It is useful when inaugurating a new journal on Anesthesia Research and Pain management to know something about the beginnings and development of the field. Earlier doctors giving anesthetics had many problems to overcome. They had to try new drugs and develop new techniques and how best to perform them. Some of these have passed into oblivion but others are now taken for granted without the thought that someone had to work them out. It is hoped that this paper will provide some interesting insights about what has gone before.

Ether and chloroform dominated the first 100 years of anesthesia, along with nitrous oxide, the analgesic properties of which Humphrey Davy suggested as early as 1799 “might be useful to relieve pain in operations where there was no great effusion of blood”. The analgesic properties of these drugs were recognized during their use as party drugs when they were inhaled.

From the beginning, there were a few individuals like John Snow and Joseph Clover who recorded their experience and developed appropriate equipment for their administration. John Snow’s ether inhaler was remarkable because he had baffles which extended the time the ether was exposed to the air flowing over it to enhance vaporization and it had a water bath to reduce heat loss which is associated with ether vaporization.

At first, the liquid drugs were administered drop by drop on to a handkerchief or cloth held over the patient's face. Then metal framed masks, such as Schimmelbusch’s, were constructed to hold gauze on
which the drops were vaporized. The benefit of this system was that air was breathed so that nitrogen was maintained in the lungs preventing alveolar microatelectasis which tended to occur when more diffusible gases such as nitrous oxide were used.

People told me of their experiences before World War II administering ethyl chloride for induction followed by ether to children when they were junior doctors with minimal training. It is not surprising that the course of anesthesia was often turbulent. It was often a frightening experience. Sometimes tonsillectomy with a guillotine was even performed on the kitchen table!

The first recorded death was 15 year old Hannah Greener who died under chloroform anesthesia in January 1848. It may be that she was very apprehensive and had high circulating catecholamines which sensitized her heart to chloroform resulting in ventricular fibrillation and cardiac arrest. In 1899, 68/83 deaths under chloroform in England occurred before the surgeon began to operate. This information stimulated Edward Henry Embley, an honorary anaesthetist at the Melbourne Hospital, Australia(1895-1917) and first Lecturer in Anaesthesia at Melbourne University (1900) to undertake a study on 284 dogs in which he demonstrated that death under chloroform was cardiac rather than respiratory failure as suggested by two previous Hyderabad Commissions in India. The report of this research occupied 20 pages of the British Medical Journal in 1902.[1] Other deaths were not uncommon – lack of availability of suction when patients aspirated vomitus was a common cause, especially with ether.

The first 35 years of the twentieth century saw the introduction of local anesthesia but the blocks were developed and done by surgeons. Equipment and machines for inhalation anesthesia were developed by Boyle in England and later by Macintosh and Epstein in Oxford, and Heidbrink and others in USA but still open drop methods were widely used. Carbon dioxide absorption was introduced with soda lime, important when using a closed circuit. In the 1940s soda lime contained 5% potassium hydroxide which produced heat when reacting with carbon dioxide. It was observed that toxic effects were observed when the inhalation agent, trichloroethylene (Trilene), was used in closed circuit with soda lime because toxic breakdown products, phosgene and dichloracetylene were produced when trilene was heated.[2]

Several new drugs were developed during the great depression of the 1930s – the longer acting local anesthetic, nupercaine in 1929, barbiturate induction agents (hexobarbitone in 1932, thiopentone in 1934), and cyclopropane in 1933. The latter had a rapid onset, produced good muscle relaxation and maintained blood pressure because it was sympathomimetic. However, when it was discontinued this effect was lost and if blood volume had not been maintained hypotension resulted (cyclopropane shock) in the recovery room (if there was one). It was popular for use with children because of its rapid induction and emergence. Operating rooms had to have antistatic floors because it was explosive. There was a major explosion in Chile about 50 years ago when six people died because of this drug. Its use was discontinued because of its inherent danger and the cost of antistatic flooring.

With the advent of further new drugs in the 1940s and 50s (e.g. d-tubocurarine, suxamethonium, lidocaine, halothane, and improved antisepsis with sulphonamides and antibiotics (penicillin), great changes began to occur while the domination of ether and chloroform ended, although ether continued to be used in
Africa and the less affluent world. It was then that pediatric anesthesia and surgery began to evolve, more complex procedures became possible and result improved.

