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From 1963-65 John Norman was a research fellow in the Department of Physiology in Leeds. He was lecturer and then senior lecturer at the Postgraduate Medical School between 1967 and 1975 becoming the professor and head of department in 1975 in Southampton.. He retired in 1988¹.



John Norman wrote 16 editorials, five reviews, 10 letters and 45 papers.

His first two papers in 1965 were related: "*Simple Methods for the Determination of the Concentrations of Carbon Dioxide and Oxygen in Blood*" and "*A system for the measurement of respiratory and acid-base parameters in blood*". The first described electrode systems for the measurement of carbon dioxide and oxygen concentrations in blood with which they achieved accuracies similar to those of the classic techniques of Van Slyke and Neill (1924) [1]. The second – a similar paper using electrodes for the determination of pH, pCO₂, and pO₂, very quick at the time, a total time of 30 minutes [2].

The topics that Norman et al. covered were blood gases and respiration [8, 13-15, 17, 19, 28, 38, 51]; muscle relaxation [6, 7, 11, 12, 16, 18, 27, 29, 48, 64, 70, 71] and cardiovascular miscellany [9, 10, 20-22, 24, 25]

¹ J F Nunn. British Journal of Anaesthesia. 1999; 83(6): 916

² Courtesy of Dr David Smith, Southampton

Blood gases and respiration

The next paper was about the oxyhaemoglobin dissociation curve, it is a physiological phenomenon that is essential knowledge for anaesthetic examinations and has great practical significance. *What is the effect of anaesthesia?* [8]. This was presented at the Anaesthesia Research Society at the March meeting in London in 1970.

In 1971, *“Does constant volume IPPV produce hypoxaemia? It was concluded that it did not [13]; this was a study of ten patients post mitral valve surgery.*

Also in 1971: *“The effect of light chloralose and pentobarbitone anaesthesia on the acid-base state and oxygenation of arterial blood in dogs”.* Over the period of the eight hour anaesthetic changes were minimal [14]. Another paper, probably resulting from the same study, questioned the use of the Henderson-Hasselbalch equation. Blood samples from anaesthetized dogs with acid-base disturbances were compared with dogs without such changes. It was found that there was no relationship between pK' and temperature, that it increased with alkalaemia and decreased with acidaemia. The variation of pK' with pH was considerable. It was thought that the use of the Henderson-Hasselbalch equation in this situation was unacceptable and could lead to large errors [15].

1972: [17] *“The effect of postoperative artificial ventilation on arterial blood oxygenation.”* Is this the same data and analysis that was used in the Anaesthesia, 1971 paper [13]?

1972: *“A comparison of the in-vivo CO₂ titration curves of arterial and mixed-venous blood in dogs”* [19].

1976: Patients spontaneously breathing under the effects of halothane (1-2%) and nitrous oxide in oxygen were studied to see if respiratory indicators changed. There was no deterioration of blood gas values over two hours and the dead-space/tidal volume ratio and alveolar-arterial oxygen tension difference did not change [28].

1978: *“Resistance of Heidbrink-type expiratory valves”* At a flow rate of 30 l min⁻¹ the average resistance of 70 valves was 318 Pa, 44% of them had resistances above the limit of 294 Pa; a nice simple laboratory project [38].

1983: *“Pre-oxygenation-how long?”* With a flow of 8 l min⁻¹ delivered via a Magill or Bain breathing attachment the end-tidal nitrogen concentrations were 4% or less within 3 minutes. The fastest time was when the reservoir bag was prefilled with oxygen and tight fitting face masks [51].

Muscle relaxants:

The first two publications, one a presentation at an ARS meeting in Birmingham in 1969 and the second its full write-up later in the year [6, 7] are the result of a very fascinating investigation and had a follow up 32 years later [76]. Tubocurarine and suxamethonium were studied during a standard anaesthetic, with nitrous oxide and halothane, in New York and London. The recovery times were significantly ($p < 0.005$) shorter in London. This was distinctly odd; even when drugs manufactured in the USA were used in the UK, the results were the same. When Americans who had lived in the UK were tested they responded in a similar manner to those in the USA. The letter in 2001 from Norman and Katz highlighted the fact that in 1947 the manufacturers (Squibs) had noted discrepancies in the dosage – “...*relatively more of the British preparation being used*”.

1970: “*The neuromuscular blocking actions of pancuronium*” [11, 12]

The first, published in ‘*Anaesthesia*’, was presented at the “Annual Meeting 1969”, presumably the Annual Meeting of the Association of Anaesthetists. The full write-up was in the BJA. Pancuronium bromide was investigated - small doses caused a slow onset of action and a reduction in twitch height of 69%. A larger dose, as might be expected, was more rapid in onset and complete block was achieved. Recovery times increased with increasing dose and repeated doses produced greater durations of action. Rate of recovery was affected by respiratory acidemia or alkalemia.

