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Chris Hull became ‘first assistant’ in the Department of Anaesthesia in the University of Newcastle-upon -Tyne in 1967 and was promoted to a personal senior lectureship in 1970ⁱ.



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He became Professor of Anaesthesia in Newcastle-upon-Tyne in 1981 following the retirement of EA Cooper. Hull was an ‘equipment man’ but also had a strong interest in pharmacokinetics.

Equipment

The first publication describes the development of a blood pressure recorder [1]. The development is described in great detail; it was made up of a two compartment brachial cuff with appropriate transducers to detect pressure changes, an air pump to inflate the cuffs and a method to deflate the cuffs in a linear manner. Artefact rejection was a major part of the device and it came with a pen recorder. It was able to produce a trend printout. The electronic control system was complex and, as was fitting at the time, was flameproof – explosive anaesthetics still being in use at this time. Under the subheading “Future Development” it was apparent that a pre-production prototype was under construction with upper and lower limit alarms, manufactured by Newmark Instruments Ltd. It only measured the systolic pressure but it was obviously the precursor of the famous Criticon Dinamap.

ⁱ Development of academic anaesthesia in the UK up to the end of 1998
J F Nunn. British Journal of Anaesthesia. London: Dec 1999. Vol. 83, Iss. 6; pg. 916, 17 pgs

ⁱⁱ Photograph courtesy of CJH.

In the following year another equipment-related publication, this time as a result of a presentation to the Anaesthetic Research Society at the 1969 Bristol Meeting. "The impedance cardiograph: development and applications." [2] He describes the shortcomings of existing instruments and explains how these faults could be overcome. One of the main problems was the summation of the cardiac signal and the respiratory signal...using the technique of 'computer of average transients' and the ECG signal as a trigger for this analysis. Using a PDP-8/L computer he was able to do the 'averaging' using only a few complexes and the resulting output changed rapidly with changes in stroke volume. These two papers together show a great technical know-how.

In 1971 another presentation to the ARS, "Development of an artefact-immune wave pulse counter"[3]. As the author states it describes the aim rather than the outcome, of which he makes qualitative comments. The detection of the QRS spike on the ECG was considered better than the peripheral pulse. He outlined all the problems associated with existing devices and then proceeded to produce a much improved, reliable version. There were no quantitative results with this presentation. I do not know Chris Hull's background but this work to-date suggests a very good knowledge of electronics. He was still unhappy with its performance and in 1973 presented a new improved version [4] to the ARS which was hosted by the University of Liverpool but held at Imperial Chemical Industries, Pharmaceutical Division in Macclesfield. The system now was "... immune to diathermy, electrode artefacts, movement artefacts, and mains pickup. Pacemaker potentials [were] also rejected, so that the true capture rate during pacing [could] be accurately assessed". This was a significant development.

In 1973 [5] a data logging system was described for the conversion of the data streams from physiological monitors in the labour ward to a magnetic tape. Data were collected at 10s intervals, processed through a 'specially constructed interface' and included both clinical measurements and information from infusion pumps; it was said that a C60 cassette tape could hold more than 20hours of recording. This is very advanced for its time.

The Anaesthetic Research Society (ARS) featured prominently in Hull's publications and in 1975 was hosted in his hometown of Newcastle upon Tyne. Both pharmacokinetics and computers were now very much in vogue and the use of the analogue computer promised to be very helpful in analyzing the resulting data of studies. According to Hull the previous attempts at computer analysis were "complex and had limited application"ⁱⁱⁱ. His version, with the help of McLeod [6], gave solutions to the pharmacokinetic data and allowed them to simulate other situations with, for example, changes in renal function, predictions of duration of drug action were therefore possible. This presentation was followed by a full paper in 1976 [7]. In this paper the technique used was demonstrated using serial plasma concentrations of fentanyl and pancuronium.

The last three publications in this group of 'equipment' related articles are about a 'demand analgesia apparatus' [8-10], 1979, 80 and 1981. The first was another ARS presentation, the second a letter and the third a full paper. The device spoke to patients ("in any language") and the dosage was limited by a reduction in the respiratory rate, it also had additional fail-safe mechanisms. Using fentanyl there was no evidence of cumulation during a ten patient study. Secher^{iv} first advanced the idea of an analgesic demand system in 1971. The 'Cardiff Palliator' was described in 1976^v and this paper of Hull's preceded Kenny's by five years^{vi}. Every six minutes the device instructs the patient to press the button twice if in pain; if the patient presses the button the device then reassures the patient that the drug is being administered. A peristaltic pump drove the drug administration. A mercury-in-rubber pneumograph transducer monitored the respiratory rate and if the interval between respirations exceeded eight seconds the cycling of the device was inhibited. The control algorithm was complex. In the discussion it was said

ⁱⁱⁱ Fleischli, G., and Cohen, E. N. (1966). *Anesthesiology*, 27, 64.

^{iv} Sechzer, P. H. (1971). *Anesth. Analg.* (Cleve.), 50, 1.

