

Historical Group

NEWSLETTER and SUMMARY OF PAPERS

No. 73 Winter 2018

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RSC Historical Group Newsletter No. 73 Winter 2018

David Knight (1936-2018)

ROYAL SOCIETY OF CHEMISTRY HISTORICAL GROUP MEETINGS

Some Chemical Consequences of World War 1

Wednesday 14 March 2018, Burlington House, Piccadilly, London

10.30-11.00: Registration, Tea or coffee

Session Chairman: John Hudson

11.00: John Nicholson, The Consequences of World War 1 on the Education of Chemists

11.30: Brian Balmer, Porton Down after World War 1

12.00: Alan Dronsfield, Fighting Cancer with Chemicals – The Mustard Gas Connection.

12.30–14.00: Lunch. This is not provided but there are various eating places nearby.

Session Chairman: Alan Dronsfield

14.00: Mike Sutton Munitions, Mergers and Military Imperatives: from WW1 to ICI

14.30: John Hudson, James Morton and the Formation of Scottish Dyes Ltd

15.00: Cliff Lea, WW1 – The Catalyst which Spurred the Development of Britain's First Onshore Oil Wells. 15.30–16.00: Tea

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appreciation of JM's activities perhaps should seek out the Wikipedia article on this company and explore some of the references therein.

Alan Dronsfield

PUBLICATIONS OF INTEREST

Ambix: The Journal of the Society for the History of Alchemy and Chemistry The following issue has been published since the summer 2017 **Chemical Heritage F**

agents. It caused the death of about 1 in 3,000 patients, in contrast to ether with a death-

them to interact electrostatically with "brain molecules" and thus show anaesthetic effects at lower doses compared to the latter group.

That John

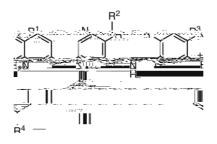
immunologically-mediated injury with some patients perhaps genetically predisposed to hepatotoxicity? - it became evident that the concept of a "safe period" between administrations had to be questioned, and the search for an ideal, and even safer, anaesthetic was not yet over. The second consideration that led to Halothane's demise was that work was being undertaken on another range of fluorinated compounds to assess their potentials as anaesthetic agents. The *Airco Inc.* company was naturally disappointed that its Fluromar anaesthetic was so rapidly eclipsed by Halothane, however it did not lose faith with the idea that another partially-fluorinated ether anaesthetic, even better than Halothane, might still be waiting to be discovered. And discovered it was – one of four commercial products, "Enflurane", "Isoflurane", "Desfluorane" and "Sevoflurane".

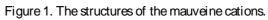
11. A. Dronsfield, M. Hill and J. Pring, "Halothane – the first designer anaesthetic", *Ed. Chem.*, 2002, **39**, 131 and *Proc. Hist. Anaesth. Soc.*, 2002, **31**, 57. Available at http://www.histansoc.org.uk/uploads/9/5/5/2/9552670/volume 31.pdf

Alan Dronsfield, Margaret Hill and John Pring

Mauveine – The Final Word? (5)

The last Final Word appeared in the summer 2014 *RSCHG Newsletter*. It was a good year for thin layer chromatography (TLC) studies of mauveine – there were three of them. The first was mentioned in the last article. John Plater described the dichromate oxidation of a mixture of *N-tert*-butyl-*p*-toluidine/aniline/o-toluidine (1 : 1.5 : 1.8), followed by de-*tert*-butylation with acid to give a mixture of mainly mauveine A and B as shown by TLC [1]. The structures of mauveines are shown in Figure 1. Next up, in a Spanish – United States collaboration, the mauveine product was synthesised according to Perkin's 1856 recipe [2]. TLC on silica gel using 6:1:3 *iso*butanol/acetic acid/ethyl acetate mixture as eluent revealed four purple spots and one red one. These were identified as pseudo-mauveine, red, R_f 0.32, mauveine A (0.56), B2 (0.63), B (0.70) and C (0.78). The Raman spectra of the separated components were obtained from the developed TLC plate using silver nanoparticles to elicit the surface-enhanced Raman spectra (SERS). SERS is a powerful extension of Raman spectroscopy which provides molecular vibrational data from exceedingly small samples. Chandrasekhara Venkata Raman (1888–1970) would have been astounded. The assignment of the normal vibrational modes of mauveine was aided by performing density functional theory calculations. Finally in November that year, Plater and Harrison disclose an





