

**A TRIBUTE TO PROFESSOR THOMAS CECIL GRAY
MARCH, 11TH 1913 – JANUARY, 5TH 2008**

Dr Anne M Florence, Liverpool

As we gather here today to mark the sesqui-centenary of the death of one great pioneer, John Snow who made chloroform anaesthesia acceptable in clinical practice, it is my, albeit sad, privilege to pay tribute to another great pioneer, Thomas Cecil Gray who died peacefully on the 5th January, 2008 in his 95th year.

Cecil was born at the Clock Inn on Scotland Road, Liverpool where his father was the Publican, on the 11th March 1913. A devout Catholic Cecil was educated initially at the Convent of the Sacre Coeur in Bath and subsequently at the Preparatory and Senior Schools at Ampleforth, the Benedictine College in North Yorkshire. It was his intention to enter the Monastery on completion of his school days. Alas, within two months of becoming a novice monk it became apparent to all, except Cecil, that this was not to be his vocation. Consequently, to the chagrin of his mother, he returned to Liverpool in 1931 to study medicine. On graduating from Liverpool University in 1937 he became a trainee in General Practice in the city before purchasing a practice in Wallasey with help from his father. At this time many General Practitioners were also part-time anaesthetists. Fascinated by the specialty, Cecil worked and studied under the guidance of Dr Robert J Minnitt, rapidly collecting the 1000 cases required for the DA examination which he passed in 1941. He immediately became a full-time anaesthetist in several Liverpool hospitals and a demonstrator in anaesthesia at the University of Liverpool.

Very early in his career as a full time anaesthetist, Cecil and John Halton, a GP colleague with a substantial anaesthetic practice in both dental and thoracic surgery, set out to investigate the feasibility of neuromuscular blockade. The paralysing properties of wourali, the South American Indian arrow poison were described in the 16th century by Sir Walter Raleigh, but it was not used medicinally until 1845, when, Sir Arnold Knight, at that time a physician in Liverpool, successfully treated cases of tetanus and hydrophobia. It is most likely that Knight had obtained a sample of the crude distillate from the *Chondodendrum tomentosum* (curare), traditionally stored in a bamboo tube, from Charles Waterton of Walton Hall, Wakefield who had experimented with this poison during his 'Wanderings in South America'.

In 1935, while working in the laboratory of the distinguished neurophysiologist, Sir Henry Dale, Harold King isolated the active constituent of this distillate

which he named d-tubocurarine. Initially manufactured in the United States, it was marketed as Intocostrin and was first used in clinical anaesthesia in Montreal in January 1942 by Dr Harold Griffiths and his assistant, Dr Enid Johnson.

Taking his responsibilities seriously, John Halton, the local Medical Officer to the RAF, was a frequent visitor to the USAF base at Burtonwood where he successfully persuaded USAF personnel to obtain a sample of Intocostrin for his use in thoracic surgery as he thought that it might overcome the disadvantages of using barbiturate as the sole agent. A sample was delivered in November 1944. Alas, John Halton soon found that the solution was unstable and consequently of unreliable potency.

Meanwhile, Cecil Gray had obtained a sample of the powdered form of d-tubocurarine, produced by Burroughs-Wellcome, which Dr Rod Gregory was using for animal studies in the Department of Physiology. Cecil sterilised the powder prior to dissolving it in water. After administering it to each other, Gray and Halton found that this preparation was safe, producing beneficial relaxation with easily achievable full recovery of muscular tone. Consequently they introduced it to their respective clinical practices.

By April 1945 they fully appreciated the great potential of d-tubocurarine chloride (curare) and within 12 months had collected a series of 1049 cases; the majority had undergone thoracic surgery with a significant number of abdominal, head and neck and orthopaedic cases included. After pre-medication with a comparatively low dose of morphine, sleep was induced with an intravenous barbiturate followed by the curare. Initially barbiturates were used sparingly to maintain a constant level of hypnosis. Cecil assisted ventilation manually, delivering a mixture of nitrous oxide and oxygen by squeezing a large reservoir bag. The muscle relaxation, resulting from the curare induced inhibition of acetylcholine activity at the neuromuscular junction, was excellent. They were not, however, convinced that the anti-cholinesterase, physostigmine, was particularly useful for the return of normal muscle tone as they were both now aware that curare was completely detoxicated in the liver and rapidly excreted by the kidneys with no evidence of latent toxicity. They did, however, recommend that it should be available at all times.

