textsuperscript{2} The unit may serve patients from all branches of medicine”. The primary role is to restore and maintain the function of vital organs, enhancing the chance of survival. I have used these criteria to determine the time when respiratory or postoperative wards could be accepted as intensive care units; viz. the unit should be able to accept patients from all branches of medicine with the object of restoring the function of vital organs. To do this they needed a unit with specialised equipment, with doctors and particularly nurses capable of using it. Nurses in each shift needed to be taught to look after mechanical lung ventilators and general nursing care of very ill patients receiving intermittent positive pressure ventilation respiration (IPPR).

Many of the Units which I found in the literature started as small side wards with two or three beds which were kept available for patients needing special equipment for treatment of respiratory failure. This included lung ventilators, suction, piped oxygen and electric supply points. Ideally a laboratory for the measurement of “blood gases” (pCO\textsubscript{2}, pO\textsubscript{2}, pH and plasma bicarbonate) and rapid access to serum electrolytes, haematology etc. should also be available.

\textbf{Radcliffe Infirmary, (1953)}

A paper by Crampton Smith, Spalding and Ritchie Russell describes how they had treated patients with combined bulbo-spinal paralysis by artificial respiration. They describe how four patients were treated in a small Respiratory Unit established in Oxford to deal with cases of respiratory insufficiency.\textsuperscript{3} The first of them was transferred to the unit on 17th August 1953. She was found to be suffering from acute toxic polyneuritis and had complete paralysis of all voluntary muscles throughout her body and had only external ocular movements. She was treated by IPP ventilation of her lungs through a tracheostomy tube for four weeks and she was discharged on November 18th fully recovered except for some diminution of her tendon reflexes. A second patient died with ‘hopeless’ damage to her lungs due to inhalation of vomit. The third and fourth patients made complete recoveries.

Table 1 illustrates the cases treated in 10 years after the Respiratory Unit opened. One-third of the patients were suffering from poliomyelitis but in the remaining two thirds the respiratory failure was caused by a wide range
of diseases, and an admirable proportion were saved from what would have previously been inevitable death.

Table 1. Results of treatment at the Respiration Unit at Oxford from 1953 -1963

<table>
<thead>
<tr>
<th>Disease</th>
<th>Number Treated</th>
<th>Dead</th>
<th>Alive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poliomyelitis</td>
<td>57</td>
<td>10</td>
<td>47</td>
</tr>
<tr>
<td>Polyneuritis</td>
<td>20</td>
<td>2</td>
<td>18</td>
</tr>
<tr>
<td>Tetanus</td>
<td>16</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Chest injuries</td>
<td>14</td>
<td>4</td>
<td>10</td>
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<td>Barbiturate poisoning</td>
<td>6</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Myasthenia gravis</td>
<td>7</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Cervical cord lesions (Trauma 3, tumour 1, myelitis 1)</td>
<td>5</td>
<td>1 (Myelitis)</td>
<td>4</td>
</tr>
<tr>
<td>Pulmonary disease</td>
<td>6</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>After chest surgery (carcinoma 3, tuberculosis 1)</td>
<td>4</td>
<td>3</td>
<td>1 (tuberculosis)</td>
</tr>
<tr>
<td>Polymyositis</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Porphyria</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Status epilepticus</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Head injury, encephalitis etc</td>
<td>13</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>153</strong></td>
<td><strong>48</strong></td>
<td><strong>105</strong></td>
</tr>
</tbody>
</table>

This 1954 publication described the reasons why a specialised Intensive Care Unit is justified for the treatment of the sort of patients described in their article. Patients with paralysis causing respiratory embarrassment are critically ill but as illustrated in their paper, if they survive, even those with both bulbar and spinal involvement may make an excellent recovery. Their treatment poses many problems and requires specialist treatment which is best carried out in a special unit whose doctors and importantly nurses, are experienced in treating these types of cases. A considerable staff of doctors and nurses is
required to give adequate treatment in the acute stage so that a unit that is to treat such cases is most conveniently situated in a large hospital which can support the required resources. Moreover, it is in large hospitals that the ancillary services required are available.

Oxford did not acquire a purpose-built Intensive Therapy Unit (ITU) until an 8-bedded ITU was opened in the Radcliffe Infirmary in April 1972. However, the management of respiratory failure was obviously intensive care, and the research into the physiology of artificial respiration in the Respiratory Unit contributed greatly to the management of the intensive care of respiratory failure.⁴

**Ham Green Hospital, Bristol (1957)**

Ham Green was an infectious diseases hospital with Dr James Macrae as its Medical Superintendent from 1948 to 1976. His remarkable range of ability is recorded in his obituary published in the British Medical Journal.⁵ After qualifying from Glasgow University in 1934 he held junior hospital posts in practically every medical and surgical specialty. In 1969 he wrote a Memorandum on Infection which starts by describing the treatment of poliomyelitis in Ham Green.⁶ (*This memorandum by Dr James Macrae was circulated locally in 1969, but was never formally published. A copy is kept in the stack room of Bristol University Medical Library*)

‘For 12 years after 1947 they treated about 1500 cases of acute anterior poliomyelitis demonstrating various degrees of paralysis. Initially these patients were treated in isolation wards which catered for many patients with other diseases.

*Even before the advent of IPPV in 1953, it was becoming painfully obvious that severe cases of polio required separate accommodation. But it was not until the 15th of August 1957 that a ward with special rooms and facilities became available.*

*Macrae wrote ‘Without knowing it, we had evolved an intensive care unit and the transformation was extraordinary. This was*
especially evident among the nurses who were able to concentrate on their duties to individual patients each with individual problems. Quite suddenly the whole business of artificial respiration took on a calmness never experienced in a mixed ward.’

Some data from Ham Green Hospital in Bristol is shown in Table 2. This table from the James Macrae’s memorandum on infection in 1969 describes the activities in two periods; the year before the special ward was opened and the first year of the special ward. Survival rates in the patients in the different causative groups were better in the patients treated in the ICU. Seventy six per cent of patients in the ICU recovered compared to only 44% in the ordinary ward.

Table 2. Data from Ham Green Hospital, Bristol.6
Outcome of patients treated in the 12 months before the special unit opened on 15th August 1957 (‘WARD’) and in the first 12 months of the special unit (‘ICU’, shown in bold). The recovery rate in the ICU was 76%; in the Ward it had been 44%. These patients were all treated for respiratory failure but by 1962 the Respiratory Unit was providing management of renal failure by dialysis.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of patients</th>
<th>Tracheostomy</th>
<th>Artificial respiration</th>
<th>Recovered</th>
<th>Died</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ward</td>
<td>ICU</td>
<td>Ward</td>
<td>ICU</td>
<td>Ward</td>
</tr>
<tr>
<td>Polio</td>
<td>17</td>
<td>15</td>
<td>13</td>
<td>11</td>
<td>17</td>
</tr>
<tr>
<td>Infective polyneuritis</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Cor pulmonale</td>
<td>0</td>
<td>2</td>
<td>_</td>
<td>2</td>
<td>_</td>
</tr>
<tr>
<td>Tetanus</td>
<td>0</td>
<td>4</td>
<td>_</td>
<td>4</td>
<td>_</td>
</tr>
<tr>
<td>Totals</td>
<td>18</td>
<td>25</td>
<td>14</td>
<td>21</td>
<td>18</td>
</tr>
</tbody>
</table>

This was probably the first ICU opened in Britain
Southampton General Hospital (1958)

Douglas J Pearce (1926-2018) was a consultant anaesthetist in Southampton General Hospital. He told me how the Respiratory Unit evolved there (Pearce D J, personal communication, 2009).

“Dr Patrick Shackleton (1904-1977) was the consultant in charge of anaesthesia. He had treated a patient for tetanus in 1953 and that really started it. In 1958 we planned a side ward in a medical ward. It was only a ward. It had three beds in it. We had to get the equipment and some oxygen. We had a Radcliffe Respirator, a Blease Pulmofoator, a Parkinson Cowan gas meter, and a humidifier. We didn’t have any blood gas sampling in those days. We were about to open and then in August a young boy was brought over from Guernsey with a shot gun injury with the most severe tetanus I have ever seen in my life. This boy came in, there was no formal opening of the unit, we were in business, and that’s how we started. The neurologists caught on to this and you got things like Guillain Barré Syndrome, strokes, and of course barbiturate poisoning in those days was quite a major thing. All these things tended to creep in, and then occasionally one or two severe post-operative things. Such was the demand for this small bed space that after the first eighteen months (in 1959-60) the Respiratory Unit was enlarged to a total of five beds. This brought all the advantages of a typical ICU at that time.7

Kettering. (Planned 1960, set up 1962)8,9

Kettering General Hospital Northamptonshire, was at the time of the establishment of its Intensive Care Unit a small hospital (180 beds). The Unit had only 4 beds but it satisfied every criterion for recognition as an Intensive Care Unit. The range of vital system failures treated is extraordinarily complete, the treatment includes haemodialysis, artificial pulmonary ventilation, and continuous ECG monitoring. The necessity of
one staff nurse for every patient was recognised. There was a bed for a
doctor when one needed to be continuously available.

**Leeds General Infirmary (1964)**

The unit in Leeds General Infirmary started as a unit for treating tetanus. Although a dedicated ICU was not opened until 1964 the Tetanus Unit was apparently treating a wide range of patients several years earlier. Professor John Norman (personal communication 2020) has described his experience when he was a medical student in the 1950s. Tetanus patients were paralysed by a continuous intravenous infusion of the short acting relaxant succinylcholine (suxamethonium) and the lungs were ventilated by relays of students as in the 1952-3 polio epidemic in Copenhagen.\(^{10}\)

In 1961 when John Norman was a senior house officer in anaesthetics and in the following year when he was a registrar, the tetanus unit existed in the amenity ward of the hospital, which was one ward of the private wing. There were a number of single rooms and two four-bedded rooms which could be taken over for anyone needing artificial ventilation. By this time (1961) their experience of treating tetanus had enabled them to offer IPPR to patients with myasthenia gravis, crushed chest, epilepsy and barbiturate poisoning. About this time the total paralysis regime (TPR) had become standard and the relaxant was curare. In 1964 a dedicated Intensive Care Unit was created in an old Nightingale ward. The consultant team was four specialists: two anaesthetists, a neurologist and an Accident and Emergency surgeon. The nursing staff was led by a sister with two or three staff nurses. Each patient was under the care of three student nurses each doing an eight-hour shift with the next 24 hours off until the patient was breathing spontaneously safely. A paralysed patient was *never* left alone – there always had to be one nurse for every patient.

**Liverpool**

Three units in the Liverpool Region were opened before 1966. They were at a) Alder Hey Children’s Hospital, b) Broadgreen District Hospital Cardiothoracic Surgical Unit and c) Whiston General Hospital. All of them have been described in comprehensive publications.
Alder Hey Children’s Hospital (1964)

An Intensive Therapy Unit was opened in Alder hey Children’s Hospital in Liverpool on 1st September 1964 to deal with acute emergencies arising within the hospital or admitted from without, but excluding surgical conditions. A leading article in the British Medical Journal stated that the Alder Hey Unit was said to be the first unit in a paediatric hospital.

Broadgreen Hospital (1964)

Broadgreen Hospital included the Mersey Regional Cardiothoracic Surgical Unit. The intensive care unit started in 1960 as a post thoracic surgical unit, with many patients receiving IPPR for a few days after surgery. The hospital immediately accepted any patient (including some from hospitals as far away as North Wales) needing treatment of respiratory or cardiovascular failure. Following four years of experience gained from the use of two side wards attached to the cardiothoracic surgical ward, a purpose built ICU was built – the first such building in this country. This unit and its successor are described in detail in a paper by the Senior Sister and two consultant anaesthetists. I was a senior anaesthetic registrar in the Cardiovascular Surgical Unit in 1964-5 and a large part of my work was in the ICU. The unit was not simply a post-surgical unit – it was a general ICU from its start in 1960. Its work was treatment of cardiovascular or respiratory failure and the treatment of whatever was the cause of these failures.

Whiston Hospital, Merseyside (1964)

This hospital achieved an early intensive care unit mainly from the energy of Dr Eric Sherwood Jones, inspired by Sister Anne White. He had heard her deliver a lecture in the early sixties on progressive patient care. It inspired him to arrange for four beds to be allocated for such care for a trial period. The experiment was successful and in 1964 a single storey ward was gutted and converted by hospital staff into an eight bedded ICU. The evolution of the Unit from 1962-1983 is described in detail and its opening by Dr Denis Melrose was
recorded in a special article in the Lancet in March 1964.\textsuperscript{14,15} The unit dealt with a wide range of conditions including major trauma, self-poisoning, severe acute asthma, acute myocardial infarction and acute renal failure, each with its own admission policy.

The object of this paper has been to investigate if the St Thomas’s intensive care unit was the first in the United Kingdom and I have found several earlier units which have provide evidence that this is not so. Part of the reason for the belief by St Thomas’s ICU staff that St Thomas’s ICU was the first in the United Kingdom is that several of the earlier ones did not publish papers about the foundation and evolution of their units until the unit was already several years old. I think that the Unit at St Thomas’ Hospital should still be highly regarded as one of the first units in the country.

References


Introduction

Alcohol and humanity’s relationship has been interwoven throughout history and alcohol has played an influential role in several ways. Its importance has been mentioned in the Christian Bible, on Egyptian medical papyri and clay tablet prescriptions of Sumerian physicians.1 In ancient Egypt, beer and bread acted as currency for the builders of the pyramids and rum played an important role in the triangular trade between New England, Africa and Europe1, 2. Disagreements in this triangular trade would act as kindling for the 1775 American Revolution.2 Alcohol has played a momentous role within the scientific and medical community as well.

French biologist, microbiologist and chemist Louis Pasteur (1822-1895) was asked to investigate the cause for the souring of a local farmer’s beetroot alcohol. He found that lactic acid produced by microscopic fermenting yeast cells was the cause. His extended studies would show that heating substances containing these felonious microorganisms would result in the sterilisation of the product leading to what is known as ‘Pasteurisation’. As his studies progressed, he linked these microorganisms to disease and produced his Germ Theory.3 Anaesthesia was not exempt from these alcoholic influences.

Carlsberg don’t make blood gas analysers, but if they did…

The polio epidemic of 1952 had a profound impact in Copenhagen, Denmark where over 300 people required artificial ventilation. This ventilatory effort

1 “Based on the prizewinning essay for the Association of Anaesthetists 2021 Thomas Boulton History Prize, and published in part in Anaesthesia News 2021; Issue 412; 13-14”.