In 1971 dacturionium bromide was investigated – this drug was not used in routine clinical practice. During the study one patient showed return of the neuromuscular block after apparent complete reversal with neostigmine – not good [16].

1972: “*Prolongation of suxamethonium-induced paralysis by propanidid*” [18]. The duration of total paralysis, of the adductor pollicis muscle, was greater by approximately two minutes in those patients given propanidid; an induction agent that had the viscosity of treacle and caused a short period of hyperpnoea; good for the uptake of volatile agents; propanidid did not last long in routine clinical use.

1975: “*Proceedings: The effect of tacrine on the neuromuscular block produced by suxamethonium in man*” [27]. This was presented at an ARS meeting in July in Newcastle upon Tyne. Tacrine increases the duration of muscle paralysis with suxamethonium significantly. Patients given

suxamethonium 1m kg⁻¹ and tacrine 15mg had a three- fold time to recovery, consistent with the work of previous investigators.

1976: "*Proceedings: A trans-Atlantic comparison of the pharmacokinetics of suxamethonium*" [29]; another ARS presentation, this time at Northwick Park. Elimination rate, efficacy and the minimal effective dose was calculated from previously collected data. The London patients had the highest values for all three. The reason for the trans-Atlantic difference was still unclear.

1988: "*Effect of suxamethonium given during recovery from atracurium*" [64]. Suxamethonium was given when the twitch response was 50% of control. A dose of 3 mg kg⁻¹ was needed to produce consistently 100% block.

1992: "*Comparison of atracurium-induced neuromuscular block in rectus abdominis and hand muscles of man*" [70]. Atracurium was administered anaesthesia with isoflurane and nitrous oxide in oxygen. Train-of-four stimulation was used over the 10th intercostal space and the ulnar nerve. Electromyograms were recorded over the rectus abdominis and hypothenar muscles. Onset of block was faster in the rectus abdominis than in the hand and recovery was faster in the rectus abdominis.

1993: "*Resistance to vecuronium*" (case report)[71]. This is a case report of the well known effect of anti-epileptic agents – patients taking them need much more muscle relaxant to maintain a satisfactory block.

Cardiovascular miscellany

This is a mixed bag:

1970: "*The effect of beta-blockade in the relationship between cardiac output and carbon dioxide*" [9] (ARS London meeting November 1969) and "*The effect of cardiac sympathetic blockade on the relationship between cardiac output and carbon dioxide tension in the anaesthetized dog*" [10]. The cardiac output increased as the PaCO₂ increased, practolol prevented it. It was concluded that the increase was due to sympathetic nervous activity.

1973: "*Fluid-loading and cardiopulmonary by-pass. A study of renal function*" [20]. Prior to going on by-pass blood was given to replace loss; in addition some patients were given Hartmann's solution (20 ml kg⁻¹). There were no differences in urine, sodium and potassium excretion.

1973: Halothane and the responses of the heart to autonomic nerve stimulation [21]. Halothane causes significant falls in heart rate, blood pressure

and the maximum rate of change of left ventricular pressure when measured at a fixed heart rate. Vagal slowing was not affected by the halothane nor was the increases in heart rate produced by stimulating the ansae subclaviae. It was concluded that the effects of halothane were not due to acetylcholine and noradrenaline release.

1973: "*Proceedings: The vagal contribution to changes in heart rate evoked by stimulation of cutaneous nerves in the dog*" [23]

1973: "*Proceedings: The use of practolol and bretylium to produce cardiac sympathetic nerve block*" [22] (ARS Edinburgh).

1973: "*Proceedings: Physiological stabilization of heart rate and blood pressure during peripheral nerve stimulation*" [24]. Presented at the ARS London meeting, at the Royal Postgraduate Medical School, Hammersmith Hospital in November.

1975: "*Proceedings: The effect of halothane on changes in heart rate evoked by stimulation to the radial nerve*" [25] (ARS Manchester).

It would appear that these last three projects did not proceed to a full write-up.

Editorials

1977 seemed to be the year for writing editorials:

1977: "*The perinatal period*" – the purpose of this editorial is a bit obscure – it recognises improvements in both maternal and neonatal well being and states that the "*anaesthetist has much to contribute*". I think it is suggesting that anaesthetic training should include neonatal work. This today is a super-specialty of paediatric anaesthetic practice [31].

1977: "*Opiates, receptors and endorphins*" – this was highlighting the the discovery of many more receptor sites (particularly opiate receptors) and how this would eventually enhance the development of new drugs [32]³.

1977: "*Learning and teaching in anaesthesia*" – Is anaesthesia learnt in the most effective way? This was his question. This was in response to decreasing pass rates in the examinations. He exhorted the use of new knowledge about how learning takes place and for some sort of continual assessment so that the trainee is aware of their progress [33].

1977: "*Trauma and immediate care*" – this was an era of training for major disaster management – every major hospital had to have a disaster plan

³ Undergraduate training 1964-9 taught only three receptors, α , β and acetyl-choline.

and many had exercises. This was an editorial in a volume of the BJA devoted to the reporting of a symposium on the management of trauma [34]⁴.

