

John E Utting

MA MB BCHIR FFARCS

The University of Liverpool appointed J. E. Utting as professor and head of department of anaesthesia in April 1977 and he retired in December 1993. The University Department of Anaesthesia was in the Royal Liverpool Hospital.



Of the 48 publications presented here 19 were investigations into the actions of neuromuscular blocking agents...it could be reasonably considered that this was his main interest. These studies came at a time when two new drugs came on the market simultaneously; atracurium and vecuronium were both first trialled in 1979.

His interest in acid-base balance and awareness is also notable.

Acid Base research

Utting's first publication, with JS Robinson, was about acid-base matters. The problem of measuring acidity of plasma and blood and the buffering components had been under investigation for some time; Rosenthal 1948, Astrup 1956, Nunn 1959, and resulted in the publication of the Siggaard-Andersen nomogram in 1960ⁱⁱ. They described the new silver/silver chloride electrode and the interpolation method for the estimation of pCO₂ in very small quantities of whole blood [1].

In 1969/70 he, together with Fadl, published four papers. The first [2] a study of maternal acid-base during the first and second stage of labour. They

ⁱ Courtesy of Liverpool Society of Anaesthetists. <http://www.lsoa.org.uk/>

ⁱⁱ Siggaard-Andersen, Ole; Engel K (1960). A new acid-base nomogram. An improved method for the calculation of the relevant blood acid-base data. *Scan J Clin Lab Invest* **12**: 177

found that arterial pCO₂ was lower than in non-pregnant women and the pH higher. This was enhanced by the end of the first stage; epidurals and drugs had little effect.

This was supplemented by investigation of the variability of pK1' during labour [3] ⁱⁱⁱ. The value determined was 6.106 at 38°C (SD 0.011), identical with non-pregnant controls.

Hyperventilation during pregnancy was the third publication in 1969 [4], a few paragraphs in Thorax. Their results showed that the 'normal' hypocapnia of pregnancy was associated with near normal lactic acid concentrations, concomitant metabolic acidosis and near normal pH. They said their results confirmed the belief that the respiratory muscles were not responsible for the lactic acid.

The last with Fadl [5], although published in January 1970, was actually a report of a presentation to the Royal Society of Medicine in April 11th 1969. It is an abridged version of an overview of their understanding of acid base changes during pregnancy.

Neuromuscular blockade

In 1970-71, with Hassan Ali as the first author, there were four papers on the subject of the method and quantitative assessment of neuromuscular block. Similar concurrent work was being done by many others.

The first - Stimulus frequency in the detection of neuromuscular block in humans [6]. To paraphrase... two methods of assessing neuromuscular block had been described; the height of the recorded twitch tensions in response to single stimuli applied at differing frequencies and reduction in amplitude of twitch tensions in response to a short train of four stimuli.

They found using the first method that as the frequency of stimulation was increased there was reduction in the amplitude of the recorded twitch response. The reduction appeared to depend on the degree of curarization. For the second method a short train of four stimuli at 2 Hz was used; again there was a progressive fade of successive twitch responses depending on the degree of curarization. It was therefore suggested that, using the first method, the amplitude of the twitch response at a higher frequency expressed as a percentage of that at the slower rate and, using the second method, the last

ⁱⁱⁱ pK1' being a component of the Henderson-Hasselbalch equation.

response of the train of four expressed as a percentage of the first might be useful in measuring degree of neuromuscular block. The latter is now the most commonly used technique.

On June 27 in 1970 the subject of quantitative assessment of residual curarization in humans was presented at the Anaesthetic research Society meeting in Aberdeen [7]. Full papers were published in 1971, parts I and II.

I [8]: This described a method for assessing the residual degree of neuromuscular blockade (after reversal) without the need for a control measure. In the study they did use control measurements but found that the control/T1 ratio^{iv} was well correlated with the T1/T2 and T1/T4 ratios, so a control measure would not be necessary.

II [9]. This paper is similar; a train-of-four stimulation pattern was repeated at 10 second intervals. They used the ability to lift the head as an assessment of recovery from neuromuscular blockade and this was found to be related to the T4/T1 ratio and that a ratio of <0.6 was associated with obvious muscle weakness; modern work would suggest >0.9 for adequate reversal.

This work has stood the test of time.

The work on atracurium started in 1982 and was spread over six years. Four were on its use in patients with renal failure (or anephric) [10-13], one about its use in a patient with myasthenia [14], one with oesophageal varices (usually indicative of liver disease) [15] and three others [16-18].

The team worked with vecuronium at the same time; renal disease [13], liver disease [15, 19], myasthenia [20] and use of neostigmine [21].