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was led by Dr Bjørn Ibsen (1915-2007), the father of intensive care, who was the first to suggest the use of positive pressure ventilation in overcoming the effects of respiratory paralysis. At its peak, Ibsen utilised about 450 medical and dental students to hand ventilate the patients. To guide this ventilation, Ibsen needed accurate readings of the patient’s pH, pCO2 and pO2. The development of the instruments to measure those clinical parameters began in Copenhagen with the beer brewing giant Carlsberg where the technology of blood gas analysis evolved.4

Søren Sørensen (1868-1939) was a chemist who worked for the Carlsberg Laboratory aiming to apply biochemical knowledge to the brewing industry. He developed the pH scale in 1909, a novel way of visualising hydrogen ion concentration in solution.5 His assistant, Gotfred Haugaard (1894-1969), approached technology company Radiometer A/S in 1937 asking them for help in developing an electric pH meter.6 When completed it was one of the first commercially available pH meters.6 During the polio epidemic doctors used this Carlsberg inspired pH meter and the time-consuming method of Van Slyke pCO2 analysis when treating patients.7 A more rapid analysis was required.

Richard Stow, an Ohioan physician, was also caring for polio patients and had developed his own pCO2 electrode based on the pH electrode.7 His instrument was unreliable and inaccurate. John Severinghaus (1922-2021) offered his help by stabilising the electrode in a sodium bicarbonate bath which not only improved the accuracy but allowed rapid analysis. Severinghaus worked alongside his long-term technician, Freeman Bradley, to establish the first three function blood gas analyser in 1959.7, 8 They combined the pH meter, the improved pCO2 electrode and Leyland Clarke’s (1918-2005) pO2 electrode. These devices revolutionised clinical care and were produced in California, Massachusetts and Copenhagen by Radiometer, the company who supplied the original pH meter to Ibsen in 1952.7, 8

**From the bubbling of beer – Nitrous oxide**

Joseph Priestley (1733-1804), a theologian, philosopher and chemist, would discover and describe numerous “airs” including oxygen and nitrous oxide.9 In 1767, whilst living in Leeds, a brewery near his home would spark a lifelong affair with “airs” and provide a bountiful supply of fermenting gas
for Priestley. He experimented with the released gas, combining it with water and created the process of carbonation. He published “Impregnating Water with Fixed Air” in 1772.\textsuperscript{10} He furthered these experiments on “airs” in 1774 by heating mercuric oxide with a burning lens and produced, characterised and identified oxygen, nitrous oxide, sulphur dioxide and other gases.\textsuperscript{11}

At 19 years old Humphry Davy (1778-1829) was appointed superintendent of the Pneumatic Institute in Bristol – a society interested in the medical potential of gases. Davy began to self-experiment with Priestley’s nitrous oxide amongst friends and colleagues at events that he termed “laughing gas” parties. The medicinal benefits of nitrous oxide were briefly mentioned in his 1800 publication “Researches, Chemical and Philosophical, chiefly concerning Nitrous Oxide, or Dephlogisticated Nitrous Air, and its Respiration”. Although there was no medicinal application by Davy, the popularised gas would find its way to future anaesthetic application with dentist Horace Wells (1815-1848).\textsuperscript{12,13}

It is unclear when Horace Wells was initially exposed to nitrous oxide. Wells may have first seen nitrous oxide used after attending a demonstration by Dr Gardner Colton in which Wells witnessed a friend, Sam Cooley, inhale nitrous oxide and injure his leg without experiencing pain.\textsuperscript{14} Recent letters between Wells and his wife suggest that he may have encountered and used nitrous oxide prior to Colton’s visit.\textsuperscript{15} After Colton’s demonstration, Wells invited him to his surgery and after Colton provided nitrous oxide to Wells, his colleague John Riggs painlessly extracted a molar.\textsuperscript{14} Enamoured with this experience, Wells perfected his craft and would hold his first public demonstration in 1845 in Boston. However, Wells provided his anaesthesia with unfamiliar equipment and likely provided a subtherapeutic dose. The patient let out a shriek of pain and Wells left the operating theatre ashamed and surrounded by jeers.\textsuperscript{14} The use of nitrous oxide was largely abandoned until the 1870s were it saw its revival in dental anaesthesia and obstetric analgesia in the 1930s.\textsuperscript{12}

A controversial cocktail – Ether

In 1540 Valerius Cordus, a German physician and botanist, described how to produce his “Sweet Oil of Vitriol” or ether. This was made by combining
sulphuric acid and wine and its preparation is comparable to a modern cocktail recipe:

"Take six ounces of strong, very biting, thrice purified wine, and the same quantity of sour oil of vitriol. Mix in a Venetian glass, and place in a small gourd with a narrow mouth, and seal the mouth with clay. Set aside thus for a whole month, or two." 16

Centuries later Michael Faraday (1791-1867) drew comparison to the intoxicating effects of ether and nitrous oxide. Similar to nitrous oxide, ether would be used and abused in "ether frolics", proving popular in the United States and set the scene for early ether enthusiasts.17 Whilst the first use of ether as an anaesthetic is classically attributed to William Morton (1819-1868), there were others in the United States that had used it before him.

William Clarke (1819-1898), a keen recreational user of ether, would be the first to use ether anaesthesia whilst a student at Vermont Medical College. He was able to successfully apply the anaesthetic to a young lady in Rochester, New York for a painless dental extraction but his sceptical Professor convinced Clarke that it was her hysterical state and not the ether that caused her unconsciousness. Clarke abandoned any further use.18 Crawford Long (1815-1878), a rural Georgian practitioner, was next to use ether anaesthesia. In 1842 he painlessly removed two small tumours from the neck of a patient. He continued this method on several patients but didn’t publish his results until 1849, a few years after Morton’s demonstration.18

Morton, a man of confidence, was responsible for the popularisation of ether anaesthesia. Morton had in fact been a student of the previously disgraced Wells and entered business with him in Boston where they both met Charles Jackson (1805-1880). Following the end of their short business venture, Morton remained in Boston and acted on Jackson’s advice to practice and hone his technique of ether administration. It was on 16th October 1846 that Morton would publicly demonstrate his technique on Gilbert Abbott who was able to have a tumour removed from his jaw without pain or distress as highlighted recently a hundred years after the event.19,20

The news of Morton’s discovery travelled fast but there were many who weren’t happy with the newly celebrated discoverer. Morton’s previous
colleagues and teachers, Wells and Jackson, as well as Georgian practitioner Crawford Long, disputed Morton’s claim. Morton sought monetary gain from his “discovery” but found little financial gain and instead received praise, medals and even an honorary MD from Baltimore.¹⁹ The fate of these other claimants wasn’t as glorious. Wells travelled to France and successfully gained French recognition for his contribution but on his return to the United States his life took a downward spiral as he became addicted to chloroform and ether. He ended his own life following his arrest for throwing sulphuric acid over two women.²¹ Jackson took his dispute to the courts and the Congress, but the ensuing 1860s civil war saw little attention given to the dispute. Years later, whilst visiting a Massachusetts cemetery, Jackson overheard that the discoverer of anaesthesia, Morton, was buried there. This sent Jackson into a neuropsychiatric disability that he would never recover from, and he died in the McLean Institute of the Insane in Massachusetts.²¹ Long was the least affected, having devoted little time to the controversy, and would return to his local practice. He died of a stroke in 1878 shortly after providing ether anaesthesia to a labouring woman.²¹

**Guthrie’s Sweet whiskey – Chloroform**

Chloroform was simultaneously and independently synthesised in 1831 in America, France and Germany by Samuel Guthrie (1782-1848), Eugène Soubeirain (1797-1859) and Justus von Liebig (1803-1873) respectively. Synthesis involved the addition of alcohol to a form of chloride and Guthrie would use whiskey and chloride of lime for a recipe known as “Guthrie’s Sweet Whiskey”²²:

> “Into a clean copper still, put three pounds of chloride of lime and two gallons of well flavoured alcohol of sp. Gr. .844 and distil. Watch the process and when the product ceases to come highly sweet and aromatic, remove and cork it up closely in glass vessels”.

²²

It wouldn’t however be until 1847 that chloroform would be availed of as an anaesthetic agent by Dr James Young Simpson (1811-1870). Simpson was a gifted man, having specialised in obstetrics and becoming Professor of midwifery in 1840 at the age of 28.²³ Simpson was inspired to use ether anaesthesia after observing Robert Liston utilise ether during surgery.
Against religious and medical doctrine of his era, Simpson successfully applied ether anaesthesia to a labouring woman. However, he noted the limitations of ether – slow onset, large dosage requirements and copious respiratory secretions. He needed a superior anaesthetic and he would find his solution with Guthrie’s Sweet Whiskey.\textsuperscript{23,24}

Simpson’s search took place not at the laboratory benchside but at the dinner table with his colleagues. Eve Simpson, his daughter, described how her father would hold regular “anaesthetic séances” with colleagues who he invited for dinner.\textsuperscript{25} It was the fateful evening of 4\textsuperscript{th} November 1847, after several unsuccessful brews were trialled, that Simpson presented his colleagues with chloroform from a brandy decanter hidden under heaps of wastepaper. As their tumblers were filled, the liquid’s vapours were deeply inhaled and each man fell into a deep sleep and awoke on the floor “under the mahogany”.\textsuperscript{25} It was clear to Simpson that he had found his answer and only four days later he successfully applied his findings. By 20\textsuperscript{th} November he had published his results. Simpson’s main interests lay in obstetrics but it would be John Snow (1813-1858) who would bring a scientific and quantitative approach to anaesthetics and become the true first anaesthetic specialist providing anaesthesia for more than 5000 procedures in 12 years.\textsuperscript{26}

\textbf{If it’s good enough for the Pope – Cocaine}

The coca leaf had been used for thousands of years by the Incan people, long before Western culture was acquainted with the plant.\textsuperscript{27} The use by the Andeans was for two reasons; first, as a status symbol for the societal elite, and secondly as a medicine used for its stimulant and analgesic properties when chewed or placed in tea.\textsuperscript{27} Western scientists observed the effects of the leaves, and a desire grew to extract the active compound and refine it following the Spanish arrival in South America in the 16\textsuperscript{th} Century.\textsuperscript{27}

By using ethanol as an extraction solvent, the active tropane alkaloid can be successfully separated from the raw coca leaves. Friedrich Gaedcke (1828-1890) first isolated the compound in 1855, terming it “erythroxyline” but it was Albert Niemann (1834-1861) who was able to properly purify the compound. In 1860 he published the dissertation “\textit{Über eine neue organische Base in den Cocablättern}” and called the substance “cocaine”.\textsuperscript{27,28} However, there was very little interest in the anaesthetic
application of cocaine following its isolation until the discovery of its anaesthetic properties by Karl Koller. Its main use was as a stimulant, especially in the form of a popular tincture – Coca wine.

Angelo Mariani (1838-1914) was the world’s first cocaine millionaire, a Corsican from a long line of chemists and doctors. He was a habitual user of the coca leaf and an adamant proponent of its medicinal benefits. He found that the most bitter leaves were also the most potent, and in an attempt to make them more palatable, he soaked them in Bordeaux wine. This process not only improved the taste but, in a similar fashion to Niemann, would further the ethanol extraction and create an even more potent elixir. He termed it “Vin Mariani”, and thanks to a novel and hugely successful advertising campaign, was able to receive endorsements from celebrities including Queen Victoria, Thomas Edison and even Pope Leo XIII. He received over 8000 physician endorsements, including from a young Vienna graduate, Dr Sigmund Freud (1856-1939).27,29

Freud was also a proponent of the use of cocaine to cure many ailments including fatigue, headache and opium addiction. He had in fact self-experimented with cocaine to treat his own opium addiction. He published his recommendation for cocaine’s medicinal application in “Über Coca” in 1884.30 During his experimentation, he noted the “numbing” effect on his tongue but didn’t utilise this and instead suggested its use to his friend and colleague Karl Koller (1857-1944). After self and animal experimentation, Koller used cocaine anaesthesia on 11th September 1884 to surgically treat a patient’s glaucoma. He presented his results to the Vienna Medical Society in October 1884 where it was received enthusiastically. Its significance was instantly recognised and by late 1885 there were over 60 publications from North America about local anaesthesia and cocaine.28

**Conclusion**

Alcohol has played a pivotal role in the development and advancement of modern medicine and anaesthesia. The discoveries found helped to provide deep sedation and unconsciousness that allowed for patients to have pain free procedures and for surgeons and dentists to developed advanced techniques.
And so, we have the ABCs of anaesthetic history – Alcohol, Beer and Cocktails. The alcohol-based solvents which allowed for the extraction of the active compound in the coca leaf and the alcohol in the wine that allowed for the creation of Vin Mariani that helped to popularise cocaine. The fermenting beer of a Leeds Brewery would inspire Priestley to pursue a lifelong curiosity of airs, discovering oxygen and nitrous oxide. The beer brewing giant, Carlsberg, with a keen interest in the biochemical process, helped in the development of the pH meter and subsequent development of the blood gas analyser. Finally, the cocktails of the controversial *Sweet Oil of Vitriol* and *Guthrie’s Sweet Whiskey* saw the advent of inhalation anaesthesia and changed the world of medicine forever.

References


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The Beginning: Cocaine

The shrub known as *Erythroxylum coca* is native to South America and contains the alkaloid cocaine within its leaves. The indigenous population were aware that chewing coca leaves enhanced physical strength, improved mental alertness and diminished hunger. The first explorers arrived in South America in 1492, and yet the first reliable account of coca leaves being chewed by the local population did not come until 1539, in a letter to Emperor Charles V from Friar Vincente de Valverde (cited by Calatayud and González). Despite the widespread practice of chewing coca leaves across South America, the propensity of the plant to induce numbness of the lips was not documented until 1653, when a Spanish priest, Father Bernabe Cobo, recounted its utility in alleviating toothache in his publication ‘Historia del Nuevo Mundo’.

“And this happened to me once, that I repaired to a barber to have a tooth pulled, that had worked loose and ached, and the barber told me how he would be sorry to pull it because it was sound and healthy. A monk friend of mine who happened to be there and overhearing, advise me to chew for a few days on coca leaf. As I did, indeed, soon to find my toothache gone.” Cobo

In 1848 the obstetrician James Young Simpson coined the phrase ‘local anaesthesia’ two years after the word ‘anaesthesia’ had been used to describe etherisation by Oliver Wendall Holmes. Simpson’s paper described a series of unsuccessful attempts to induce local anaesthesia by topical application of

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2 Parts of this article have appeared in the *British Society of Orthoapaedic Anaesthetists Spring (BSOA) Newsletter* 2021 and are being reproduced here with the permission of the Editor of BSOA newsletter.
chloroform.³ Although Simpson did not identify a local anaesthetic agent, he was able to describe the proposed benefits of local over general anaesthesia comprehensively. The principles that Simpson outlined remain valid today and represent a truly remarkable scientific leap for the time.

1845 saw the design of the hollow needle by Francis Rynd, which was first used to inject morphine into the trigeminal nerve for neuralgia.⁴ The combination of Rynd’s needle and the Charles Pravas’ metal syringe was revolutionary, providing the first practical solution for injecting drugs into deep anatomical structures. The combined apparatus was first used by Alexander Wood to inject narcotics in 1855.⁵ The use of the syringe and needle soon expanded beyond narcotics and provided the basic equipment required for the inception of regional anaesthesia.