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Mauveines of known and unknown structure

powder Test for Aniline. A few drops of aniline are agitated with water, and the solution separated from undissolved amine by passing it through a moist filter. A small quantity of a clear solution of bleaching-powder gives a deep-violet coloration with the filtrate" [13]. In 1840, Carl Julius

The book is very clearly structured and has a glossary, so "dipping" is facilitated. The author condenses and combines sources as listed in his bibliography (history and philosophy of science books, scientific biographies,

speakers were former consultant anaesthetists with an interest in the historical/chemical aspects of their speciality. David Wilkinson, representing the President of the Royal College of Anaesthetists, "topped and tailed" the conference. The day was judged to have been a success, with several of our guests expressing a wish to attend our next whole-day conference on "World War 1 – Some Chemical Outcomes".

Alan Dronsfield

Anaesthesia Ignored: Why Doesn't Chemistry Give us the Answers?

David J. Wilkinson (Retired Consultant Anaesthetist, St. Bartholomew's Hospital)

Mankind has been using combinations of plant extracts for centuries in the hope of treating a variety of ailments. It is not surprising that the relief of pain and/or the creation of an unconscious state so that traumatic injuries could be treated more humanely would prove to be a feature of many early herbal manuscripts. The creation of a 'soporific sponge' and 'dwale' are two examples of this type of product and were undoubtedly used effectively for centuries. Using combinations of powerful alkaloids, the difference between therapeutic and harmful dosages would have been very difficult to determine especially as there were no standard preparations of each plant.

In Japan in the late-eighteenth century, Seishu Hanoaka produced a duplicatable product which was a combination of six plants after some thirty years of experimentation. Mafutsusan was an effective orally administered general anaesthetic and its preparation and use were taught throughout Japan during the early part of the nineteenth century. It was not until Western influences and the speed and simplicity demonstrated by ether inhalation to create a similar state that the practice disappeared.

With the demonstration in the USA that ether could create an anaesthetic state and the subsequent development of chloroform anaesthesia in the UK, the search was on for other potential anaesthetic agents. The only requirement for the trial of such agents was that they should be a volatile liquid! Innumerable products were tried, sometimes on animals first but often they were given to patients without any preliminary trials. Although several agents proved to be effective there were also series of cases that experienced very unpleasant side-effects.

By the start of the 1930s there were a series of gases and volatile liquids that were recognised as effective anaesthetic agents and chemists started to manufacture more potential agents. Halogenated hydrocarbons and ethers were the predominant agents and the ability to fluorinate such products that developed in the late 1940s changed the face of inhalational anaesthesia.

However, before chemists are blamed for not providing what anaesthesia would like to have, it should be recognised that the understanding of the receptors involved in anaesthesia is still at a rudimentary level and so it is very difficult to develop agents for indeterminate endpoints! The structural differences between complex ethers, hydrocarbons, and noble gases, all of which create an anaesthesia state, does little to solve this problem. It is to be expected that as soon as anaesthesia can determine exactly what it wants then a chemist should be able to manufacture it for our use. Until then we await research outcomes and in the meantime, seek to minimise adverse effects from the agents available for our use.

