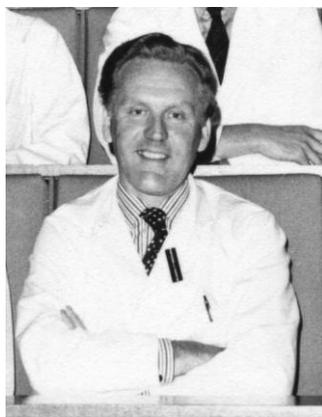


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MD MB BS Lond FFARCS
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Andrew Thornton moved to Sheffield in 1963 (he had been a research fellow at Guy's Hospital) and became Professor in 1971. He left in 1983 to take the chair of anaesthesia in the Chinese University of Hong Kong. Professor Andrew Thornton's work can be



classified under four main headings - clinical reports, general scientific studies, dental sedation and adverse reactions to drugs. They range from 1958 to 1988.

Clinical reports:

The first reports from Andrew Thornton were from his time in the army and described the management of a crushed chest injury using intermittent positive pressure ventilation (IPPV) and continuous curarisation. Anaesthetists had been using curare to create a 'balanced' anaesthetic since about 1942 but its use in intensive care was, obviously, later, because the first intensive care unit was not established until 1953 during the infamous polio epidemic in Denmark. The second publication from Guys Hospital was an assessment methodology for the efficacy of bronchodilators (antispasmodics) [1, 2].

From here on the publications become more specifically associated with anaesthesia [3]. By 1963 he had moved to Sheffield, had his Fellowship of the Faculty of Anaesthetists (F.F.A) and was working in the Regional Cardiovascular Centre [4-6]. Sheffield was to be his base for most of his academic life. These papers on various problems associated with anaesthesia for cardiac surgery were associated with two papers on the estimations of blood loss during surgery [7, 8], a

problem that has not been solved satisfactorily today (2009); of the methods tried the colorimetric technique was considered the most useful/convenient.

In 1963 there was a most extraordinary investigation into the aetiology of cot death [9]. This involved the study of six infant cadavers where spontaneous respiration was simulated. The cadavers were positioned supine, laterally and prone, and a variety of different pillows were tested. The bottom-line of this study was that the position did not seem important but that the nature of the pillow was. In the views of the authors the best pillow studied consisted of a covering of loose mesh material having a large number of small holes. The pillow was filled with curled plastic pieces forming a loose slightly springy network. This seems to have been the first study to analyse this problem in a physical way; a truly innovative approach.

Two papers on the assessment of Citanest [10, 11], two on the problems associated with chronic respiratory disease and anaesthesia (a common problem in the industrial midlands) [12, 13], and then some interesting early work on postoperative epidurals with an infusion of fentanyl [14], adding knowledge to previous work in 1979 and 1980 by Behar et alⁱ and Bailey et alⁱⁱ respectively, and total intravenous anaesthesia [15] using etomidate.

Science

The investigation of basic physiological entities (like physiological dead space and analysis of respiratory gases) was still underway in the early nineteen sixties and Andrew Thornton was amongst the investigators. [16-19]. In 1960 he was collaborating with John Nunn at Guys Hospital, London.

At the same time computer technology was rising fast but its use in anaesthesia research was of the analogue variety; these computers were useful for

ⁱ Behar, H, Olshwang D, Magora F, Davidson, J.T. Epidural morphine in treatment of pain. *Lancet* 1979; 1: 527-9.

ⁱⁱ Bailey, P.W, Smith, B. E. Continuous epidural infusion of fentanyl for postoperative analgesia. *Anaesthesia* 1980; 35 1002-6

the teaching and research into the distribution of drugs and gases [20-23]. The examples described in the B.J.A. article of 1968 included hydrodynamic and electronic analogues that were able to mimic the complex relationships involved in carbon dioxide and oxygen stores, and in the uptake of general anaesthetic agents. With digital computers dominating the scene in the 21st century these analogue systems were the easiest to program for complex inter-related exponential functions... the hydrodynamic systems were also great visual demonstrations[22].