Albert Niemann successfully isolated an alkaloid extract from coca leaves in 1860 and named it cocaine.⁶ Niemann even described the numbing effect of cocaine on the lips at this time, but perhaps being laboratory based, did not see the potential clinical application.⁷ Niemann died shortly after isolating cocaine, but his work was continued by Wilhelm Lossen who determined its molecular structure in 1865.²

Mantegazza was an Italian neurologist who was working on isolation of cocaine at the same time as Niemann. He is mainly known for describing the psychological effects of cocaine, following a series of experiments on himself, that sadly left him afflicted with addiction.²

“I sneered at the poor mortals condemned to live in this valley of tears while I, carried on the wings of two leaves of coca, went flying through the spaces of 77,438 words, each more splendid than the one before.” Mantegazza²

French entrepreneur, Angelo Mariani saw the marketing potential of cocaine after reading Mantegazza’s paper and decided to grow his own coca leaf, macerate it with red wine and sell it as a health tonic to the masses. His product ‘Vin Mariani’ became a favourite of Pope Leo XIII (1878-1903) who awarded it a papal gold medal.⁸
The success of ‘Vin Mariani’ was heard across the Atlantic, where the American biochemist John Pemberton was inspired to produce a similar product. Prohibition laws in North America prevented the use of wine in the preparation, so Pemberton settled on a formulation of carbonated water, syrup and extract from the caffeine-rich kola nut to flavour the drink. In 1886, the drink known as Coca-Cola was launched and it was not until the Pure Food and Drug Act of 1906 that cocaine was removed from its formulation.

Carl Koller (Figure 1) was a budding ophthalmologist at Vienna General Hospital who was familiar with the particular challenges involved with anaesthesia for ophthalmic surgery. Anaesthetic facemasks interfered with the surgical field. Chloroform anaesthesia rendered patients incapable of cooperation with the surgeon and increased bleeding by engorging the ocular vasculature. The lack of fine suture material available for closing ocular incisions at the time, meant that the corneal wound was left unstitched at the end of surgery. The high incidence of postoperative vomiting associated with ether and chloroform, increased the risk of extrusion of globe contents during retching. The culmination of these risks forced many surgeons to choose patient discomfort over general anaesthesia.9

Figure 1 Karl Koller (Public domain image)
As a medical student, Koller had attempted to find an agent that would induce local anaesthesia, without success. It was only when he joined the research team of Sigmund Freud years later and was given a sample of cocaine that the long-awaited *Eureka!* moment for local anaesthesia history arrived. The envelope containing the sample leaked a little and Koller absent-mindedly touched his finger to his lips, noting that they became numb. In that moment, Koller was able to unlock cocaine’s potential, because he possessed the motivation and clinical experience that his predecessors had lacked.9

Koller applied the cocaine solution to the eyes of frogs and found that he was able to touch the cornea with no sign of distress. He and a colleague subsequently applied cocaine to their own eyes, resulting in both insensate corneas and great excitement. In 1884, Koller performed the first ophthalmic operation under local anaesthesia on a patient with glaucoma. The technique was demonstrated at a conference in Heidelberg and published in English shortly afterward, rocketing Koller to scientific stardom.2

**Development of Cocaine**

Cocaine instantly revolutionised eye, nose and oral surgery. The following period in history saw a flurry of experimentation to expand the use of cocaine by the pioneers of the age. On hearing of Koller’s work, the American surgeon William Halsted began a series of experiments to demonstrate that practically every peripheral nerve in the body could be injected with cocaine and render its area of innervation temporarily insensate to facilitate surgery.10 The description of the first brachial plexus block involved cocaine infiltration to the overlying skin and subcutaneous tissues, exposing the plexus and then injecting a small amount of cocaine directly into the nerve (likely to be upper trunk). An excellent block was reported with no subsequent nerve injury despite apparent intraneural injection.2

Sadly, Halsted produced only one publication on the topic, as he and his colleagues fell foul of cocaine addiction. Halsted was unable to continue in his clinical role as a surgeon due to addiction and all but one of his colleagues died of addiction-related complications.10
Early Neuraxial Blocks

The American doctor James Leonard Corning was the first to administer spinal anaesthesia in New York in 1885. He described injecting cocaine solution between two inferior dorsal vertebrae of a dog. He noted that the dog exhibited incoordination and weakness in its hind quarters within 5 min, which resolved within 4 hours. He attempted to replicate the procedure in a human subject for the treatment of spinal weakness, seminal incontinence and addiction to masturbation. Corning injected cocaine solution into the T11/12 space. As no effect was noted in 6-8 min, the injection was repeated. There was no motor block but the legs were ‘sleepy’ in another ten minutes. The patient’s response to pin-prick and electric current was impaired in the legs, genitalia and the lumbar region. The patient had headache and vertigo next morning, suffering from what we now know as post-dural puncture headache, indicating that the dura had probably been punctured.

Heinrich Quincke was a German physician whose particular research interest was cerebrospinal fluid (CSF). He performed lumbar punctures in late 19th century and removed CSF in an effort to treat diseases such as tuberculosis, meningitis, and cerebral tumours, with little success. The bevel point needle used for these lumbar punctures became known as the “Quincke needle”. Quincke worked in the same laboratory as the surgeon August Bier who went on to utilise the Quincke needle for his role in the development of spinal anaesthesia.

August Bier performed the first spinal anaesthetic on a human in 1898, which was reported as part of a six-patient case series. (The appendix of this paper contains the English translation of the original Bier publication). The landmark patient was a 34-year-old labourer who required resection of a tuberculous ankle joint. Following his initial success, Bier decided to further experiment on himself. There are obvious practical difficulties in administering a spinal anaesthetic to oneself, so Bier recruited his colleague August Hildebrandt to assist him. The injection was generally without any pain except for when the needle pierced the dura. Unfortunately, the syringe did not connect properly to the needle and a large amount of cerebrospinal fluid leaked out along with the cocaine and no clinical effect was produced.
Bier subsequently managed a successful injection of the cocaine solution into Hildebrandt. Bier has described the time sequence of the loss of various sensations in great detail in his original article.\textsuperscript{14} Bier performed a rigorous set of tests on Hildebrandt to check block adequacy including pinching the skin, hitting the legs with a hammer, extinguishing a cigar on the skin, ripping out pubic hair followed by firm traction to the testicles... methods certainly that would be frowned upon in modern times. Although they celebrated that evening with lashings of wine, the severe headaches the following day were understood by Bier to be primarily a result of the CSF loss during the procedure. Both Hildebrandt and Bier had quite a few side effects and both did not feel well for several days.

Details of the technique were published the same year and met with rapturous enthusiasm and the technique was swiftly and widely adopted. However Bier was aware of the side effects and Whitacre and Dimitru have highlighted this in their description of the development of anaesthesia in Germany at the beginning of the last century.\textsuperscript{15}

**Improving Safety**

The rapid rise in the clinical use of spinal anaesthesia with cocaine inevitably led to complications. In 1901 a report of 15 deaths associated with the technique was published alongside other reports of effects including respiratory arrest and severe hypotension.\textsuperscript{16} Thereafter began a multifaceted approach to improving safety. One such measure was the work of Arthur Barker, a British surgeon and early champion of sterile technique. His 1907 paper describes the sterile precautions that he took when performing over 100 spinal anaesthetics.\textsuperscript{17} Barker scrubbed the skin with a brush and hot soapy water, applied antimicrobial compresses and washed them away with saline. This reduced the risk of meningitis and local infection.

Cocaine was well known to have toxic effects which limited its use. In 1894, Schleich demonstrated the technique of injecting wheals of dilute cocaine (as little as 0.01%), first starting with the skin incision, creating a continuous line of wheals and then once the incision is made, injecting further aliquots of cocaine throughout the dissection (Fig 2).\textsuperscript{18} Previously 5-20% solutions were routinely used, which explains why toxic effects were commonplace.
Using the minimum possible dose of a drug remains a key principle in modern times.

Figure 2 The Schleich method of local anaesthesia using dilute cocaine solution

In 1903 Heinrich Braun elegantly illustrated that the toxicity of cocaine was directly proportional to its rate of absorption, and therefore any means of inhibiting absorption of the drug should increase the margin of safety. This can be achieved by the use of a physical tourniquet, such as the commonly employed Esmarch bandage, to directly reduce the blood flow. And can also be achieved through the use of a “chemical tourniquet,” such as adrenaline, which reduces blood flow by causing vasoconstriction. The chemical tourniquet has the added benefit of utility beyond extremity surgery.

Harvey Cushing introduced blood pressure monitoring into the operating theatre in 1903. This is now included in the minimum standards of monitoring recommended by the Association of Anaesthetists of Great Britain and Ireland (AAGBI). However, in 1903, the physiology behind hypotension under spinal anaesthesia was not understood, and therefore monitoring did very little to improve its management initially. It was not until 1915 after Porter and Smith explained the effects of sympathetic nerve blockade under spinal anaesthesia that the consequent hypotension was appropriately managed.

Probably the best solution for avoiding cocaine toxicity was to invent another, less toxic agent. While Lossen determined its molecular formula in 1860s, it was Willstätter and Müller in 1898 who derived the structure of
cocaína que proporcionó la base necesaria para desarrollar nuevos agentes.\textsuperscript{22} En 1905, el químico Alfred Einhorn aisló procaina y encontró que era superior en perfil de efectos secundarios comparado con la cocaína.迅速 became the most popular local anaesthetic agent in use, and yet the high incidence of severe allergic reactions associated with benzoic ester local anaesthetics remained. This prompted the search for a completely novel agent that did not prove fruitful until 1943 when Nils Lofgren and Bengt Lundquist developed lidocaine (lignocaine).\textsuperscript{9}

Equipment began to improve with the introduction of the atraumatic ‘pencil point’ spinal needle, designed to part the dural fibres rather than cut them. The round-ended Greene needle was introduced in 1923, followed by the Whitacre needle in 1951, which has a blunt tip and an opening just proximal to it. The Whitacre remains in use today with only minor modifications. The developments in spinal needles are described in detail by Calthorpe.\textsuperscript{23}

**Wooley & Roe**

In 1947, Graham performed spinal anaesthesia on two patients which sadly left them both with permanent painful spastic paraparesis. A court hearing in 1953 concluded that the local anaesthetic ampules had been contaminated with the phenol solution used to sterilise them. The coloured phenol solution had entered the ampoule through microscopic cracks in the glass but was not present in sufficient quantities to have been detectable by eye. The judge ruled for the defence and neither complainant received compensation.\textsuperscript{24}

The 1922 book “*Regional Anaesthesia: Its technique and clinical application.*” by Gaston Labat was a comprehensive textbook describing practical block techniques. This book provided the instruction required for those practicing regional anaesthesia to expand their techniques and is partly credited with the rise in popularity across the English-speaking world.\textsuperscript{25}

The introduction of halothane in 1955 combined with public fear of paralysis following the Wooley & Roe case, led to a reduction in the popularity of spinal anaesthesia in the United Kingdom (UK) for many years. Notably, the case did not affect the popularity of spinal anaesthesia in the USA, where regional anaesthesia practice continued to grow. The application of the
The modern era

The rise and fall in popularity of regional anaesthesia throughout its history has shaped the culture surrounding its delivery in the UK today. Regional anaesthesia has, at times, been perceived as a technique delivered by a small group of specialists but has more recently experienced a deserved surge in popularity. This has in no small measure been helped by the availability of aids to deliver it safely and by many outcome studies. Anaesthetists in training are encouraged by the increased number of providers, as well as the wealth of on-line resources available to supplement clinical experience. Regional techniques are now considered core skills as a result.

References


time/2020119.article; 2007).
A Brief History of Extracorporeal Membrane Oxygenation (ECMO)

Dr Olivia Baker
Addenbrookes Hospital, Cambridge

Extracorporeal membrane oxygenation (ECMO) is a type of life support machine used in intensive care settings for people with life-threatening conditions that compromise heart or lung function. ECMO is designed to support cardio-respiratory function for prolonged periods whilst managing an underlying, reversible, pathology. To begin to understand the history of the current-day ECMO machinery, we must cast our minds back to the history of the cardiopulmonary bypass machine of the late 1800s and early 1900s. We then move to the 1930s, when American surgeon John Gibbon first began his personal, decade-long quest to improve extracorporeal oxygenation. Later, following the second world war, 1950s and 60s saw the pivotal movement to provide prolonged periods of cardiopulmonary support. It was in the 70s that the first successful human cases using ECMO were reported. With an intriguing history, intertwined with inspirational researchers and a fortuitous young girl, the history of ECMO is a moving story that tells the power of academic innovation and persistence.

The History of Cardiopulmonary Bypass

ECMO has saved the lives of many patients with severe acute cardiopulmonary failure, for whom conventional mechanical ventilation provides insufficient organ support, and has successfully bridged many acutely unwell patients pre-and postoperatively. It has proven to be an invaluable tool in intensive and critical care settings, from neonates to children to adults.

The history of ECMO begins with primitive cardiopulmonary bypass. In 1812, French physician and physiologist Le Gallois first proposed the concept of extracorporeal circulation to preserve essential organ function.1 In 1858, Brown-Sequard, perhaps most famously known for his description of spinal cord transections, demonstrated that injecting oxygenated blood into amputated dog and human limbs could elicit a neuromuscular reflex.1 Later, Austrian-German Max von Frey and Austrian Max Gruber invented the rotating film oxygenator, a model that current membrane oxygenators are
based on. In 1895, Jacobi rejected the “complicated” cylindrical oxygenator, instead opting to use dog lungs as an oxygenator to maintain the function of isolated organs.¹ Jacobi’s experimental procedure bears a striking similarity to Lillehei’s cross-circulation model of the 1950s. With a proven concept and experimental foundations to build up, it was in the 1930s that research into extracorporeal oxygenation accelerated.

John Gibbon (1903-1973), surgeon, dedicated researcher, and fifth-generation physician, first began working on extracorporeal oxygenation in the early 1930s. He graduated from Jefferson Medical School in Philadelphia in 1927 and soon met his wife, Mary, who became his partner in life and research.² In the 1930s Gibbon was working in Harvard, Massachusetts, and one case is said to have inspired his lifelong dedication to this field. A 53-year-old woman developed massive pulmonary emboli postoperatively following a cholecystectomy. At the time, the treatment for massive pulmonary emboli was limited to an emergency pulmonary embolectomy (or Trendelenburg procedure). This operation carried such a high mortality that it was often referred to as an early post-mortem.³ Following the woman’s death, Gibbon hypothesised that a method of removing blood from the patient’s venous system, bypassing the lungs, and readministering blood into the arterial system, had the potential to save her and future patients’ lives.⁴

In 1935, Gibbon assembled a feline model of massive pulmonary embolism to test his hypothesis. By clamping the pulmonary artery, either partially or completely, venous pressure rose, arterial pressure dropped to levels incompatible with life, and spontaneous respirations stopped.⁵ After clamping, the feline circulation was redirected through the artificial oxygenator, leading to an improvement in arterial blood pressure to a level compatible with life (around 100 mmHg systolic), and reintroduction of spontaneous respiration.