1978: *"The preoperative assessment of patients"* – a description of the Goldman Cardiac Risk Index for assessing patient pre-operatively.

1979: *"Immunology in anaesthesia and intensive care"* – another editorial preceding a special issue on a symposium on immunology in anaesthesia and intensive care [42].

1979: *"Anaesthetic pharmacology"* – an editorial in a volume of the journal devoted to reviewing anaesthesia pharmacology. It was surprising to see that there was a comment suggesting that the practice of administering volatile agents in uncalibrated vaporisers was still happening [39].

1980: *"Muscle"* – a very short editorial – preceding reviews of the subject of anaesthesia and muscle [43].

1980: *"The intensity and duration of I.V drugs"* – a discussion of pharmacokinetics and in particular the way in which the results are presented. It was suggested that for the clinician it might *"be better to give some idea of the dispersion of results using standard deviations or tolerance limits"* [44].

1981: *"Metabolism and anaesthesia"* – another prelude to a symposium [46].

1983: *"Mechanisms of general anaesthesia"* – prelude to a symposium on neurophysiology [53]

1983: *"The i.v. administration of drugs"* – this is a lengthy editorial on more complex pharmacokinetics and shows the advances made by the use of computers. *"Pharmacokinetics is advancing from the descriptive to the predictive phase"* [52]. 1987: *"Complications and medico-legal aspects of anaesthesia"* – another prelude to a symposium [61].

1997: *"Anaesthetic pre-registration house officers"*. Classically, in the UK, pre-registration house officers (first year of medical practice following graduation) are attached to medical and surgical firms. This editorial is about having pre-registration house officers in anaesthesia. The aim, evidently, was *"not to create anaesthetists but rather for them to learn from us how to be doctors starting out with knowledge of the management of the acutely ill patient"* [72].

⁴ The only exercise the author was involved in was at night, in a railway yard, and one of the racing ambulances carrying a 'flying squad' did in fact fly off the end of a ramp causing major trauma to the ambulance and minor injuries to the hard-hat wearing rescuers.

1999: *"Monitoring spinal cord function during aortic surgery"* and *"Assessing paralysis"* – in the same journal.

The former editorial highlights the devastating effects of iatrogenic paraplegia or paraparesis and the techniques available to monitor spinal cord function – it reads more like a review than an editorial. The latter discusses the problem of different rates and depths of neuromuscular blockade when measured at different sites [74, 75].

Reviews

- 1976: *"Septicaemia"*
- 1978: *"An assessment of acid-base balance"*
- 1987: *"Education in anaesthetic safety"*
- 1988: *"Do we need more muscle relaxants?"*
- 1992: *"One-compartment kinetics"*

Letters:

- 1977: *"Performance of the Lack circuit"* (much concern about adverse comments from Barnes et al.⁵ following their assessment of a pre-production model of the breathing system)
- 1979: *"Neuromuscular blocking drugs"*
- 1982: *"Co-axial breathing circuits"* (see below)
- 1983: *"Rebreathing and the Bain circuit"* (see below)
- 1983: *"The Lack system"* (this is a detailed response to criticism of the Lack breathing system which Nott, Walters and Norman had assessed –in 1977, 1982 and 1983 [35, 50, 54])
- 1984: *"More about the pharmacokinetics of vecuronium and pancuronium"*
- 1985: *"Nosworthy anaesthetic record"* (extolling the virtues of pre-computer anaesthetic record cards, perforated, enabling data analysis)
- 1990: *"Complications of the use of EMLA"*
- 1998: *"Drug designers in anaesthesia"* (a debate about who was the earliest drug designer – Charles Suckling with halothane or David Savage with pancuronium)
- 2001: *"Trans-Atlantic variation in response to neuromuscular blocking drugs"* (manufacturer noted difference, as above)

⁵ Barnes, P.K., Seeley, H.F., Gothard, J.W.W., Conway, C.M. *Anaesthesia* 1976;31: 1248

Odds and Ends:

"Propofol: clinical strategies for preventing the pain of injection" – only i.v. injection in the antecubital fossa caused no pain, but pain on injection elsewhere was reduced by combining lignocaine in with the propofol [65].

"Use of anaesthesia. Preoperative assessment of patients" – the British Medical Journal is, by and large, aimed at physicians and general practitioners. This was an article under the section titled *"Today's Treatment"* outlining the importance of patient assessment at the time, 1980. Six years earlier, JB Burn had written about a preoperative assessment clinic⁶. So in 1980 there was the problem of anaesthetists still seeing patients the night before or just before surgery; if there was a problem it was too late and there was pressure not to disturb the surgical list [45].

"The British Journal of Anaesthesia. An informal history of the first 25 years" [77]. Fifty one of John Norman's publications were in the BJA and so it is fitting he should write such a history!

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⁶ Burn JMB. Lancet 1974;ii:886-8

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