Intravenous sedation

Andrew Thornton's main interest seems to have been in the field of dental sedation; in 1969 intermittent methohexitone was the investigative drug of choice. [24-28] A letter to the editor of the British Medical Journal has his team of Dixon, Hatt, Mann and Perks writing about their experience with methohexitone which is in response to, and supportive of, a paper by Robinson et al (Birmingham)ⁱⁱⁱ. This paper by Robinson had caused an uproar which led to the threat of libel action by Mr S.L. Drummond-Jackson^{iv}. In brief it was shown that airway obstruction, hypoxaemia and hypotension were common during the use of repeated doses of methohexitone, and it was suggested that some of the deaths associated with dentistry were caused by the technique. The references listed include detailed accounts of the research methodology; it included psychological testing of the patients to assess the 'banishment of fear of dentistry', aspiration of radio-opaque dye (testing of laryngeal competence), measurement of cardiovascular and ventilatory parameters and oxygenation. '*Methohexitone and its application in dental anaesthesia*' [26] is a review article and covers all aspects of the subject.

The use of methohexitone (references 1969 -1971) tailed off and diazepam took its place [29-31], (references 1970 - 1973). Associated with these

ⁱⁱⁱ Wise, C., Robinson, J. S., Heath, M. J., and Tomlin, P. J., British Medical Journal, 1969, p525 and 540

^{iv} Drummond-Jackson, S. L. Ed. (1967). *Intravenous Anaesthesia* - S.A.A.D. 3rd edn. p. 155. Swindon: Swindon Press

studies were reports on anxiety [32] and patient responses to dental surgery with and without sedation[33]. Letters discussed the 'dental anaesthetist of the future [34, 35]. This was followed by another 'new' agent Althesin (removed by the manufacturers in 19xx), references are dated 1976, [36, 37] this was quickly followed by flunitrazepam - 1976-1980 [38, 39]. Midazolam took over in 1982 [40-42] and is still in use today.

Adverse reactions to drugs

A different set of papers on drug interactions and allergy began in 1975 when collaboration with John Watkins began [43-49]. In 1975 it was known that there were alterations in the concentrations of components of the complement system and white cell numbers when sampling blood from patients with an anaphylactic type of response to intravenous drugs, thiopentone, methohexitone and Althesin in particular. In letters to the British Journal of Anaesthesia and Anaesthesia a request was made for anaesthetists to send blood samples to the Sheffield research unit if a patient had experienced an anaphylactoid type of response. This was the attempt to overcome the problem of the rarity of the 'anaphylactoid' event.

A paper in 1976, "Identification and quantitation of hypersensitivity reactions to intravenous anaesthetic agents" advocated the measurement of plasma complement C3consumption and conversion in sequential blood samples taken at intervals over the 24 h following an adverse response. Irrespective of the actual mechanism involved, it was said to provide a simple and convenient method for assessing hypersensitivity reactions.

Cremophor El, a detergent, a mixture of some 50-60compounds, was used to solubilise some intravenous agents. In 1978 its role in adverse reactions to intravenous anaesthetic induction agents was suspected. It was used in Althesin and Eponol (propanidid), two popular agents at the time. Again, in a letter, it was stated that there was no established correlation between intradermal skin testing and systemic responses.

The request for blood samples from the British anaesthetic workforce worked and almost 100 samples had been received by 1979. It was once more stressed that the clinical features of the anaphylactoid response are predominantly a result of the release of histamine, without involving IgE antibodies. Skin-testing pre-judges the mechanism of the reaction whereas examination of changes in complement, the immunoglobulins, and IgE specifically is the best approach.

Andrew Thornton contributed to the safety of dental sedation by the systematic study of the effects of various agents on cognition, respiration and the cardiovascular system. This work spanned the years 1969 -1983, a considerable body of work with a team of collaborators that included RE Atkinson, NR Bennett, PR Clarke, CD Day, RA Dixon, PS Eccersley, MJ Harrison, SD Hatt, TJ Hughes, D Lamb, P Mann, VC Martin, ER Perks and S Woodhead.

The publications of most interest are these rigorous assessments of cardio respiratory changes during dental sedation but the investigation into cot death and the use of analogue computers are also of note. His co-authorship of papers published in Nature[50] and in the Journal of Applied Physiology[21] must have also been very gratifying, the first on the genetics of human serum cholinesterase and the second on the electronic analogue for the distribution of carbon dioxide in the body.

Andrew Thornton was also involved in the organisation of a supernumerary Senior House Officer training scheme in the area served by the Sheffield Regional Hospital Board, later the Trent Regional Authority, which was a significant improvement on existing training methods and he was also co-author of several books – Aids to Anaesthesia, Basic Sciences and Clinical Practice (with Tom Healy and Michael Harrison), Techniques of Anaesthesia with Management of the Patient and Intensive Care (with Cyril Levy) and Adverse Reactions to Anaesthetic Drugs.

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