Gibbon’s rotating oxygenator was based on von Frey and Gruber’s model. Two cylinders, one inside another, rotated in opposite directions creating a blood film along the inner surface that was directly oxygenated by injected gas.⁶ Initial experiments proved that the functions of heart and the lungs could be carried out by the oxygenator for about 40 min following complete bypass.⁴ In 1937, Gibbon published his findings in a paper called “Artificial Maintenance of Circulation During Experimental Occlusions of Pulmonary
Artery”. In one instance, the cat survived for five days after one hour on bypass, the longest postoperative survival. The cause of death was euthanasia, performed due to wound infections at the cannulation sites. Gibbon concluded that this mechanical aid to the circulation in the presence of a partial or complete occlusion of the pulmonary artery has been satisfactorily demonstrated. He also concluded that his apparatus allowed a bloodless operative field to facilitate complicated or prolonged cardiac surgery, to support severe cardiac or respiratory failure, or as an adjunct to major surgery.

Over the following decade, Gibbon worked to improve his original model. He found creating turbulence to disrupt laminar blood flow in the oxygenator greatly improved the efficiency of oxygenation. Following a short hiatus during the Second World War, increased funding gave Gibbon opportunities to upscale his experiments to canine models. In the 1950s, he began performing cardiac operations on dogs, and his operative mortality rate dropped from 80% to 12% over 3 years.

In 1953, following 22 years of work on cardiopulmonary bypass, Gibbon got the opportunity to use his heart-lung bypass machine on a human being. An 18 year old girl was admitted for the third time in 6 months with fulminant right heart failure secondary to a severe atrial septal defect and permanent left-to-right shunt. She was not expected to survive, perhaps not this admission, and required urgent cardiac surgery. This complex surgical repair required a bloodless field to operate safely and efficiently. Gibbon performed the septal repair, during which the patient was completely dependent on extracorporeal support for 26 of a total 45 min spent on bypass. The operation was successful, and the patient’s recovery was reported to be uneventful. At the time, various others were trialling alternative bypass machines in human but Gibbon’s was the only patient to survive. However, Gibbon himself knew his apparatus was not perfect: the film oxygenator induced excessive haemolysis, and the formation of bubbles and foam in the blood risked multiple potentially fatal gaseous microemboli.

Around the same time as Gibbon returned from the war, a physician called Banning Gray Lary was working in Illinois. Lary (1924-2013), born in Kentucky, was an accomplished American surgeon and researcher. He is remembered for multiple pivotal contributions to cardiac surgery, including
first demonstrating that intravenous administration of oxygen can maintain life. Lary started his career as an army recruit following the bombing of Pearl Harbour and trained recruits in America while his company was assigned to North Africa. After discovering his natural clinical acumen, Lary was sent to Chicago to study medicine at the University of Illinois, which is where he uncovered his passion for surgery. Lary graduated and married his wife, Katherine, in 1948. It was during his time in the Cole laboratory in Illinois, researching hepatobiliary disease, that Lary made his landmark discovery in surgical history. Lary’s paper, presented in 1952, described intravenous administration of tiny bubbles of oxygen into dogs that were breathing pure nitrogen. For the first time, the dogs lived. Previous attempts had been fatal; the key appeared to be reducing bubble size before administration by adding a wetting agent to oxygen before forcing it through a filter. His discovery in the early 1950s created the foundations upon which the safer cardiopulmonary bypass models could be built for use in humans and eventually lay the foundations of using ECMO.

Looking back, we might have expected mass euphoria in the medical community following Gibbon’s successful ASD repair in 1953. However, the response felt short of anticipation, thought partly to be due to the parallel work on alternative bypass models. Clarence “Walt” Lillehei, born in 1918, was an American cardiac surgeon based in Minneapolis, Minnesota. In 1954, Lillehei was heading a laboratory dedicated to developing pioneering techniques for open-heart surgery. At the time, the only method to create a bloodless field for complex open cardiac surgery was the creation of a blood-free field by induced hypothermia. However, hypothermic methods allowed for only very short window of time which was not enough for long operations to correct multiple congenital defects. Lillehei developed a technique that bypassed the patient’s cardiopulmonary circulation, similar in principle to Gibbon’s model, but using donor lungs as oxygenators instead. Canine lungs were used as dogs were found to possess a unique physiological characteristic, the “azygous factor,” meaning that they can survive for up to thirty minutes if a blood supply via the azygos vein is maintained. Capitalising on this phenomenon, Lillehei diverted blood from the pulmonary vein of one dog into the arterial circulation of another dog. Venous blood was then removed from the recipient dog and pumped directly into the pulmonary artery of the donor dog for oxygenation via the donor dog’s primitive lungs, with flow controlled to prevent donor exsanguination.
With both the superior and inferior vena cavae occluded, complete cardiopulmonary bypass of the recipient dog’s heart was achieved permitting a blood-free zone in which to operate.

In 1954, despite ethical considerations and some resistance, regulatory boards approved the use of Lillehei’s method in humans. Interestingly, Lillehei only initially intended to use the cross-circulation model for a short period, as an inexpensive model to practice cardiac surgery without requiring a pump oxygenator. However, initial success inspired him to use the model in humans. The first open-heart surgery using controlled cross-circulation was carried out in 1954 by Lillehei on a 12-month-old boy with a ventricular septal defect. The child’s lightly anaesthetised father acted as the donor lungs and a simple mechanical pump acted as the heart. The boy survived the operation and immediate postoperative period, however, unfortunately, succumbed to pneumonia 11 days postoperatively. The Minnesota team continued to use the cross-circulation model in the following year, and 28 of 45 operated patients were reported to have survived, using parental donor lungs.

Despite Gibbon’s and Lillehei’s successes in the early to mid 1950s, the issue of formation of residual gas emboli following direct oxygenation of the blood remained. In 1954, Richard DeWall (1926-2016) was working in Lillehei’s group at the University of Minnesota. After realising the proficiency at which DeWall was working as a perfusionist managing the cross-circulation apparatus, Lillehei challenged DeWall to find a way to solve the so-called “bubble problem”. There was significant ethical hesitancy surrounding the use of healthy donors in the cross-circulation model, with one especially morbid description “the first operation in history to have the potential for 200% mortality”. Following the death of a donor, DeWall focused on improving Gibbon’s oxygenator. DeWall’s solution, finalised in 1955, introduced a novel silicone membrane to “defoam” blood and reduce the formation of gas emboli. Then blood was passed through a plastic helical coil to further remove any remaining bubbles. Alongside colleague Vincent Gott, DeWall improved the model to create a cost effective, sterile, disposable, portable and safe oxygenator that could be easily transported. The bubble oxygenator was first used on a patient in 1955; a 3-year-old boy with a ventricular septal defect who underwent
uneventful open cardiac septal repair.\textsuperscript{6} It was used for hundreds of operations in subsequent years.

\textbf{From Cardiopulmonary Bypass to ECMO}

The cardiopulmonary bypass machines were pivotal historical research that facilitated complicated intracardiac surgery and improved morbidity and mortality outcomes significantly in children with congenital heart defects. These were the inspiration for the development of ECMO. However, these machines, due to their direct oxygenation of blood via bubbling, were unsuitable for use for more than a few hours while complex cardiac surgery could take much longer to perform. In the 1960s and 70s, Robert Bartlett, a Michigan-born physician, sought to modify existing cardiopulmonary bypass apparatus to facilitate longer-term use in neonates. Therein began the heartening story of a migrant newborn and a dedicated surgeon, later coined the Father of ECMO, that has saved thousands of lives ever since.

Robert Bartlett was born in 1939 in Ann Arbor, Michigan, USA whose father was a surgeon.\textsuperscript{9,11} He was awarded a Bachelor of Arts (BA) degree from Albion College in 1960 and graduated from the University of Michigan Medical School with a distinction three years later.\textsuperscript{12} After graduating, Bartlett spent the years 1963-66 at Peter Bent Brigham and Children's Hospital in Boston, Massachusetts as a surgical intern. From 1966-70 he was a National Institute of Health trainee in academic surgery at Harvard Medical School, where he completed his general surgery residency with an additional year as a resident in thoracic surgery.\textsuperscript{13} In 1970 he moved to Southern California to continue his clinical work and research into long term cardiopulmonary bypass at the University of California in Irvine. It was during his time on the West coast that Bartlett pioneered the use of ECMO for acute respiratory failure in neonates. In 1980 he returned to the Midwest to become a Professor of General and Thoracic Surgery and Director of the Surgical Intensive Care Unit at the University of Michigan. Bartlett has remained involved with the University of Michigan ever since.

During his time in Boston, junior resident Bartlett and colleagues noticed high mortality rates of up to 50\% in neonates requiring surgery for congenital heart disease.\textsuperscript{11} They hypothesised that continuing cardiopulmonary bypass in the immediate postoperative period would
drastically improve mortality outcomes. However, such intervention was not possible with the then available cardiopulmonary bypass machines. Bubble oxygenators directly oxygenated blood which was harmful to blood and organs after hours, through the effects of systemic gaseous micro-emboli. By oxygenating blood across a silicone membrane, thereby mimicking a natural mammalian lung, membrane oxygenators could be used for longer periods with a lower risk of harmful sequelae. Multiple academics were working on designing disposable membrane oxygenators, including Latvian Theodor Kolobow, who created the silicone rubber spiral coil membrane lung, which became the standard device for many years. Alongside his colleague Zwischenberger, Bartlett coined the term "extracorporeal life support" (ECLS), later known as ECMO, to describe the use of membrane oxygenators for longer periods up to days or weeks.

In 1972, J Donald Hill was the first person to successfully treat a human with ECMO. A 24-year-old male sustained multiple traumatic vascular and orthopaedic injuries and developed respiratory failure postoperatively refractory to maximal mechanical ventilatory support. ECMO using a membranous heart-lung machine was used for three days, reversing the shock-lung syndrome. The patient miraculously made a full recovery. Also in 1972, Bartlett successfully used ECMO in the first paediatric case, a 2-year-old child who had developed heart failure following cardiac surgery for transposition of the great vessels. By the mid-1970s, it became clear that these modified cardiopulmonary bypass machines could effectively provide temporary cardio-respiratory support for patients with severe postoperative cardiac or respiratory failure for a period of several days. In 1975, Bartlett conducted the first successful use of ECMO in a neonate and neonates with severe acute respiratory failure soon became the poster child of ECMO history. That very first child was Esperanza (see below).

Baby Esperanza was born at term in tumultuous circumstances. Her mother, from Baja in Mexico, sought American citizenship for her unborn child. During the expectant mother’s journey across the border, her membranes ruptured. She was forced to find a hospital urgently and Baby Esperanza was born in Orange County Medical Centre in California. This was rather fortuitous, as Bartlett was working in California in Irvine at the time. The baby was born cyanotic and severely hypoxic. Despite maximal mechanical ventilation with 100% oxygen, the neonate could not sustain adequate
oxygenation. With probably not full maternal consent, Dr Bartlett used ECMO in a final attempt to reverse her severe, and almost certainly fatal, respiratory failure. It is worth noting that at the time, ECMO, still in its relatively experimental phase in human, was only indicated in moribund patients believed to have no chance of survival with conventional treatment. The mother appears to have absconded after this leaving the baby an orphan who was named Esperanza (meaning hope in Spanish) by the hospital nurses.

Baby Esperanza spent six days on ECMO. After stopping ECMO, she was weaned off ventilation a few days later and spent months in the hospital neonatal intensive care to later make a full recovery. It was later concluded that Esperanza had persistent pulmonary hypertension, secondary to meconium aspiration with a patent ductus arteriosus and a total right-to-left intracardiac shunt.

Baby Esperanza was raised by a foster family in America. Dr Bartlett lost contact with the family when they moved away from California but were reunited when a Missouri paediatrician contacted Dr Bartlett about a “most unusual young girl in his office”. The paediatrician described obscure scars on the child’s right neck and left chest and a plastic catheter in the lower lobe of her right lung. Bartlett and Esperanza were reunited. Since this ground-breaking case, ECMO has become a well-established bridge to recovery in neonates with severe acute respiratory failure, shifting a high predicted mortality to a 50% survival rate, and as a modality for the management of severe acute respiratory distress syndrome in adults.

Now 82 years of age, Bartlett has held a post at the University of Michigan since he returned in 1980. He currently holds an Emeritus Professorship of surgery at the University of Michigan medical school but no longer practices clinical medicine. He has been awarded numerous awards for his contributions to surgery and has published three books. In 2002 he received the Medallion for Scientific Achievement from the American Surgical Association for the development of continuous haemofiltration and ECMO for treatment of the critically ill patient. This is the highest honour for surgeons in America and at the time of award had only been received 16 times in the last 120 years. Despite his numerous awards, he claims his biggest contribution to the field of medicine and surgery is the numerous
professionals he has trained, educated, and collaborated with for decades during his career. Although retired from active practice, Bartlett’s contributions to medicine remain at the core of treating acute cardiorespiratory failure, and in the fields of surgery and critical care. Many of the basic principles of ECMO have remained the same since his pivotal work in the 1960s and 70s.

Conclusion

As a newly qualified doctor thrust into the NHS at the start of the pandemic, circling the unfamiliar corridors of critical care, I remember clearly the thick coiling tubes protruding from patients’ necks, like menacing red serpents. Little did I know about the intriguing history of ECMO and the physicians and scientists whose life work many critically unwell patients have depended upon since the 70s. The story of Baby Esperanza is extraordinary and emotive but merely scratches the surface of the vision and dedication of those involved in cardiac surgery and intensive care medicine spanning over a century.

References

The first experiments with central neuraxial blockade were by New York neurologist Dr James Leonard Corning (Figure 1) who injected 111mg of cocaine into the lumbar epidural space of a healthy male patient in 1885. He had intended to inject it into the intrathecal space but there was no flow of cerebrospinal fluid (CSF). He had injected a large dose but it was certainly, and fortunately, almost all in the epidural space.


In 1901 the first epidural via the caudal approach was independently described by two Frenchmen, Jean-Anthanase Sicard and Fernand Cathelin who both used cocaine. In 1909 Walter Stoeckel, a German obstetrician published his 141 cases of caudal epidural analgesia for labour pain. His success rate was 50%. He used procaine which was first synthesized in 1905, and there were no reports of headache.
The Spanish military surgeon Fidel Pagés Miravé developed the technique of “single shot” lumbar epidural anaesthesia and analgesia in 1921.²

Eugene Bogdan Aburel, a Romanian obstetrician, injected local anaesthetics via a silk catheter to perform lumbar obstetric anaesthesia in 1931.³ This allowed repeated injections throughout labour without the need to repeat the procedure.