There were two deaths in the early stages of the study which may have been related to the occurrence of hypoxaemia induced myocardial anoxia. This emphasised the importance of adequate oxygenation throughout and limitation of opiate use. Synergism occurred with both ether and cyclopropane; in

particular, they observed increased contraction and irritability of the gut which was not seen with barbiturates.

Their first public dissertation “A Milestone in Anaesthesia – d-tubocurarine” was presented to the Anaesthetics Section of the Royal Society of Medicine on 1st March 1946. They declared that curare was beneficial, as an adjuvant to barbiturates, for every thoracic and abdominal operation. It was of particular benefit in the poor risk patient and in the presence of peripheral circulatory insufficiency as it avoided the necessity for deep planes of anaesthesia and for thus high doses of opiates. The preparation of curare, available from Burroughs–Wellcome, in nearby Crewe, was of constant potency producing good muscle relaxation during light planes of anaesthesia. They did, however, stress that adequate ventilation and oxygenation were essential for the safety of the technique. They warned that “The road lies open before us, and with a grave and insistent warning to the inexperienced that we are dealing with one of the most potent poisons known, we venture to say that we have past yet another milestone, and the distance to our goal is considerably shortened.”¹

Many hours of discussion on the use and potential dangers of d-tubocurarine followed within the hallowed walls of 1 Wimpole Street occupying many of the regular monthly sessions of the Section. This pioneering advance was, initially, treated with suspicion and scepticism.

On the 12th April, 1948 Cecil Gray presented a detailed report of the use of curare in 8500 cases anaesthetised by a group of enthusiastic colleagues within the Liverpool Region who had willingly adopted the technique of hypnosis, muscle relaxation and controlled ventilation with the mild anaesthetic and analgesic, nitrous oxide and oxygen. The anti-cholinesterase, prostigmine, was now used routinely for reversal of curare with atropine added to eliminate its parasympathetic activity. Hyperventilation to achieve significant hypocarbia did not feature as an essential component of the technique until it was described by Geddes and Gray in 1959.² The absence of serious morbidity or mortality attributable to the drug fully supported Cecil’s belief that curare, while probably the most potentially dangerous drug in use at that time was, obviously, one of the least toxic. Bronchospasm was the only untoward event encountered on two occasions in this large series. The first occurred in a severe asthmatic and the second during bronchoscopy under very light anaesthesia. It was strongly felt that curare could not be implicated.³

Meanwhile Gray and Gregory had studied the effects of Intocostrin on the heart-lung preparation of a dog. Using concentrations far in excess of those used in clinical practice they found no deterioration in cardiac activity even when

thiopentone and adrenaline were administered singly or in combination, or hypoxia induced. There was evidence of improvement in contractility when cardiac activity was deliberately impaired.⁴

The basic principles of this pioneering work which became known as the 'Liverpool Technique', a triad of hypnosis, muscle relaxation and reflex depression with controlled ventilation using nitrous oxide and oxygen to provide a degree of hypocapnia has survived with modification, nationally and internationally, to this day. Advances in pharmacology and physiology have enhanced the safety and universal acceptability of this technique of anaesthesia. With the advent of new inhalational agents, in particular, hyperventilation is no longer necessary and, over the years, a multitude of new neuromuscular blocking agents have replaced curare.

Cecil Gray must also be remembered for his major contribution to education and standards of training in anaesthesia. Acutely aware of the inevitable changes in the practice of medicine and, in particular, anaesthesia which would follow the establishment of the National Health Service in 1948 he saw an obvious need for the specialty to develop an examination structure similar to the Royal Colleges of Physicians and Surgeons. Formal training to a high standard and post-graduate education in anaesthesia was essential. Following his appointment as Reader and Head of the Department of Anaesthesia in the University of Liverpool he opened negotiations with the Dean of the Liverpool Medical School and the Board of Clinical Studies which culminated in enrolment for the first Post-graduate Course in Anaesthesia in October 1948. Most of the surgeons tacitly agreed to the presence of trainees in the operating theatre. The following year the proposals for a full-time course received official recognition by the Hospital Authorities. They empowered the Academic Department to select junior staff for employment in the hospitals of the Region. It was agreed that all trainees would be free to attend lectures until 11.00 am each day including Saturday. All participants were required to have had previous experience in anaesthesia. This unique course, the first in the United Kingdom, rapidly became extremely popular and over-subscribed.