^v Evans, J. M., McCarthy, J. P., Rosen, M., and Hogg, M. I. J. (1976). *Lancet*, 1, 17.

^{vi} Gillies, G.W., G.N. Kenny, and C.S. McArdle, *Journal of Medical Engineering & Technology*, 1986. 10(2): p. 55-7.

that a microprocessor-based system was being developed by Janssen Scientific Instruments.

Electrical Hazards

Electrical hazards have been a topic of editorials and comment from the early days of anesthesia and Hull published four[11-14]. The first in 1973 was in the Annals of the Royal College of Surgeons of England and it was a special edition dealing with all aspects of hazards in the operating theatre... Hull's contribution was about electrical hazards. He explained the problem associated with 'transcardiac' current, 50mA upwards can cause ventricular fibrillation but, unless the heart is damaged, a current of 5 A when switched off may still be followed by sinus rhythm. The contact between the source of the current and the body tissues is of importance; dry skin is very protective, wet hands are not. He mentions the merits of good maintenance of cables and the American system of isolating transformers. This is followed by a section on microshock.

Microshocks are possible when intravascular leads are present (pacemakers) or electrolyte filled catheters. The current will be so low as to be not sensed by the patient or physician, the resulting VF unexpected. Isolated circuits are mandatory, battery driven devices ideal as long as they are not earthed.

Five years later he writes a detailed account of electrocution hazards in the operating theatre and goes into great detail...it is a worthwhile read for those interested in the subject even 30yrs later. It is the only paper where the author has seen 'Murphy's law' quoted. The 1979 Anaesthesia editorial quotes T.L.Martin from "Malice in Blunderland"^{vii}, "Nothing can be made foolproof, because fools are so ingenious". This is an editorial following the death of a 20yr old by electrocution in an operating theatre, in modern parlance 'all the holes in the Swiss cheese lined up' and death was the result. He laid out the problem (paraphrased) of the costs of

^{vii} Malice in Blunderland, McGraw-Hill, New York, 1973

maintenance of, or replacing of, old equipment and the appropriate communication required between maintenance staff and the theatre managers/users.

Modeling

The development of electrical analogue computers as referred to above [7] facilitated the study of drugs in a way that minimized or avoided human or animal experimentation. In 1978, with Van Beem, he addressed the problem of the model not accounting for the observed effects of muscle relaxants [15]. To the simple two-compartment model for pancuronium they added a receptor compartment and then the model behaviour came to resemble the observed effects in animal experiments. The model, with parameters consistent with renal failure, showed a biphasic response, small doses of pancuronium demonstrated marginal resistance with normal recovery, whereas large doses resulted in delayed recovery in a dose-dependent manner.

Another paper in 1980 used the model to compare fazadinium and pancuronium and was used to compare potencies [16]. A 'general solution' to the three-compartment model was published in the appendix. ^{viii}

At this point we will continue with the muscle relaxant studies but opiates were also scrutinized [17, 18].

In the B.J.A. of February 1983 his editorial addressed the pharmacokinetic problems associated with atracurium [19]. It was in this issue that the first account of the pharmacokinetics of atracurium was published^{ix}. Hull outlines the differences between the clearance of atracurium (by the Hofmann reaction) and the clearance of previous muscle relaxants by a combination of liver and kidney function. However despite conceptual differences, and a possible array of different models, he

^{viii} The author wishes to thank Chris Hull for the use of his pharmacokinetic algorithms in his own research.

^{ix} Ward, S., Neill, E. A. M., Weatherley, B. C., and Corall, I. M. (1983). *Br.J.Anaesth.*, 55,113.

explains how the conventional two-compartment model would be equally valid for atracurium.

“How far can we go with compartmental models?” [20] was the subject of an editorial in *Anesthesiology* in 1990. The discussion in the editorial was centred on two papers in the same issue that were trying to evaluate the effect of age on pharmacokinetics^x. Both papers were introducing a way of looking at data that he thought might be confusing. He advocates the use of simple rather than complex models – the greater the complexity the more uncertain being the value of some of the variables used. He discusses the use of an “effect” compartment and how this minimizes the measured differences between drug concentration and effect. He wants clarification over the various terms relating to parametric and nonparametric models. The problem he is addressing is really complex; (the fact that thiopentone is partitioned into lung tissue in the early distributive phase) and he points out the limitations of both studies but both studies suggest arrived at similar conclusions – distribution of thiopentone from the central compartment to the periphery is slowed with age and that body weight is poor at predicting the pharmacokinetics. He then goes on to describe how the problem might be resolved.

His final (team) paper on the pharmacokinetics of muscle relaxants was in 1996 [21]. They studied cisatracurium in an attempt to elucidate the differences between the young and the elderly. The clinical difference of interest was the slower onset in the elderly. Other differences were marginal.

His other pharmacokinetic publications are [17, 18, 22-27].