The Argentinian physicians Alberto Gutierrez and Vincent Ruiz used epidural anaesthesia extensively for surgery in 1939. Also in 1939 the Italian Achille Dogliotti popularised lumbar epidurals and developed the loss of resistance and the hanging drop techniques.⁴

In 1941 Americans Robert Andrew Hingson and James Southworth popularised the technique of continuous caudal anaesthesia using an indwelling needle.⁵ Dr Hingson collaborated with Dr Waldo Edwards, an obstetrician, in using caudal anaesthesia for childbirth and they described the first successful use of a flexible catheter for continuous caudal anaesthesia in labouring women in 1943. Southworth along with Hingson and Edwards described the use of continuous caudal analgesia for lower abdominal and lower limb surgery.⁶

The Cuban physician Manuel Martinez Curbelo described the placement of a lumbar epidural catheter in 1947.⁷

Dr Charles John Massey Dawkins (Figure 2), consultant anaesthetist at UCH, pioneered epidurals in the UK in 1942.⁸ Dr Philip Bromage (Figure 3) was taught epidurals by Dr Massey Dawkins, and encouraged by Dr J Alfred Lee. He steered the practice of epidural anaesthesia into the modern era. He published a single author textbook “Spinal Epidural Analgesia” in 1955 while working in Chichester.⁹ In 1955 he was invited to speak in North America where he helped popularise epidural analgesia and anaesthesia. In 1978 he published his textbook “Epidural Analgesia” while working in the USA.¹⁰ He developed the Bromage scale for assessment of the motor block; this was subsequently modified by Breen and colleagues.¹¹
Figure 2. CJ Massey Dawkins (1905-1975)
(https://rcoa.ac.uk/dr-charles-john-massey-dawkins)

Figure 3. Professor Philip Bromage (1920-2013)

John Bonica founded the University of Washington Department of Anesthesiology in Seattle in 1960 and helped popularise regional anaesthetic techniques for childbirth. He published many books and papers on pain
relief, including “Principles and Practice of Obstetric Analgesia and Anesthesia” in 1967,\textsuperscript{12} and which is now in its 5\textsuperscript{th} edition.\textsuperscript{13}

A new design of the catheter made of flexible nylon was introduced by Alfred Lee (Figure 4) in 1962.\textsuperscript{14} It was closed-tipped with a lateral opening about 1 cm from the tip. This was designed to facilitate insertion and cause less trauma. More new catheters with two or even three holes were introduced following Lee’s introduction of the single orifice catheter. The innovations in epidural catheter design are discussed in an excellent review of the epidural catheters by Toledano and Tsen.\textsuperscript{15}

![Figure 4, J Alfred Lee (1906-1989)](https://rcoa.ac.uk/dr-john-alfred-lee)

**Figure 4, J Alfred Lee (1906-1989)**
https://rcoa.ac.uk/dr-john-alfred-lee

Although cocaine was the first drug used for local and regional anaesthesia, concomitant development of the local anaesthetic drugs occurred at the same following the introduction of lignocaine in 1948, bupivacaine in 1957 and further agents; these are discussed elsewhere.\textsuperscript{16,17}

The discovery and characterisation of opioid receptors by Goldstein led to the development of specific drugs and their antagonists.\textsuperscript{18-21} This also opened the field for the use of opiates by the epidural and spinal routes, the first such use being described by Behar and colleagues in 1979.\textsuperscript{22}
The bolus dose use of both local anaesthetics and opioids while still continuing is being replaced by the use of more and more continuous infusions from 1970s onwards.

References

Some of the history of circle systems in anaesthesia

Dr Patrick Magee PhD, FRCA
Retired Consultant Anaesthetist, Royal United Hospital, Bath
patrick.magee1953@btinternet.com

Circle systems in anaesthesia are designed to be used at low fresh gas flow (FGF), with the carbon dioxide (CO₂) being absorbed and the unused oxygen (O₂) and anaesthetic agent being recycled and rebreathed. In the modern system the vaporiser is invariably placed outside the circle (VOC), although historically they were also used inside the circle (VIC). Their complexity and safety lie in knowing what gas composition the patient is receiving when low FGFs are used.

The earliest record of the recognition of the problem of rebreathing CO₂ was in the 18th century by Reverend Stephen Hales of Teddington (1677–1761).¹ ² He is better known by modern clinicians for his direct measurement of blood pressure in a horse, but he was a polymath with a wide range of scientific interests. In his publication entitled ‘Vegetable Staticks’, concerning the transport of sap in plants, he alludes to the feeling of suffocation within one minute while breathing air from an enclosed bag.³ This feeling was delayed after he had designed a breathing system with unidirectional valves and a cloth soaked in vinegar or sal tartar. Later researchers from the 18th century who were better known for other aspects of research into respiratory gases, also studied the subject of carbon dioxide (CO₂) absorption. These included Joseph Black (1728–1799) examining the use of chalk, Joseph Priestley (1733–1804) examining the use of lime water, Carl Scheele (1742–1786) examining the use of milk of lime, and Humphry Davy (1778–1829) examining caustic potash. Results heretofore had been inconsistent due to the different CO₂ absorption media, but it was Antoine Lavoisier (1743–1794) who clarified that air breathed from an enclosed space became unfit to breathe due to both diminishing oxygen, and increasing carbon dioxide levels.

In the 19th century, both William Morton (1819–1868), and John Snow (1813–1858) recognized the need to avoid rebreathing exhaled gas, and their equipment for delivery of ether was designed with unidirectional valves.⁴ ⁵ Snow retained a non-rebreathing valve in the mask for use with a chloroform
vaporizer. In 1849 Snow used an experimental closed absorption system with non-rebreathing valves on anaesthetized animals and on himself, but did not pursue it clinically. After Snow’s death in 1858, the mantle of closed breathing systems fell to Joseph Clover (1823–1882), who designed a closed system which allowed intermittent breathing of chloroform, thereby economizing on its consumption. Later designs of anaesthetic equipment in the 19th century were characterized by a lack of understanding of equipment dead space and of CO₂ accumulation.

The first mention of oxygen being added to a breathing system was by Duroy at the French Academy of Sciences in 1850. An attendee at this lecture was Claude Bernard, who plagiarized the concept and published it in the Journal de Pharmacie et Chémie. However, it was another 18 years before the idea was even reintroduced, and a further 50 years or more before the need for oxygen in clinical systems became more widely recognized.¹

Theodore Schwann (1810–1882), better known for his work on neural structure and function (e.g., Schwann cells), was a German-born Professor of Anatomy and Physiology at Liège University in Belgium. He devised a breathing system for mine rescue in 1853, which included unidirectional valves and a CO₂ absorber of lime in caustic soda, oxygen supplementation and pressure regulation.¹ In 1868 an American dentist, Alfred Coleman (1828-1902), introduced an ‘economizer’, a system to recycle nitrous oxide. However, it fell out of favour due to a long hose which increased dead space and due to the lack of added oxygen.¹ Meanwhile, outside of anaesthesia, in 1878 a diving engineer, HA Fleuss (1851–1933) based in London, designed a diving rebreather set, in which oxygen was provided and CO₂ was absorbed by a rope soaked in caustic potash.⁷

By the early 20th century, there was a preference for high flow, non-rebreathing systems, the hazards of hypoxia and hypercarbia in the use of low FGF systems having been recognized. However, this did not stop further design of closed systems. EI McKesson (1881–1935), designed a ‘fractional rebreathing’ system, in an attempt to economize on the use of volatile agents by using intermittent ventilation to allow the gas from the anatomic dead space to be saved. In 1906 Franz Kuhn (1866–1929), a German surgeon, made a number of contributions to intubation and invented a device with two soda lime canisters and unidirectional valves. However, it fell out of use
because of concerns of possible interaction between chloroform and soda lime. Indeed, the design was later criticized by Ralph Waters (1883–1979), the well known American anesthesiologist, on account of its long, single tube dead space which could become depleted of oxygen and from which CO₂ could not be absorbed.⁸ In 1915 Dennis Jackson (1878–1980), a US based experimental pharmacologist, ingenious inventor and occasional anaesthetist, designed a closed circle absorber system for animal use out of laboratory scraps and milk bottles, using liquid alkali to absorb CO₂.⁹ He recognized the problem of dead space and introduced a fan rather than valves, a precursor perhaps to the Revell circulator. He tried to interest clinicians in his system by modifying it to a simpler ‘to and fro’ system using a cake tin and a shower cap. It is worth noting that McKesson had unsuccessfully tried to use the Jackson’s system.¹

By 1899, it had been noted that soda lime was a better absorber of carbon dioxide than other substances, and its quality had been greatly improved, particularly for use in gas masks in WW1. Ralph Waters designed his own system in 1925 using a canister and a bag, formally introducing soda lime to clinical anaesthetic breathing systems.¹⁰ Waters’ system was a ‘to and fro’ rebreathing system, rather than a circle system, for ease of use and to maintain its proximity to the patient.¹¹ His original design had a 10 L reservoir bag, which was reduced to 5 L by the 1940s, when chloroform was being more widely used. Originally the oxygen inflow was into the tail of the bag, but this was moved to the elbow on the patient mask to facilitate changes in inspired gas concentrations. The ‘to and fro’ system facilitated mask anaesthesia in the 1920s, when intubation was relatively infrequent.

The need for a circle system became apparent as the use of nitrous oxide and flammable volatile agents increased. Drägerwerk of Lübeck, having started in the 1880s as a manufacturer of pressure regulators for carbon dioxide to preserve the quality of beer in barrels, developed the first circle system to fulfil this need. This was developed for use with the volatile agent Narcylene (acetylene) in 1924 for use with the Drager Narcylene anaesthetic machine. Subsequently, the first anaesthetic machine incorporating a circle system for use with nitrous oxide and ether, the 'model A' was developed in 1926.¹² This was the first anaesthetic machine incorporating a circle system, the model A, from the original designs of both Kuhn and Schwann. It is an unfortunate sequel of WW1 and indeed the first half of the 20th century, that the cross-
fertilisation of information and ideas to improve design internationally, that might otherwise have occurred between German and American designers, was lacking. Although Thomason and Jackson had been the first in the USA to describe a functioning circle system, credit is more often given to Brian Sword (1889–1956) and Richard Foregger (1872–1960), who made such a system commercially available. Sword was an anesthesiologist (anaesthetist), and Foregger, who founded the US company which manufactured the machines, was an Austrian emigré to the USA who had started life as a chemist and engineer, who could turn his knowledge and skills to most things. His mother had taught Foregger to speak Russian, and one of his earliest jobs was working for a British company on the construction of the Siberian railway.

While it was clear that the use of low flow circle systems was justified by the need to absorb carbon dioxide, to recirculate exhaled gases and to reduce operating room pollution, the arrival of cyclopropane from around 1935 added further impetus to their usefulness. Cyclopropane was expensive and highly flammable, but gave rapid and smooth onset of anaesthesia and recovery. Its use had started to diminish in popularity by the 1960s, and is now no longer available for use in most parts of the world. Nevertheless, the concept of circle systems was not completely lost, even if its use in anaesthesia was. In 1961, the breathing system of the first cosmonaut, Yuri Gagarin, was a circle system, although almost certainly used with high FGF. The danger with low flow circle systems prior to the introduction of respiratory gas monitoring and pulse oximetry was that it was difficult to be sure that the patient was not receiving an hypoxic or hypercapnic gas mixture, or that inadequate or excessive anaesthesia was not being delivered. One might use the Brody equation to calculate the oxygen consumption, and the Severinghaus equation for nitrous oxide uptake, or indeed the uptake of other volatile agents, but these are not easily undertaken on the back of an envelope during a busy operating list.

The demise of the clinical use of circle systems was due to a number of other factors too such as many connections in the systems with the potential for leaks, poorly designed valves, poor absorber design with gas channelling and an increase in dead space as the soda lime was consumed. There was an increasing use of muscle relaxants in combination with nitrous oxide and less volatile agent, which could be given more accurately at high FGF. Of
course, paralysis came with the need for ventilators, which usually needed high FGF to function (in the absence of a separate high pressure gas source). In addition, the new halogenated agents had to be used with agent specific vaporizers, designed for use with vaporizer outside the circle (VOC) with high FGF, which by this time was considered safer. There was a fear that newer potent agents would give dangerously high concentrations if used with vaporizer inside the circle (VIC), unlike ether, which was more forgiving. In the USA, the Copper Kettle vaporizer was introduced, which was harder to use safely in low FGF closed systems, so its use with VOC with high FGF was emphasized. In fact, the introduction of the non-flammable agent halothane in 1956 saw the demise of low FGF circle system anaesthesia in favour of mechanically simpler, and inherently safer open (semi-closed) systems used with high FGF.\textsuperscript{1}

In the continued absence of reliable gas monitoring, the next interesting historical phase was the mathematical analysis of the performance of circle systems. In 1960, WW Mapleson, a physicist in the department of Anaesthesia in Cardiff, did a mathematical analysis of circle systems, both with VIC and VOC.\textsuperscript{15} He showed that the inspired anaesthetic agent concentrations were critically dependent on FGF and on alveolar ventilation. At low FGF, the inspired anaesthetic agent concentration was considerably less than that dialled up on the vaporiser when used VOC, with the risk of awareness; when used VIC at low FGF, the inspired anaesthetic agent concentration was considerably higher than the dialled vaporiser concentration, with the risk of toxicity. The lower the FGF, the more extreme were these differences between the dialled and the inspired concentrations, with both VOC and VIC. The higher the FGF, the more like an open system did a circle system behave, with inspired concentrations corresponding more closely to vaporiser concentrations in both VIC and VOC.

In follow-up laboratory and clinical studies from Cardiff in 1960, Galloon and William Mushin (1910–1993; Professor of anaesthesia), confirmed how differently VIC and VOC systems behaved at low FGF and in the presence of artificial ventilation, and how anaesthetic uptake varied with system geometry and anaesthetic absorption.\textsuperscript{16,17} In 1972 Forbes demonstrated in a clinical study that there was an increasing discrepancy between system delivered O\textsubscript{2} concentration and patient FiO\textsubscript{2} at low FGFs, but that it was
predictable. In 1968 Eger and Ethans laid down some simple rules for the way components in a circle system should be combined to minimise carbon dioxide rebreathing. Other research in the 1970s by Jorgensen and Jorgensen, and by Snowdon et al, focussed on CO₂ clearance by systems with different geometries and the presence or otherwise of different absorbers.