By 1952 the course had expanded its horizons with the recruitment of students from Singapore, Malaysia, Hong Kong, the Indian subcontinent, South Africa and Australia. Financed by their own governments these doctors held supernumerary posts in hospitals throughout the region, providing an enthusiastic, reliable and valuable service.

Cecil's profound interest in medical education and organisational ability was recognised by his election as a Founder Member of the Board of the Faculty of

Anaesthetists of the Royal College of Surgeons in 1948 and subsequently as Dean of the Faculty in 1964. In 1959 he was appointed to a Personal Chair in Anaesthesia in the University of Liverpool and in 1966 became its first Post-graduate Dean, remaining in this role until 1970. He was subsequently appointed Dean of the Faculty of Medicine from 1970 until his retirement from the Chair of Anaesthesia in 1976.

He wrote numerous papers and edited several text books. His last publication in 2003 was the biography of Dr Richard Formby, the founder of the Liverpool Medical School initially at the Royal Institution before it moved to the Infirmary in 1844.

Cecil was invited to deliver numerous eponymous lectures. The first was the Clover Lecture of 1954 entitled the 'Disintegration of the Nervous System', a 'perversion' of the title of Sir Charles Sherrington's great work 'The Integration of the Nervous System' published in 1906 while he was Holt Professor of Physiology in Liverpool. In his lecture Cecil outlined the animal research and clinical experience which had led to the development of the theory of the triad of anaesthesia and a technique for the safe use of curare in anaesthesia. This contribution made by Cecil Gray and his departmental colleagues to the understanding of the nature of the state of anaesthesia and the practical application of neuromuscular blocking drugs was as significant for anaesthesia as that of Sherrington was for neurophysiology.⁵

Many honours, national and international, were bestowed upon him. Probably, one of the most significant was the award of the Sims Commonwealth Travelling Professor. As the first anaesthetist to receive this award from the three Royal Colleges of Physicians, Surgeons and Obstetricians and Gynaecologists it provided the opportunity for him and his wife to travel to Australia for 3 months to engage in educational activities and the interchange of ideas.

Cecil was President of the Anaesthetic Section of the Royal Society of Medicine, The Association of Anaesthetists of Great Britain and Ireland, the Liverpool Society of Anaesthetists and the Liverpool Medical Institution and was actively involved with the Medical Defence Union for many years as Vice-President and subsequently Honorary Treasurer. He also devoted time to serve on the Liverpool Bench between 1966 and 1983.

Cecil, a man with great charm, talent and boundless energy, was a gifted teacher with the ability to inspire students, trainees and colleagues with devotion and enthusiasm. No problem was insurmountable. His advice, either deliberately

sought or volunteered, was always sound; consequently he had a profound influence on the careers of many whose subsequent progress he followed assiduously with pride. A good friend and mentor of many, friendships made were enduring even when he might have thought that a friend had gone astray. Many years ago at an International Congress, many thousand miles from here, one of his 'prize trainees', whose own research supported the views of an Australian colleague that 'Normocarbica was a desirable goal', dared to argue with the Chairman of the session, knowing that he, himself, firmly believed that hyperventilation induced hypocarbica was the ideal goal. He graciously conceded the argument and retired to the Bar with the two renegades. This did not end life-long friendship, respect and admiration.

A devoted family man, Cecil was a generous, entertaining host with a wicked sense of humour, a true native of Liverpool. An accomplished pianist and opera lover his musical interests included membership of the Royal Liverpool Philharmonic Society, Liverpool Welsh Choral Society and the Verdi Society. He also had a passion for amateur dramatics and was a player and producer with the Irish Players for over twenty years. Cecil will be greatly missed by many.

References

1. Gray TC, Halton J. A Milestone in Anaesthesia – d-tubocurarine chloride. *Proceedings Royal Society of Medicine* 1946; **39**: 400-10
2. Geddes IC, Gray TC. Hyperventilation for the maintenance of anaesthesia. *Lancet* 1959; **2**: 4-6
3. Gray TC. The use of d-tubocurarine in anaesthesia. *Proceedings of the Royal Society of Medicine* 1948; **41**: 559-68
4. Gray TC, Gregory RA. The Effect of d-Tubocurarine Chloride on the Heart-Lung Preparation of the Dog. *Anaesthesia* 1948; **3**: 17-20
5. Gray TC. The Disintegration of the Nervous System. *Annals of the Royal College of Surgeons of England* 1954; **15** : 402-19