Miscellany

In 1969 Hull was part of a team at the Royal Victoria Infirmary in Newcastle investigating methods of preserving liver function in cadavers[28, 29]...they worked on pigs and the 1969 presentation to the Surgical Research society indicated real success. A variety of regimens were used but the one that

^x Avram MJ, Krejcie TC and Henthorn TK. *Anesthesiology* 72;403-411,1990 and Stanski DR and Maitre PO *Anesthesiology* 72;412-421,1990.

seemed to succeed was that used in Group 3. In this group “the liver was cooled and stored for a similar period [20-25minutes] by perfusion with a preservative solution containing high concentrations of potassium, magnesium, and bicarbonate, together with Dextran, glucose, and insulin.” It was shown that ischaemic changes were minimal and subsequent function excellent. Although the first liver transplant had taken place in 1963 it remained an ‘experimental’ technique until the eighties because the survival rate was at that time very poor^{xi}.

In 1979 they investigated extracorporeal hepatic support using the pig liver [29]. Calves were connected to a pig liver on two occasions and these perfusions were tolerated for 6-7 hours. Some calves with induced liver failure also had repeated perfusions and survival was prolonged, one made a complete recovery. The immunological response was relatively benign. This work demonstrates the complexity of the work being carried out at the RVI in Newcastle and potentially of great clinical significance.

The topic of pain management occurs in several papers – a 1983 clinical trial of alfentanil for short surgical procedures [30] compared with fentanyl. Alfentanil had more post induction apnoeas and more postoperative nausea and vomiting when associated with ergometrine. Three years later alfentanil for gall bladder surgery [31] and the following year a case report of alfentanil for a caesarean section complicated by aortic stenosis [32].

An interesting study of extradural diamorphine vs. the same drug intramuscularly showed no significant difference in pain relief...however, analgesia was more prolonged when the diamorphine was given by the extradural route [33], this was in 1983.

Lignocaine and propofol associated pain was addressed in 1985 [34], and the whole topic of control of pain in the perioperative period in 1988 [35].

Three publications in the 1990s are of a non-clinical nature. In 1994 is an article, which is well worth reading, on the responsibilities of being an expert

^{xi} http://en.wikipedia.org/wiki/Liver_transplantation

witness [36]. It covers many practical aspects of the methodology that should be followed and how to produce the report. Not least amongst the many gems is the advice that the report should not depend on whether one is an expert for the defence or the prosecution, and to determine, within the limits of the evidence available “the most probable sequence of events” and causation. Anybody who is asked to take on the role of an expert witness should read the article carefully.

“Awareness is due to negligence during general anaesthesia for caesarean section” [37], a very strongly worded proposition which was opposed by J Thorburn of the Western Infirmary Glasgow. These were in fact arguments around the subject of the use of volatile anaesthetic agents during caesarean section and the opposing risks of awareness (too little) and uterine haemorrhage (too much). In most debates the proposition is strongly worded, as here, and it does not take into account the variability of response between patients (as is pointed out by Thorburn). The modern concepts of open disclosure of adverse events *without blame* have not quite permeated this debate. Thorburn’s comment about there being “clear evidence of stress response” in many instances of awareness is not reassuring... a stress response may occur during surgery without awareness and is therefore has low diagnostic strength.

The final publication, on anaesthetic risk [38], was a record of a talk given to the Medico-Legal Society on the 8th January 1998, it was given at the Royal Society of Medicine; he was replacing Professor Aitkenhead (Nottingham) who was unavailable. He explains to a mixed audience that adverse events during anaesthesia can range from ‘misadventure’ – where nobody could have predicted the event, through slips and lapses to bad decision making due to ignorance. He also explained that equipment could be designed in such a way that due to the ergonomics errors are likely to happen, he called them ‘latent errors’. He described the early deaths from anaesthesia in the 1800s and the early attempts to determine the causes of sudden death, and moved on to more recent studies including the

CEPOD^{xii} studies, AIMS studies^{xiii} and the use of closed claim records. Showing the safety of new monitors is difficult, the classic is the pulse-oximeter – Hull reports that Moller in 1993^{xiv} studied 20000 patients, there was a 19 fold increase in the detection of hypoxaemic episodes and half the number of ischaemic changes, but he was unable to show any difference in mortality. It was obviously a complex topic – and at that time, from reading his final comments it looked as though, at that time, there was the threat of withdrawal of legal aid for medical negligence claims. This was an interesting talk at the end of his career.

Hull had a range of interests...from ‘mechanical’ electronic devices, to the complexities of pharmacokinetics and dynamics, from clinical problems to medico-legal argument. He was the sole author for 50% of his publications, a significant body of work.

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^{xii} <http://www.ncepod.org.uk/studies.htm>

^{xiii} Runciman WB. The Australian Patient Safety Foundation. *Anaesth Intensive Care* 1988;16(1):114-6

^{xiv} Moller, JT, Pedersen, T, Rasmussen, LS, et al (1993). *Anesthesiology* 78,436-444

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