Renal / Liver disease

[10]: In 21 anephric patients it was possible to give incremental doses of atracurium without evidence of cumulation. Even with high doses there was no evidence of residual curarization. It was stated that "This finding would seem to be compatible with what is known of the pharmacology of the drug."

[13] This was a comparative study in patients with or without renal function using vecuronium, atracurium, and tubocurarine. Vecuronium was given to 21 normal and 21 anephric patients and there "*were no gross difference between the two groups in the effect or in the duration of action of either initial or incremental doses, except in two anephric patients who were resistant to the agent.*" The duration of action of increments of atracurium and vecuronium

^{iv} In the train of four stimulus pattern the resulting muscle twitches are labelled T1, T2, T3 and T4.

were not greatly different, the behaviour of vecuronium was similar to that of atracurium. However tubocurarine was shown to be longer acting and *“considerably less predictable. This was particularly so in the anephric group, in which its action sometimes persisted after neostigmine had been given.”*

[15] The effects of atracurium and vecuronium were described in patients with portal hypertension and liver dysfunction. There was no evidence of gross resistance. However, ...” *the method of elimination would suggest that atracurium may be the better drug in patients with severe liver dysfunction, but the use of small doses of vecuronium is not contraindicated in this type of patient.”*

Myasthenia is an uncommon condition. If anaesthesia is required the patients can be exquisitely sensitive to neuromuscular blocking agents. Two papers are presented here, one with atracurium and one with vecuronium [14, 20]. A third is about an association with carcinoid [22]. The two papers with atracurium and vecuronium are similar...in each case they used one fifth of the normal induction dose; for vecuronium this was found to be too small so they subsequently doubled the dose. They found that with these diminished doses they could maintain satisfactory muscle relaxation and good reversal with neostigmine at the end.

The third paper has to be at the extreme end of rarity. The carcinoid syndrome is rare (about 1:100,000) and myasthenia is rare at about 1:30,000; the combination 1:3,000,000,000. Vecuronium was used, in reduced dosage, as it does not release histamine.

‘Awareness’

Using the Google Ngram viewer with the keywords *‘awareness during anaesthesia’* the topic started to take off around 1967, and first peaked in 1976. A second peak occurred in 1999, probably associated with the use of BIS, a processed EEG monitor.

The first investigation [23], in 1970, assessed recall and dreaming under nitrous oxide and muscle relaxant anaesthesia. Tape-recorded music was used as a stimulus. No episodes of awareness were detected. However, 44 per cent of the patients dreamed and two-thirds of them could recall details. Hypocapnia, part of the ‘Liverpool technique’ (or Gray’s technique), did not prevent dreaming.

This study coincides with his work with the train-of-four pattern of electrical stimulation to determine the magnitude of neuromuscular blockade so it is not surprising that at this time patients were not always adequately

paralysed with the neuromuscular blocking drugs and often moved. Patients who did move were more liable to dream than those who did not. Half of the patients described waiting for surgery as the most unpleasant part of their surgical experience, 20% considered postoperative pain was the worst, the third ranked complaint was being asked to lift their head when they were unable to do so. Unpleasant dreams came fourth.

Did premedication or the use of volatile agents influence dreaming [24]? This 1971 paper had four groups of patients, an unpremedicated nitrous oxide only (with muscle relaxant, as above), a group with morphine premedication, another using halothane and the last with methoxyflurane. In group 1- 57% of patients dreamed; group 2 - 23%; group 3 - 0% and group 4 - 23%. Awareness was not definitely diagnosed but a number of dreams were associated with the site of the operation.

In 1972 a letter to the British Journal of Anaesthesia [25] highlighted the problem of awareness further. In a study of 90 patients two presented strong evidence of being conscious during the surgery. This study was to show that giving halothane for fifteen minutes either at the beginning or the end of the anaesthetic did not abolish the risk of dreaming, or in this case, overt awareness. This was strong message that the 'Liverpool technique' was unsatisfactory.

This work was later presented in the Phillip Gett^v memorial lecture [26].

Miscellaneous

A study of **perioperative complaints** [27]. One hundred patients were given a personality assessment (Eysenck and Eysenck, 1964) a day before their operation. The day after a standard anaesthetic the patients filled in a questionnaire about their experience. The patients "neurotic" score was higher than the general population; upper abdominal operations had greater scores than other procedures. The lie score was also higher than the general population! Pain, preoperative anxiety and the passage, or presence, of a nasogastric tube were also major complaints.

The lie score is of interest ... the lie scale was "*included to detect individuals "faking good".*" One of the questions on the lie scale, for example was

^v Phillip Gett was Director of the Intensive Care Unit at Sydney Hospital. He was shot by a robber in New York in 1974.