Davy, Nitrous Oxide and Bristol

Frank James (Royal Institution of Great Britain, London)

Frank James began by noting that his talk continued where his Wheeler Lecture of 2015 had finished. In this lecture he had discussed the fundraising endeavours of Thomas Beddoes and others in the mid-

Nitrous Oxide in Anaesthetic Practice: Some Reflections

John Pring (Retired Consultant Anaesthetist, West Cornwall Hospital, Penzance)

If only Davy, instead of saying "As nitrous oxide in its extensive operation appears capable of destroying physical pain, it may probably be used with advantage during surgical operations in which no great effusion of blood takes place" had declared "Hey, lads, this nitrous oxide will make a good anaesthetic – let's investigate!" he would have ended up twice as famous as he is now, and we would not have had to wait another forty years for anaesthesia!

Nitrous oxide is a colourless, slightly sweet-smelling gas, which boils at -88°C, and is produced by the thermal decomposition of ammonium nitrate above 250°

Surgical Relaxation: Crum Brown to the Present Day

Ann Ferguson (Retired Consultant Anaesthetist, Broadstairs)

"Relaxation" a term widely used in surgery and anaesthesia incorrectly implies that the subject still has control of their voluntary muscles. A more accurate term is *pharmacological paralysis*, and it is carried out, under very controlled conditions, by anaesthetists, not surgeons. How and why we do this, depends very much on the surgery.

The drug that everyone has heard about is curare, brought to Europe in 1744. It acts on the junction between a motor nerve and the muscle, causing flaccid paralysis. Neuromuscular blocking drugs, as exemplified by curare are unusual and perhaps unique in that knowledge of their mechanism of action and their use as tools in physiological experiments preceded their widespread clinical use by almost a century. Many physiological discoveries concerning cholinergic transmission have depended on the use of curare or tubocurarine. Claude Bernard showed, working with frogs, that curare paralyses motor nerves, but has no effect on the nerves of sensation. Alexander Crum Brown, doctor, chemist (eventually professor in Edinburgh) together with Dr Thomas Fraser, together won the Macdougall Brisbane Prize of the Royal Society of Edinburgh in 1868 for their paper "On the Connection between Chemical constitution and physiological action. Part one on the physiological action of the salts of ammonium bases derived from strychnia, brucia, thebaia, codeia, morphia and nicotia". This paper has considerable historical importance, as it constitutes one of the earliest attempts to make a systematic study of the relationship between the chemical structure and the pharmacological action of a drug. They showed that strychnine kills, but the same dose of methylated strychnine causes paralysis. It would be a mistake to suppose that they were trying to synthesize drugs which would cause neuromuscular blockade; they were merely trying to see how a change in the chemical structure of a substance changed its physiological action.

In the nineteenth and twentieth centuries, curare was tried as a cure for tetanus and there were attempts to use it in anaesthesia.

But cocaine had a number of drawbacks and chemists and physicians searched for an alternative. They were informed by a knowledge of the main structural features of cocaine, the correct structure being announced by Richard Willstätter in 1894. Several products were marketed, the most successful being *Novocaine*. This was used widely over the period 1905-1955. It was non-addictive and, unlike cocaine, was reliable in its action with virtually no cases of patient-collapse being reported.

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All of these developments took place in Germany, but the next major development was in Stockholm in the late 1930s. Attempts to synthetize an alkaloid, gramine, resulted in production of an isomer which was found to have local anaesthetic activity. A few analogues were produced, but none was better than procaine so the project stalled. However, one of the undergraduates who had helped, Nils Lofgren, returned to the subject for his PhD thesis, producing many homologous series of compounds as an exercise in structure activity relationships, then a 'new'

Anaesthesia: Present and Future: The Chemist's Challenges

David J. Wilkinson (Retired Consultant Anaesthetist, St. Bartholomew's Hospital)

In the decade following 1960, American chemists Ross Terrell and Louise Croix synthesised hundreds of fluorinated hydrocarbons for Ohio Medical Products in a search for more

A Common History

The two talks on *A Common History*, opening the main proceedings, were chaired in turn by the CEO of the RSC, Robert Parker, and the Executive Director of the GDCh, Wolfram Koch. First, Bill Brock (University of Leicester) spoke on "Anglo-German Chemistry 1821-1914". The Anglo-German chemical connection stems in considerable part from succession of the Elector of Hanover to the British throne in 1714 as George I. The personal link was broken only in 1837 when Queen Victoria inherited the British throne but could not inherit the throne of Hanover under Salic law. Hanover was annexed by Prussia in 1866.