The 1980s saw a plethora of analytical work by late Professor Cyril Conway (died 1986), Professor of Anaesthesia at Westminster Hospital Medical School, in which he showed that CO₂ clearance at low FGF depends on the extent of gas mixing in different systems, and on ventilatory pattern. He showed the dependence of alveolar oxygen and anaesthetic agent on FGF (confirming the 1960 Cardiff results), fresh gas composition, minute ventilation and gas uptake. Conway recommended an adequate period of high FGF at the start of an anaesthetic in order to denitrogenate (where N₂O is used), and mandated gas monitoring, which by this time was available.

More of Conway’s work validating his model in relation to anaesthetic uptake with modern agents, and with the fate of nitrogen during low FGF anaesthesia was published posthumously in 1986.

The renaissance of circle systems in the 1990s was driven by the introduction of modern, expensive volatile agents, and the availability of excellent respiratory gas monitoring and pulse oximetry. By this time there were also soda lime canisters of much improved design, better unidirectional valves made with modern materials, and a more precise mathematical understanding of the pharmacokinetics of volatile agents. There still needs to be an appreciation of the fact that gas monitors draw 100–200 ml per min of gases for sampling and analysis, which is not usually returned to the circuit. This may be a significant loss of gas volume with low FGF. In addition, further recent research reveals the need for a continuing understanding of what FGF is necessary at different phases of the anaesthetic administration to oxygenate, denitrogenate and load adequate volatile agent, and a continuing need for understanding of equipment dead space. Above all, we are in an era in which environmental pollution must be considered; volatile agents have a threefold capacity for atmospheric warming compared to carbon dioxide, and 5% of the NHS carbon footprint is from anaesthetic gases.
intravenous anaesthesia (TIVA) may be considered an even better option in the future.

References


This is a short history of the Cape Engineering Company named after ‘The Cape of Good Hope’, a canal side pub in Warwick. It sprang from the discovery that Ron Walton who later became managing director, lived not far from me, and from my biography of Captain GT Smith-Clarke who became involved with Cape. It was started in disused aircraft hangars (Figure 1) by TG ‘Gerry’ Turner, Alvis Home Sales manager who had negotiated with the Ministry of Defence during WW2. He left Alvis in the late 1940s setting the company up with a nucleus of employees who according to Ron Walton, were ‘poached’ from another company; Warwick Productions. Turner was joined by George S Webley who had been manager at the Alvis Fighting Vehicles and during WW2 managed the Alvis shadow factory in Stratford on Avon. Towards the end of WW2 in August 1944 Webley had actually engaged Ron as ‘assistant to the Technical Assistant’ at 25/- plus 3/6 war bonus (£1.45) a week in Stratford.
In 1928, Philip Drinker and colleagues at Harvard Engineers, built a machine to breathe for paralysed or asphyxiated patients. As all will know the patient was encased in an airtight cabinet with their head protruding through a rubber collar. A pump reduced the pressure within the cylinder to sub-atmospheric, so causing the patient’s chest to expand and draw air into the lungs. It was made of metal and was colloquially called ‘the Iron Lung’ but medically described as a cabinet respirator. An improved version of the Iron Lung (Figure 2) was made by J H Emerson in 1931 and became known as the Emerson Iron Lung. Drinker, having patented his machine, sued Emerson but lost.

![Emerson Iron Lung](image)

**Figure 2. ‘Emerson’ Iron Lung**

In 1937 there was a poliomyelitis (polio) outbreak in South Australia and there were very few Iron Lungs to cope with cases of bulbar paralysis/respiratory failure. The Both brothers, Edward and Donald, inventors and engineers, made a primitive but effective wooden version of the Iron Lung (Figure 3).

Edward Both, sometimes known as Australia’s Edison, visited London in late 1938 to market an ECG machine he and his brother had designed. The BBC broadcast an appeal for a child dying of respiratory failure due to poliomyelitis and Edward Both set to work and made one of his wooden Iron Lungs. William Morris, Lord Nuffield, heard about it and he and Robert
Macintosh, newly appointed Professor of Anaesthetics at Oxford, evaluated the machine (*YouTube has a clip*). So impressed was Nuffield that in early 1939 he turned over part of the Morris Motors factory at Cowley to mass produce Both ‘Iron Lung’ (actually made of blockboard). Nuffield aimed to manufacture 5000 machines for distribution throughout Britain and the Empire though only 1700 were completed before the onset of the war.\(^1\) There was considerable opposition from the medical establishment not least because of the need to train nurses to care for patients in Iron Lungs.

Figure 3: Early ‘Both’ Iron Lung, Jamestown, South Australia 1937

Captain GT Smith-Clarke retired as Chief Engineer of Alvis in 1950 and became Chairman of the Coventry Hospital Management Committee (HMC 20). He’d been involved with the Coventry and Warwickshire Hospital from the 1930s and from 1935 was chairman of the hospital board. At the advent of the NHS in 1948 he became vice chairman and when he retired from Alvis in 1950 reverted to chairman.

Polio became epidemic from 1950 and in April 1952 the Senior Administrative Medical Officer of the Birmingham Regional Hospital Board (BRHB) was concerned about the quality and quantity of breathing machines for polio victims with bulbar paralysis. They were 13 years old and in poor condition from damage and deterioration during the war. Neither ‘patient
friendly’ nor easy to operate; the original model had been designed in a hurry to cope with the 1937 South Australia polio epidemic. Access to the patient was poor, limited to only two ‘portholes’ near the patient’s head. Nursing staff found it difficult to nurse patients within the cabinets; for full nursing procedures the patient had to be withdrawn from the coffin-like cabinet and then only for a limited period because of apnoea. The heavy cabinet with no wheels was difficult to move (Figure 4). The pump unit, providing the ‘negative’ pressure, had poor respiratory speeds, was noisy and hard to operate manually if there was an electricity failure. There was no alarm if the pump failed or the cabinet leaked.

![Figure 4. Both mechanical respirator (Nuffield Iron Lung) before modifications](image)

At some time, during a ward visit, as part of his hospital rounds, Smith-Clarke had also been horrified at the distress and discomfort endured by a female patient being nursed out of the iron lung and particularly when the airtight collar was forced over her head on return to the cabinet.

The Senior Administrative Medical Officer of the BRHB convened a subcommittee to look into possible improvements of the 48 Both/Nuffield cabinet respirators in the Region. On 8th May 1952 Smith-Clarke was co-
opted on to the BRHB Iron Lung Committee for his engineering skills. Doubt was expressed by some members that anything useful could be done to improve matters. Together with JDF Williams, the hospital physicist, a Both respirator was completely dismantled in a disused hospital air raid shelter. There were no working drawings of machine so Smith-Clarke made drawings for the parts required and took them to Alvis, where patterns were created. The Managing Director of Alvis had the larger castings made and machined while Smith-Clarke machined smaller parts in his workshop. He redesigned the pump which was modified in the hospital workshop. It is a measure of their dedication to the task that modifications to the first machine were completed in a matter of weeks by August 1952. All five of the Both machines in Coventry were converted and over the next 18 months were in almost continuous use at the Whitley isolation hospital without any failures.

The details of the many modifications made to the Both cabinet respirator are taken from the minutes of the BRHB in early 1953 where the report of the sub-committee was approved. These consisted of: splitting the neck collar, fitting large observation windows, have multiple portholes and small holes for drips, and make fine adjustments to the pressure within possible. A tilting mechanism, illumination and warmth by electric light bulbs inside the cabinet, a simple patient alarm, and rubber wheels were added. The pump speeds were made more useful and the pump quieter and easier to work manually, in the event of a power failure, by elongating the manual lever with a detachable extension for extra leverage. The Ministry of Health approved the modifications and Cape won the contract. They produced some 500 sets of Nuffield/Both respirator with the improvements made by Cape (Figure 5).

The company also made other non-medical equipment. Cape had a contract to make a mechanism that flipped out fins on bombs, resulting from Turner’s Ministry of Defence connection when working for Alvis.

Recognising the disadvantages of the Both design, even in its modified form plus informal discussions with medical and nursing staff, Smith-Clarke also built a one-quarter scale model of a new cabinet breathing machine by August 1952. Charitable monies were sought to build a prototype. A Coventry Iron Lung Fund was inaugurated, which raised £500 in a short time. This was supplemented by a donation of £800 from the Coventry Coronation
parade. By the late autumn of 1953 the Coventry Evening Telegraph had a
photograph in it showing Turner and Webley with the ‘new Coventry type
iron lung’ (Figure 6A).

![Iron Lung](image)

**Figure 5. ‘Both’ mechanical respirator (Nuffield Iron Lung) after
modifications**

The accompanying article described the modifications made to the Both
machine and the kits of parts the company had produced. It states that the
new revolutionary iron lung was designed by Smith-Clarke and that the new
apparatus will be made of glass fibre and stainless steel. The first eight
machines had fibre glass (*top*) covers, which turned out to be costly and
difficult to make.

The Mark 2 was constructed of aluminium alloy and stainless steel. A
much-improved neck seal was incorporated utilising a wrap-over collar, and
the pump unit was extensively modified to provide an inspiratory/expiratory
ratio of 1/1.5 and better speeds. Called at first the Coventry Mechanical
Respirator, the new iron lung became known as the Alligator (Figure 6B)
(from its description in the Lancet by Dr J F Galpine, Medical
Superintendent, Whitley Hospital, also known as the ‘Fever’ or the
‘Isolation’ Hospital).² What is not mentioned is that the design with rounded
top reduced the internal volume improving efficiency. The jaw-like opening
also meant less ward space was needed. Junior and infant models were made.
Figure 6. A. The Coventry Evening Telegraph of November 27, 1953 with a picture of Turner and Webley with the new Coventry type Iron Lung; B. The new Coventry Respirator, the Alligator

Later models had nameplates with ‘Alligator’ and ‘G Smith-Clarke’ facsimile signature. It was robust and very successful and made in batches of ten. Cape made cuirasses and rocking beds for patients out of the cabinet for nursing. Using the pump motor and gearing, Smith-Clarke redesigned the Stoke Mandeville hospital rocking bed and made it quieter and more robust (Figure 7). It worked at the rate the patients were accustomed to and it was economical to manufacture. Cape continued to make non-medical equipment but cabinet respirators were the foundation of a very successful business.

After the Copenhagen polio epidemic when Dr Bjorn Ibsen, a local anaesthetist, started using intermittent positive pressure respiration (IPPR) because of the shortage of ‘iron lungs’, Smith-Clarke designed and constructed a prototype IPPR ventilator (Figure 8). It was superbly engineered and contained some unique design features, having an infinitely
variable stroke volume between 200 and 1500 ml and a variable speed gearbox that allowed stepless speed changes to give breathing rates if 1-40 per minute. The inspiratory and expiratory valves were opened by cams and closed by springs just like valves in car engines (DER Fox, a Cape employee, told me that the prototype used Morris Minor valves) and if electricity failed, it had a crank handle for manual operation.

Figure 7. The Coventry Rocking bed

Cape began manufacturing the ventilator after appropriate trials and standardisation. It became the Cape IPPR (Figure 9) and sold well. GT Smith-Clarke waived all royalties on the machines.
Figure 8. The Smith-Clarke prototype mechanical respirator

Figure 9. The Cape IPPR ventilator
In May 1956 Smith-Clarke entered into an agreement with Cape Engineering Company Limited that they should have the sole permitted use of his trademark; “G. Smith-Clarke” (facsimile signature) which he had registered in October 1955. It was for use on the mechanical breathing machines manufactured by Cape to Smith-Clarke’s design and he received £500. Ron Walton joined Cape in October 1956 by which time the need for Both modification kits was fading out. The company were making 2 to 3 Alligators and about 10 Cape IPPRs per week but fewer junior and infant Alligators. Some 150 Alligators were manufactured between 1954 and 1967 and about one third sold worldwide. In 1957 Ron made the journey to the 4th Polio Conference in Geneva in a large Austin van to demonstrate the Alligator (Figure 10).

Figure 10. Ron Walton demonstrating the ‘Alligator’ in Geneva in 1957

Cape Engineering was acquired by E & HP Smith of Birmingham in 1962 but they put it up for sale in 1970 and Webley and Turner bought it back. Ron Walton progressed from works manager to works director and later managing director. The company became a group, Cape Warwick Holdings, in which Ron took a share-holding. It comprised several subsidiary companies. Apart from the ‘iron lungs’, Cape Engineering made the foot operated suction pump devised by GT Smith-Clarke and a pump for the cuirass used to aid the breathing of polio patients when they were out of the
iron lung. Ron was involved in the manufacture of cuirasses using glass fibre and set up a separate department for making other devices using this relatively new material. Cape continued making ‘iron lungs’ but also kidney dialysis machines, a subcontract under licence from Lucas. Other medical equipment included anti-embolism stockings and the pneumatic leggings for the prevention of pulmonary emboli during and after surgery for which they also made the pumps. Additional products made were Microflow air filters and fish boxes. Pressoturn Bulk Material Handling and Capecraft, which was the sales company for Cape Warwick, also made medical trolleys, X-Ray trolleys and full set ups for hospital Central Sterile Supply Departments particularly for new hospitals in the Middle East. In 1977 they displayed ventilators at a medical equipment exhibition in Dubai.

Cape made a semi-electronic IPPR, the Cape 2000, but its biggest success was the Cape Waine anaesthetic machine (Figure 11).

![The Cape-Waine anaesthetic ventilator](image)

**Figure 11. The Cape-Waine anaesthetic ventilator**
This had been suggested by Dr TE Waine, consultant anaesthetist at the Coventry hospitals. He approached Cape with the idea of combining the Smith-Clarke and Cape IPPR with an anaesthetic machine and the resulting large appliance was sold widely.

Dr Waine was known at Cape as ‘Curly’ Waine; he had a bald pate and he was careful about royalties on ‘his’ machine. A full description of the Cape Waine anaesthetic machine and ventilator can be found in the British Journal of Anaesthesia. Waine’s co-author, DER Fox, was originally Cape’s service engineer, visiting hospitals and becoming involved with anaesthetists.

In the late 1950s, Dr W Howlett Kelleher of the Western Hospital in Fulham that had many polio patients in cabinet respirators, came to Cape with a proposal to make a rotatable Alligator to aid postural drainage of the lungs, reduce the incidence of bed sores and enable physiotherapy. He was accompanied by Baroness Felicity Lane Fox after whom the St Thomas’ Respiratory Unit was later named. Kelleher later published the details of the new version of the Iron Lung (Figure 12). Cape made 11 (8 according to Richard Hill) of them. Dr Geoffrey Spencer later ran the Tommy’s (St Thomas’ Hospital) unit; it was said to be the first ITU in Britain.

Cape Warwick Holdings was bought by Thomas Tilling in 1976 and Ron Walton then was Divisional Manager. The company participated at a medical equipment exhibition in Dubai in 1977. Later Ron became Chairman of Penlon, also part of Tilling, and Vessa who made electric wheelchairs. In 1983 a ‘dawn raid’ was made on Thomas Tilling by British Tyre & Rubber (BTR), a conglomerate driven by its chairman Sir Owen Green. With the introduction of the Salk vaccine in 1957, the demand for more ‘iron lungs’ was diminishing but many patients still needed them.