"Are all your habits good and desirable?" Eysenck's view was that a lie score of 4 or 5 would suggest the answers were not acceptable. However if they excluded all patients with high lie scores the results from 28 patients would have been rejected. Other workers have questioned the validity of the lie score (Knowles and Kreitman, 1965).

An interesting foray into patient satisfaction. At least the use of nasogastric tubes has been minimised over the last four decades.

Postoperative pain: 1976 [28]. Smith and Utting were commenting on the poor quality of postoperative pain management. To quote *"The drug treatment of postoperative pain is fundamentally unsatisfactory with the drugs at present available; any improvement is likely only to be marginal. The hope would seem to be that the subject will be given more prominence in the education of both doctors and nurses. Patients, too, should be told that asking for an analgesic drug is not necessarily a sign of frank cowardice."*

The money motive: [29]... this was based on a paper that was read at a symposium on *Money and Medicine* in Manchester, November 1975. It is worthy of a 'full read'. It describes the social state at the time, about the union fights with the government of the day and the call for doctors to go on strike^{vi}. He describes reasons why doctors have higher than average salaries, about the proximity of doctors to the public and the confidence that the public has in doctors. "...our strength becomes our weakness: our proximity to our patients may make them think highly of us, but it also makes us think highly of them. It is difficult deliberately to ignore someone in such close proximity merely to obtain one's own way." He expressed the view that striking would diminish goodwill. He also attacked the time spent in private practice at the expense of the 'main activity', work in the National Health Service.

He stated that it was the freedom in the practice of medicine that was more important than the money motive, and that it was of even greater importance to the patient.

^{vi} A strike was called by junior doctors and some NHS consultants involved in private practice, who had rarely been seen before in the NHS hospital, turned up to 'man-the-pumps'. There was no compulsion to strike and no hard feelings to those who felt it against their principles.

Human misadventure in anaesthesia: [30] Since the early audit by Beecher and Todd of anaesthesia related mortality^{vii} many morbidity and mortality studies have been published. This presentation by Utting was based on the data collected by the two other authors (T.C. Gray and F.C. Shelley) about anaesthetic accidents reported to the Medical Defence during the period 1970 to 1977. In general usage "*misadventure is taken to be an unlucky chance or accident*". He made the point that human misadventure in anaesthesia is not as frequent as human failure. Six hundred and two anaesthetic accidents were reported during the eight-year period; 60% were either deaths or cerebral damage. He made the point that cerebral damage can be a greater catastrophe than death. Faulty technique was thought to be responsible for half the events and failures of postoperative care another major, and avoidable, cause. "*Over all error was deemed to be twice as common a cause of death and cerebral damage as was misadventure.*"

It was good to see the understanding of misadventure being dissected with human failure (error) being part of the picture...this was to be further dissected by subsequent investigators; JT Reason being, probably, one of the most well known^{viii}.

Pitfalls in anaesthetic practice [31]; this was part of a symposium on complications and medico-legal aspects of anaesthesia which follows on from the previous section, but almost a decade later. It is a comprehensive article and has a section on 'Defensive anaesthesia'; that is to protect the anaesthetist from litigation. To quote - "*Features of practice which are more of medico-legal importance than direct patient benefit*"; note-taking, preoperative investigations on fit, healthy young patients, peer pressure for 'good medical practice'. He describes the problem of not re-using halothane within a 28 day period when the danger of halothane hepatitis is really rare and one may be forced by peer pressure to use something that may have greater risk, It is a good read.

Anaesthetists, lawyers and the public: [32] This was a letter in response to a previously published article about anaesthetists, lawyers and the public. Utting writes a strongly held opinion about medics vs. lawyers. He had obviously spent 15 years sitting in Courts of Jurisdiction and also, occasionally, acting as

^{vii} Beecher. H.K and Todd. D.P. Ann. Surg. 140:2-35 (1954)

^{viii} Reason JT. Human Error. Cambridge University Press. 1990

an expert witness. He was of the view that the competence, expertise and dedication of doctors exceeded that of lawyers. He described the apparent injustice of an anaesthetist culpable of a medical accident not being reprimanded but a porter being dismissed for the theft of £2. He believed that we, the medical profession, should be less inhibited about criticising our colleagues.

The era of relaxant anaesthesia [33] This is an editorial on the 50th anniversary of the introduction of curare. He describes the 'tetrad' of anaesthesia, "narcosis, reflex suppression, muscular relaxation and "controlled apnoea" ". By controlled apnoea he meant controlled pulmonary ventilation. It is an historical review.

As we get older we get more interested in history and the same is true here. In 2002 he writes on the subject of "*Matthew Turner: surgeon-apothecary of eighteenth-century Liverpool. His life and background*" [34].

Utting has a relatively small number of publications compared with some other academics but they are of high quality, have stood the test of time and show a great deal of thought, both scientific and social. A really interesting bibliography.

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