George II founded the University of Göttingen in 1734 and this attracted British students. Edward Turner, a future professor of chemistry at University College London, studied there under Friedrich Stromeyer (1766-1835). A galaxy of later British chemists studied under Liebig at Giessen, Bunsen at Marburg and Heidelberg, Wöhler at Göttingen, and Hofmann in Berlin, and elsewhere in Germany. Among these were Williamson, Frankland, Tyndall, Dewar, and Ramsay. Germany had good laboratories and offered the PhD degree (introduced in England only in 1919). Germany was cheaper than England to live in, and had superb countryside. Germans also travelled to England, most famously Hofmann to establish the Royal College of Chemistry in 1845, with laboratories opened in 1846 facing onto Oxford Street, and the industrialist Ludwig Mond. A rift was caused by the Great War and particular the 1914 letter signed by ninety-three German intellectuals including Baeyer, Fischer, Haber, and Ostwald. The rift began to heal after 1929. The PhD now being available in Britain, Germany became more of a destination for post-doctoral workers such as Todd.

The next talk was given by Brigitte Osterath a science journalist from Bonn and contributor to *Nachrichten aus der Chemie*, who spoke on "Searching for Traces of August Wilhelm von Hofmann". August Wilhelm von Hofmann co-founded the German Chemical Society in Berlin in 1867 and became its first president, and its father figure. The idea for establishing a chemical society in Germany was brought back by Hofmann from London where he had lived and taught at the Royal College of Chemistry (RCC) for twenty years. Early on he became involved in the Chemical Society of London of which he was President from 1861 to 1863. In London, numerous sites associated with Hofmann remain today, including his home in 9 Fitzroy Square and the former site of the RCC at 299 Oxford Street, both with plaques. In Berlin, though, almost all memories of him were destroyed in WWII or demolished later on. Even at the site where the German Chemical Society was founded in 1867, little of its former glory remains: the building was demolished when a railway line embankment was built in 1876 – nowadays, the homeless reside under the underpass. Beside it, in front of the university library of the Humboldt University of Berlin, the German Chemical Society (GDCh) has now installed a Historic Chemical Landmark plaque.



Delegates listening to Brigitte Osterath's talk on "Searching for Traces of August Wilhelm von Hofmann". Images are the copyright of the RSC and are kindly reproduced with their permission

Chemistry and Global Challenges

The next four talks came under the heading of Chemistry and Global Challenges, alternately chaired by Nevilles.

The Council Chamber housed numerous historical exhibits and placards. There were essays by Bill Brock on the Albert Medal, on Hofmann's celebrated Friday evening discourse at the Royal Institution on 11 April 1862, concerning colouring matters from coal, and on

molecular sciences? New challenges in the history of chemistry and the molecular sciences", concluded the conference.



Group photo in Bymarka recreation ground, where the 11ICHC conference dinner took place. Photo credit: Mentz Indergaard, NTNU

The social programme included demonstration of a fifteenth century distillation furnace at the University Museum, an excursion to Sverresborg Open Air Museum, an organ concert at the Nidaros Cathedral, a conference dinner, a stroll along the Trondheim fjord, and a full-day excursion to the UNESCO World Heritage Site of Røros, a seventeenth-century mining town.

To add a personal note, I was pleased that the ICHC was well attended after a couple of conferences where attendance had been declining. Once again, however, British attendance was low, only six in total including Hasok Chang as a keynote speaker and myself. This was doubtless partly a result of the high cost of living in Norway, which seems to become more and more eye-