In the early 1980s a more user-friendly version was devised to allow flexibility for more physically able patients who lived at home (Figure 12). Portable Iron Lungs were designed for this purpose and twenty were built by Cape Warwick into which Cape Engineering had been merged after being closed by BTR. Cape Warwick suffered the same fate a few years later. By 1989 BTR had decided that making more cabinet respirators of any type was unprofitable. In The Observer 19th May 1991 it was announced that ‘Profits fall leads firm to quit iron lung production’. The manufacturing rights were
eventually sold to a small company DHB Tools in Leamington Spa. They had previously worked with Cape Warwick and even employed some of the workforce including the designer of the Portable Iron Lung, Dr John Wines. In 1992 at the behest of Geoffrey Spencer, they made five improved Portable iron lungs called the Spencer-DHB for the Lane Fox Respiratory unit. Cape (Warwick) Holdings was dissolved in August 2016 but there is another Cape Warwick in Burton on Trent who make hospital sanitary ware etc.

Figure 12. The rotating ‘Alligator’ (top) and the ‘Alligator’ for home use (bottom)
References


Further Reading:


Coventry, Alvis and the Iron Lung. A Biography of Captain GT Smith-Clarke (available from Hughes & Company, 8 Church Street, Pershore Worcestershire, WR10 1DT UK; or directly from Dr Adrian Padfield: a.padfield@sheffield.ac.uk)
Richard Steevens was a year 1687 medical graduate of Trinity College Dublin (TCD). He practised in the city, was one of the founding fellows of what is now the Royal College of Physicians of Ireland (RCPI) and also became Professor of Physic at TCD. He died, unmarried, in 1710 having made his will the previous day. It stated:

“I give and bequeath all my real estate unto my sister Grizell Steevens for and during the term of her natural life and no longer, and from and after her decease I give and bequeath the same to provide one proper place or building within the city of Dublin for a hospital, for maintaining and curing from time to time such sick and wounded persons whose distempers and wounds are curable”.

Grizell, also single, decided to give effect to her brother’s wishes during her own lifetime and surrendered his estate to trustees in 1717, retaining £100 from the £600 it generated annually. A total of £16,000 was spent before Dr Steevens’ Hospital opened in 1733 with eighty-seven beds.¹ It was Dublin’s second general hospital, and was supported by, among others, Dean Jonathan Swift, the author of Gulliver’s Travels. It rapidly became a vital institution in the city’s provision of healthcare. Perhaps the best-known doctor to have worked there during its 244 years existence (it closed in 1987) was Abraham Colles, of Colles fracture and fascia fame, but there were other notables, including many Presidents of both RCPI and the Royal College of Surgeons in Ireland (RCSI). The building, after a lavish refurbishment, now serves as the headquarters of the Health Service Executive, the body responsible for the provision of government funded health and social care to the Irish people.

On New Year’s Day 1847, the evening edition of a Dublin newspaper, The Pilot, carried a report of what it referred to as an important operation – the first in Ireland under what is now termed general anaesthesia.² Over the
following decades most anaesthetics in the country were administered by junior surgeons, medical students or the nursing staff. In late 1886, Dr Paul Piel was appointed to provide anaesthesia two mornings per week to patients of the Adelaide Hospital, Dublin, thereby becoming the first doctor to be employed in a designated anaesthetic post on the island of Ireland. His salary was £50 per year. There were a limited number of similar appointments to other hospitals in Dublin, Belfast and Cork during the remaining years of the 19th century.

In early 1899 the Governors of Steevens’, as it was known, decided that an anaesthetist should be appointed to their hospital. Dr Thomas Percy Claude Kirkpatrick (Figure 1), who had been born in Dublin thirty years earlier to the King’s Professor of Midwifery at TCD and his wife, and was known to his friends and professional colleagues as “Percy” or “Kirk”, was the successful candidate.

Figure 1. Photograph of Dr Thomas Percy Claude Kirkpatrick, Werner & Son, c.1940 Courtesy of the Royal College of Physicians of Ireland (VM/1/2/K/8).
‘Kirk’ had been educated at Foyle College in Derry, or Londonderry, from which he entered TCD, where he obtained a First Class Honours degree in History before commencing his medical studies. Graduating MB in 1895, he proceeded MD in the same year, and was appointed Resident Surgeon to the County Donegal Infirmary in Lifford, in the North-Western part of the island. Returning to Dublin in 1897, he had to wait until his 1899 appointment as anaesthetist to Steevens’ for his first hospital position in the city. At the end of that year, he joined the visiting staff at the Incorporated Dental Hospital of Ireland, also as an anaesthetist.

Kirkpatrick was promoted to the post of Assistant Physician to Steevens’ in 1900, becoming full Visiting Physician in 1903. As a practising physician, his particular interest was in what was then termed venereal disease. He was also on the staff of Dublin’s Westmoreland Lock Hospital. Syphilis in particular was rampant in the city in the early 20th century, its incidence being far higher than in any of the large cities in Britain. To encourage his patients to attend, Kirk held a clinic in Steevens’ at a discreet early morning hour to facilitate anonymity.4 He also continued to practice anaesthesia there, but more especially in the Dental Hospital and various smaller Dublin institutions, for the remainder of his medical career.

From the time of his 1899 appointment, he had a great interest in dental anaesthesia. He delivered a paper in 1901 to the Dental Students Society of Ireland on “The Asphyxial Factor in Nitrous Oxide Anaesthesia” in which he gave a clear account of the dangers of restricting the amount of oxygen delivered to the patient and cautioned against the use of 100 per cent nitrous oxide, which was still commonplace. He also advocated for separate dentists and anaesthetists where general anaesthesia was used.5 Two years later he wrote on the use of chloroform in dental anaesthesia, a practise which he considered to be entirely unjustified.6 His paper provoked a predictably negative response from Edward Lawrie of Hyderabad Chloroform Commission fame, who expressed his displeasure by writing not to the journal in which Kirk’s paper had been published, but directly to its Dublin author.

Kirkpatrick contributed to the literature over the following few years on ethyl chloride, Somnoform (a proprietary mixture of ethyl chloride, methyl chloride and ethyl bromide), and the General Anaesthetics Bill of 1908. He
also devised and published on a modification of the inhaler introduced by HJ Paterson at the Dental Hospital of London. One of the more interesting of his anaesthesia papers is one from 1910 in which he reported a personal series of 5,142 anaesthetics given in the Dental Hospital between late 1899 and 1909. The anaesthetic agents used most frequently by him were nitrous oxide alone (87% of cases), Somnoform (4.5%), nitrous oxide and ether (also 4.5%), ethyl chloride (1.7%) and ether alone (1.5%). He was appointed Lecturer in Anaesthetics to TCD in 1910 – this was the first recognition of the specialty by an Irish academic institution, and one of the earliest anywhere; he held the position until 1948. Also in 1910, he became Registrar of RCPI and General Secretary of the Royal Academy of Medicine in Ireland (RAMI). Both roles were to last even longer than his Trinity lectureship, 44 years in all.

Kirk had been a lover of books from childhood and corresponded with noted medical bibliophiles such as William Osler and Harvey Cushing. He knew literally everything about books - how and where they came to be written, which font or type was used, what paper they were printed on, and how they were bound and distributed. His position in RCPI afforded him the opportunity to indulge this interest and also his specific passion for medical literature and medical history. His own major works include the History of the Medical School in Trinity College Dublin published in 1912, the Book of the Rotunda Hospital from 1913 and his 1924 History of Doctor Steevens’ Hospital Dublin 1720-1920, considered to this day to be a classic of its kind and re-published as recently as 2008. In addition to scientific papers, he wrote numerous pamphlets and articles on Irish hospitals, medical journals and other historical topics, and on the life histories of many Irish doctors.

Kirkpatrick was also a collector. Where Irish medicine was concerned, he gathered, recorded and safeguarded, whether from newspapers, periodicals or large tomes, information about both leading and obscure individuals and institutions. His work over the years culminated in the development of by far the most extensive collection in existence of biographical material relating to Irish doctors. Where over ten thousand of these were concerned, he stored the information accumulated by him in individually labelled envelopes – there is no doubt that but for his efforts, clues to a great number of medical lives would long since have been consigned to oblivion.
Dr Kirkpatrick attended Steevens’ daily, including Sundays, when he was to be found not on the wards but in one of Dublin’s hidden treasures, the hospital’s Worth Library, which opened in 1742. It was the gift of a Dr Edward Worth who had assembled a collection of some 4,500 superbly bound volumes published before that time. Kirk’s great pleasure was to dust and otherwise care for them; they remain in mint condition to this day.

The Society of Anaesthetists originated in London in 1893; it joined the Royal Society of Medicine as the Section of Anaesthetics fifteen years later, while in 1932 the Association of Anaesthetists of Great Britain and Ireland was founded. It was not until 1946, the centenary year of Morton’s public demonstration of ether anaesthesia in Boston, that the first all-Ireland anaesthetic group, the Section of Anaesthetics of the Royal Academy of Medicine in Ireland, came into being. Kirk was elected inaugural President, while the first scientific address was delivered by his fellow Irishman, Ivan Magill.9

Thomas Percy Kirkpatrick died in 1954, in Steevens’, where he was still a staff-member over 55 years after his appointment as anaesthetist. Whether because of the esteem in which he was held, sheer hard work or popularity he had, during his lifetime, achieved high office in almost every medical and non-medical body of which he was a member.

Reference has already been made to his roles in RCPI and RAMI. In 1936, a special Honorary Professorship of Medical History was created for him in TCD, and as with the other positions, he held it until his death. He also served for a time as Chairman of the Board of Governors in Steevens’, and as President of both the Bibliographic Society of Ireland and the Irish Historical Society. The Royal Irish Academy, an All-Ireland institution, is considered to be the island’s leading body of experts in the sciences and humanities. Membership is by election only, following a rigorous peer-review selection procedure conducted by both national and international referees. A member from 1906, Kirk was elected President forty years later. The only other medical doctor to attain that position in the 235 years of the Academy’s existence to date was William Stokes, of Cheyne–Stokes respiration and Stokes–Adams attack fame.
Away from medicine and academia, Kirk was an accomplished gymnast in his youth, and enjoyed sailing. The Strollers Club was an amateur singing, not walking, group founded in the mid-19th century. Although he is reputed not to have been able to sing, he became President and until his final illness never missed a meeting or a dinner during his sixteen years in the role. He was also President of his gentleman’s club, the Friendly Brothers, where he was regarded as a gracious host and witty speaker, but at his best when making punch for friends after dinner, or acting as marker in the billiards room, where his lively conversation entertained everyone.

Kirk bequeathed his compilation of newspaper cuttings on Irish doctors (now termed the Kirkpatrick Newspaper Archive), his personal and professional papers, and also his collections of books written by Irish doctors, medical books published in Ireland, and manuscripts relating to medical matters, to RCPI. Included were 1100 books, some 3500 pamphlets and 126 manuscript items, all of which had been catalogued by him. His papers and the manuscript collection comprise the College’s Thomas Percy Claude Kirkpatrick Archive. Some idea of its extent may be gauged from the fact that the catalogue alone of its contents is well over 200 typescript pages long. The legacy as a whole serves as a truly outstanding resource for researchers.

The Kirkpatrick Archive includes a Register of Anaesthetics administered in Steevens’ during 1900, the one full year during which Kirk was anaesthetist to the hospital. It contains 306 records in all, 268 of which relate to anaesthetics given by him. Individual entries contain the date and type of operation, the patient’s name, age and preoperative condition, anaesthetic agent or agents and equipment used, remarks concerning the course of the anaesthetic, and information regarding the patient’s postoperative recovery. The names of the operating surgeons are conspicuous by their absence. Patient ages ranged from three months to eighty-two years, with a mean of twenty-four years. Fewer than ten were aged sixty years or over. Where anaesthetic agents were concerned, Kirk used gas (nitrous oxide) and ether in seventy per cent of cases, gas alone in seventeen per cent and chloroform, which he was soon to all but abandon, in ten per cent. For gas and ether, or gas alone, he preferred Clover’s apparatus, and he specifically mentioned Frederic Hewitt’s modification on a number of occasions; whether that was the version he employed at all times is unclear. He generally used Krohne
and Seseman’s version of Junker’s inhaler when administering chloroform and referred to Skinner’s mask in one case, and to catheters or mouth tubes a few times, but not often. The average duration of anaesthesia was about half an hour for both the gas/ether and chloroform groups, but just four minutes for those patients in whom gas alone was used. The longest anaesthetic was for one of the gas/ether patients, a lady who underwent surgery lasting almost four hours for intestinal obstruction secondary to tuberculous peritonitis. She died of haemorrhage fifteen hours postoperatively.

Books and manuscripts etc. owned by Kirk, but which had not been bequeathed by him to RCPI, were sold at auction in April and November 1855 by Sotheby’s of London. The two sales took place over five days during which over 1100 lots were sold; 310 items were from the seventeenth century or earlier while thirty-seven were incunabula, i.e. they had been printed before year 1501. The oldest artefact was a manuscript written in 1473, while the earliest printed book dated from 1480. The proceeds amounted to £13,709, equivalent to approximately £400,000 today. The highest lot price was £320, achieved for a collection of 650 books on the history of medicine.

Three of the more interesting items offered for sale were:
- A second edition (1855), of John Snow’s *On the Mode of Communication of Cholera* (sold for £17). The second edition of this book was the first in which Snow referred to the role played by the Broad Street pump in the 1854 cholera outbreak in Soho, London. Another copy of this edition was sold by Christies, New York for U.S. $52,500 in 2010.

Three years after his death, a large plaque in Kirk’s memory was unveiled close to the front door of Steevens’. In 1967, the first eponymous lecture of the Faculty of Anaesthetists at RCSI, now the independent College of Anaesthesiologists of Ireland, was inaugurated in his name (Figure 2). It was delivered on at least seven occasions over the following twenty years or so,
but not since. For some years, RCPI had an annual Kirkpatrick Award competition, open to all, for history of medicine research but this also appears to have fallen by the wayside.

Figure 2. Invitation to the inaugural Kirkpatrick Lecture of the Faculty of Anaesthetists, RCSI. Courtesy of the Royal College of Physicians of Ireland (MS/90).

In conclusion, Thomas Percy Claude Kirkpatrick is remembered in Ireland as an early anaesthetist and venereologist but, most of all, and especially by researchers in the field, as the single individual who, in his lifetime, did most to salvage and integrate the ephemeral material on which Irish medical history is based. He was, and remains, the historian without peer in Irish medicine.

Acknowledgements

The author wishes to acknowledge the assistance given to him by Ms Harriet Wheelock, Keeper of Collections, RCPI and Ms Francesca Charlton-Jones, formerly of Sotheby’s, London in the preparation of this paper.
References

10. Dr Steevens’ Hospital Register of Anaesthetics, 1900 (TPCK/2/2/3). Royal College of Physicians of Ireland Archive, Dublin, Ireland.
Understanding of respiratory physiology was greatly advanced in five decades from 1872 to 1922. Perhaps most notable in the many aspects elucidated was the oxygen-haemoglobin (Hb) dissociation curve, which is fundamental to understanding oxygen delivery and the parameters which the anaesthetist and intensivist may have to manipulate. Now taken for granted (Figure 1), it took much scientific work to produce. The essential features were developed through 50 years of scientific collaboration between Great Britain and Ireland, France, Germany, Denmark, and The Netherlands. This project required the development of techniques for accurate sampling and measurement of gases in air and blood.

Figure 1. Oxygen-haemoglobin dissociation curve (from Creative Commons CC BY-NC)

3 A version of this paper was presented at the Euroanaesthesia 2016 meeting held in London.
In 1872, Prof Eduard Pflüger, the Chair of Physiology in Bonn, was the first to understand that metabolism occurs solely in the tissues, and to recognise that the respiratory role of blood is merely to transport oxygen and carbon dioxide. By this time, Joseph Clover in London had instigated use of nitrous oxide for British dental anaesthesia. Use of pure nitrous oxide of course caused the patients to turn blue. The Nitrous Oxide Committee of the Odontological Society of Great Britain had tried various mixtures of nitrous oxide and oxygen, and in 1872 produced its second report. This noted that addition of oxygen produced much struggling and excitement, with imperfect anaesthesia. Clover’s nitrous oxide-ether apparatus of 1876 did not incorporate oxygen. If the facepiece was lifted too soon, the patient would rapidly “come out” of the nitrous oxide narcosis and, as the blood was not sufficiently saturated with ether, commence to struggle. However, once “under”, Clover lifted the mask regularly to allow the patient to breathe room air. It was probably difficult for many other anaesthetists to match Clover’s skill.

Paul Bert, the French physiologist, worked on gaseous partial pressures and in 1878 produced the first in vivo relationships between oxygen pressure and oxygen content. He reintroduced the idea of using oxygen with nitrous oxide. Noting that nitrous oxide must be administered pure to achieve anaesthesia, Bert inferred that the required tension of the gas was 1 atm. Or, looking at it the other way, to achieve 1 atm. nitrous oxide under normal conditions, one had to give it as 100%. BUT if one put the patient in apparatus where the pressure was increased to 2 atm., one could achieve the desired tension by a mixture of 50% nitrous oxide and 50% air. In 1880 came Fontaine’s ‘anaesthetic car’ – an air-tight tank, designed in accordance with Bert’s suggestion. The pressure in the tank was increased by pumping in air, which passed through a refrigerator to prevent the temperature rising by more than 1 or 2 degrees above ambient. From a large cylinder, the mixture of nitrous oxide and oxygen (at 10 atm. pressure) was passed through a separate tube to the patient’s facemask. By 1883 Bert realised the practical disadvantages/ expense of using nitrous oxide under pressure. So, he recommended a technique of using pure nitrous oxide for induction, followed by a mixture of 79% nitrous oxide and 21% air.

In 1884 John Scott Haldane, residing at 17 Charlotte Square in Edinburgh, was registered on the General Medical Council, and in the following year he
attained a MD from the University of Edinburgh. He went to Dundee in 1886 and performed experiments on sampling air with the Professor of Chemistry, Thomas Carnelley. They found that the air in homes of the poor had high percentages of carbon dioxide, hydrogen sulphide and bacteria. Later that year, Haldane went to Berlin for some exchange learning in the laboratory of Prof Ernst Salkowski, a leader in physiological chemistry. Next, Haldane took up an appointment in Oxford as a Demonstrator in Physiology.

In 1889 compressed oxygen became readily available in metal cylinders, enabling progress in inhalation anaesthesia. This facilitated the development of Hewitt’s nitrous oxide/oxygen apparatus in London.

In 1891, Christian Bohr, Professor of Physiology in Copenhagen, suggested that oxygen and carbon dioxide were secreted by the lung. This was incorrect, but it would take twenty years before scientists began to accept publications disproving it. Importantly, he also characterised dead space. J S Haldane and J Lorrain Smith went to Christian Bohr’s laboratory in Copenhagen in 1893, where Haldane observed Bohr’s methods of gas and blood-gas analysis, using the haematarometer. Haldane also took the opportunity to introduce the game of golf to Denmark! He supported Bohr’s theory that lung actively secreted oxygen into the blood. The following year (1894) Haldane experimented on gas and blood-gas analysis in coal mines in England. A blood sample suffused with gas was placed in dilution in a tube and its colour compared with that of an adjacent tube of ‘normal’ blood. In time this would develop into the ‘Haldane Haemoglobinometer’.

Also in 1894, C Gustav von Hüfner, Professor of Physiological Chemistry in Tübingen, Germany reported experimental evidence that 1g of Hb can bind with 1.34 ml of oxygen when fully saturated. This matched his theoretic value based on iron content. There was scepticism to his publication initially.

In 1899, Lorrain Smith then at the pathology laboratory in Queens College, Belfast investigated the effects of high oxygen tension on the lungs of animals. He was able to demonstrate inflammation and congestion, which became known as the “Lorrain-Smith effect”.

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JS Haldane devised his haemoglobinometer utilising a colorimetric method in 1901. The pink tint of a standard volume of blood saturated with carbon monoxide was compared with that of a standard solution. In 1902 came the Haldane-Barcroft blood gas analysis apparatus. Oxygen in a sample of blood was liberated by ferricyanide and the increased pressure was measured by a gauge, from which one calculated the volume of oxygen. Carbon dioxide was liberated by tartaric acid and similarly determined.

Christian Bohr described the “Bohr effect” in 1903 in Copenhagen. We now simply state this as “the decrease in oxygen affinity when the pH of blood falls”. In his original research, Bohr noted the reduced affinity for oxygen of dog and horse blood as the carbon dioxide content increased (causing increased acidity). The following year (1904), Bohr and his colleagues Karl A Hasselbalch and August Krogh, published this in the Scandinavian Archives of Physiology. They showed graphically that the oxygen-haemoglobin dissociation curve was shifted to the right by increasing carbon dioxide content.

The role of carbon dioxide in driving breathing was described in 1905. Haldane developed apparatus to snatch the last of the air from a full expiration – so called ‘Alveolar air’. He reasoned that the carbon dioxide in alveolar air was equivalent to that in arterial blood. With J Gillies Priestley he used the apparatus on the top of Ben Nevis (1343 m) and down Britain’s deepest mine, Dolcoath (a tin mine in Cornwall, -622m). The measurements were compared with the results from Oxford and a low-pressure chamber in the Brompton Hospital, London. They found that the weight of carbon dioxide in a given volume of alveolar air was constant, whatever the barometric pressure. They concluded by further experiments that carbon dioxide is the trigger to breathe, rather than oxygen. Haldane also tested the limits by experiments in a closed box, where very low oxygen tension became the drive. Haldane and Priestley then began to look at the influence of muscular work, but it was Nathan Zuntz in Berlin, who published the relationship between barometric pressure and altitude, as well as the metabolic needs of exercise (1906). In 1908 Prof Arthur Keith, the British anthropologist (Royal College of Surgeons) demonstrated differential expansion of the various components of the lungs.
Søren PL Sørensen in Copenhagen developed in 1909 the pH notation: the negative log of hydrogen ion (H\(^+\)) concentration. He found this useful because H\(^+\) concentration in the body is low relative to other cations; in a paper on enzyme activity he needed to write seven zeros after the decimal point.\(^{19}\)

In 1910 August Krogh and his wife Marie in Copenhagen produced seven papers disproving oxygen secretion by the lung.\(^{20}\) In the same year Zuntz organised an expedition to the Canary Islands (Tenerife) to investigate the effect of altitude on the position of the oxygen-haemoglobin dissociation curve. The team included C Gordon Douglas (a young Oxford colleague of JS Haldane) and Joseph Barcroft, the Cambridge physiologist. At the Alta Vista hut (3350 m) the members of the expedition had their blood sampled. J Barcroft showed that the dissociation curve was shifted to the right when PCO\(_2\) was adjusted to sea level value (40 mm Hg), the inference being an increase in acidity. However, when equilibration was done with subjects’ alveolar PCO\(_2\) at high altitude, the dissociation curve had the same position as at sea level. Barcroft argued that the pH of arterial blood was normal after acclimatization, from which he inferred that an increase of (? lactic) acid balanced the decrease in carbonic acid.\(^{21}\)

JS Haldane led an expedition to Pikes Peak (4300 m) in Colorado for more high-altitude experiments in 1911 – on the invitation of Prof Yandell Henderson of Yale. He took with him his laboratory technician, Mabel P Fitzgerald, and his colleague C Gordon Douglas. The results of the Pikes Peak experiments were reported in 1912. Haldane believed that acclimatisation was due to ‘the increased secretory activity of the alveolar epithelium…’.\(^{22}\) (This was wrong – we now know that acclimatisation increases red blood cell 2,3 DPG.)

Joseph Barcroft and EP Poulton, in Cambridge in 1913, made the oxygen-haemoglobin dissociation curve reproducible by standardising the conditions for plotting.\(^{23}\) Collaboration between the Physiological Laboratory, Oxford and the Institute of General Pathology, Copenhagen led to publication in the following year by Christiansen, Douglas and Haldane of what came to be known as the ‘Haldane effect’.\(^{24}\) This may be simply stated as ‘deoxygenation of blood increases its ability to carry carbon dioxide, and vice versa’. In fact, reduced Hb is about 3.5 times as effective as oxy-Hb in
carrying carbon dioxide. These actions facilitate uptake of carbon dioxide in venous blood and its release in the lungs.

After the introduction of chlorine gas as a German weapon by Fritz Haber in 1915, JS Haldane began work on a gas mask to protect against chlorine gas attacks in World War 1. Through 1916-17 Haldane’s oxygen apparatus was supplied to many hundreds of British and American forces in France. ‘Haldane equipment’ comprised a pressurized oxygen cylinder, a pressure regulator, a reservoir bag attached to the regulator, and a tight-fitting mask with non-return valves. The poison gas phosgene had to be dealt with from 1916. It is colourless with just a slight odour of musty hay. This is the gas for which oxygen therapy was primarily used in World War 1. Haldane argued against the notion that administration of oxygen is at best only palliative (not removing the cause of the problem). He wrote “the respite afforded by such measures as the temporary administration of oxygen is not wasted, but utilized for recuperation”. This represented a paradigm shift. He was duly awarded the Queen’s Medal by the Royal Society in 1916.25

Hasselbalch in Copenhagen in 1916, produced the log form of Lawrence J Henderson’s (1908) equation pertaining to buffers in the blood:

\[
\text{pH} = pK + \log \left[ \frac{\Delta}{[HA]} \right]
\]

This became known as the ‘Henderson-Hasselbalch equation’.4 In Groningen (north-east Netherlands) in 1918, Hartog Hamburger described the ‘Hamburger effect’ in carbon dioxide transport26, now better known as the chloride shift.

Towards the end of World War 1, Haldane investigated the puzzle of why addition of oxygen could be of little help to gassed victims whose breathing was shallow. At the 15th Canadian Field Hospital in Taplow, Buckinghamshire he devised experimental apparatus to investigate this, recalling Arthur Keith’s work on the varied opening of parts of the lung. He was assisted by Col. Jonathan C Meakins and Capt. J Gillies Priestley. Their resulting paper recognised the mismatch between ventilation and perfusion (1919).27
In 1920 the oxygen secretion theory (which Haldane had supported) was attacked. J Barcroft in Cambridge closed himself for six days in a glass cabinet with oxygen reduced to just 10% (equivalent to altitude 6000m) and used the direct method of sampling his arterial blood. His results refuted the Pikes Peak findings. Unluckily, Haldane dismissed the report! Next, in 1921-22, Barcroft led another high-altitude expedition at Cerro de Pasco (4330 m) in Peru. His team included JH Doggart (Cambridge) and JC Meakins (by then Professor of Therapeutics at the University of Edinburgh). They obtained good measurements and discovered diffusion limitation.

Thus, by 1922, all the ‘basics’ of the oxygen-haemoglobin dissociation curve had been discovered. In that year Haldane published his book _Respiration_. This set the bar for others to aspire to and did much to hasten understanding of respiratory physiology. Some refinements which came after 1922 include the following.

- Adair equation (GS Adair, 1925)
- Carbamino carriage of carbon dioxide (JKW Ferguson and FJW Roughton, 1934)
- Function of 2,3-diphosphoglyceric acid in erythrocytes: decreasing the affinity of oxygen and allosterically promoting release of remaining oxygen molecules bound to haemoglobin (R Benesch and RE Benesch, 1967).

While the pH notation is still considered convenient by analytical chemists and some physiologists, most clinicians now alternatively use actual H⁺ concentration in nmol/litre. This method aids understanding in treating severe metabolic acidosis with sodium bicarbonate, using 50-100 mmol quantities.

In the new millennium, several authors have referred to John Scott Haldane as ‘the father of oxygen therapy’.

References


7. *ibid*; 98.


11. *ibid*; 133.


Correspondence

Sir,

I very much enjoyed the paper on anaesthesia for liver transplantation by Dr Mike Lindop in the Proceedings for the Cambridge meeting 2019; 52: 21-22. However, I have to cast doubt on the statement that for the first liver transplant by Professor Roy Calne in 1968, the anaesthetist was Ronnie Millar (misspelled ‘Miller’ in the Proceedings).

As I was including Ronald Alexander Millar in another historical project, I contacted Dr Lindop to ask if he had a primary reference for Millar’s involvement. He held a copy of the original operation note, but this had a blank space for the anaesthetist(s) names(s). However; he was able to tell me that the exact date of the operation was 2 May 1968. I then contacted the theatre staff of Addenbrooke’s Hospital, Cambridge, who kindly sent me a copy of the theatre book for the day, showing that there were two anaesthetists: Drs Keates and Powell. There was no mention of Dr Millar. They told me that the operation note was typed from Professor Roy Calne’s dictation – he either didn’t know the name of the anaesthetist or didn’t think it important.

I also contacted Dr Aileen Adams, who recalled that George Keates (Consultant Anaesthetist at Addenbrooke’s) died some time ago, and Dr Powell who was a Senior Registrar at the time had moved somewhere else (not known to Dr Adams) to take up a Consultant post.

I established that Ronnie Millar was later Professor of Anaesthesia at the University of Glasgow, followed by being Professor at the Memorial University, Newfoundland, Canada. He died in 2015.

Alistair McKenzie

Editor’s notes:
  1. Dr Lindop was sent a copy of this letter but did not wish to make any comment
  2. This letter is published a year late, as no Proceedings was published in 2020.