The first half of the twentieth century saw a slowly increasing number of doctors becoming part or full-time anesthesiologists and then some began to take a special interest in children. National Societies began to evolve and by 1955 representatives of 26 Societies met and formed the World Federation of Societies of Anaesthesiologists. There were also 12 official Society observers (including USA) and four other societies had members there. There were still relatively few who specialized in Pediatric Anesthesia. The Association of Paediatric Anaesthetists of Great Britain and Ireland, which had many overseas invited members (always less than 50%) was founded about 1974 and led the way. It is a young subspeciality.

In 1946 Margaret McClelland returned to Melbourne after spending the war years training and working in London. She had a sessional appointment at the Children's Hospital and was the first anesthetist to use muscle relaxants in infants there. In 1952 she was appointed half-time director of Anaesthesia and became full time in 1956 when the staff at the hospital became salaried instead of honorary as was customary in public hospitals in Australia at that time. This was a major step forward as parents were often unable to pay private fees so that children’s doctors had relatively poor incomes until the hospital was able to pay them.

The first registrar with anaesthetic duties was appointed in 1951 and then, in 1953 an anesthesia training program developed including 6 or 12-month of rotations in the Children's Hospital. The standard of pediatric anaesthesia was enhanced. With more people being trained the standards improved, morbidity and mortality decreased and patient care improved.

Equipment was developed and by the 1950s specialized pediatric delivery systems were available – the T piece introduced by Philip Ayre in Newcastle, UK (1937) \(^3\) and modified by Jackson Rees in Liverpool by the addition of a bag which allowed greater control of respiration. Non-rebreathing valves designed by Digby Leigh, and Stephen and Slater and miniature circle absorbers were made by Bloomquist in North America and Ian MacDonald in Melbourne. The purpose of these items was to minimize the anesthetic dead space for small patients. This could also be reduced by endotracheal intubation or by using a Rendel Baker – Soucek low dead space mask.

Monitoring was minimal but effective. The pulse was observed more diligently. Changes in rate, rhythm and pulse pressure could be identified. In Pediatric anesthesia a precordial or esophageal stethoscope was very valuable once one's ear was trained to notice differences. Heart rate, rhythm and intensity of heart sounds and breath sounds could easily provide essential information. Nowadays few doctors appreciate how the intensity of heart sounds gives a good idea of changes in cardiac output. The sounds are created by the force of valve closure. If cardiac output is reduced by blood loss or myocardial depression the back flow of blood caused by the elastic recoil of the aorta and pulmonary artery is reduced and the valves are closed less forcefully. The sounds produced are softer. The stethoscope is therefore a very sensitive monitor of the vital functions. It may seem hard to believe in these days of sophisticated monitoring that before infant open heart surgery began about 1970 pulmonary blood flow and hence pulmonary hypertension in infants with ventricular septal defect was reduced by applying a constriction band to the
pulmonary artery. The tightness of this could be assessed by tightening the band until the heart sounds suddenly diminished, then releasing it until the sounds became louder as cardiac output became adequate, then fixed there.

Blood pressure could be measured with a traditional cuff in bigger children but was more difficult and often not measured in infants. In the mid-1970s Roche produced the Arteriosonde, an automated blood pressure recorder which could be used for babies.

Probably the greatest advance in the later twentieth century was the introduction of the pulse oximeter which gives warning of developing problems. The main problem with babies was knowing when a low reading occurred whether it was a poor contact of the probe, a failing heart or inadequate ventilation. Listening with a stethoscope has often differentiated these when the heart was failing.

The capnograph is another useful monitor of ventilation and correct endotracheal tube placement but it also declines with falling cardiac output and may be a sensitive warning of the increased metabolism in malignant hyperpyrexia when it increases.

The Laryngeal Mask Airway, introduced by Archie Brain, probably produced the greatest change in anesthetic practice in the latter part of the twentieth century. While it provides a good and usually safe airway, cases of aspiration of regurgitated fluid around the cuff have occurred.

Cocaine was found to have local anesthetic properties in 1884 by Kohler. In 1898 two of six patients who received spinal anesthesia by the famous German Surgeon, August Bier, were children. Children must have been included in hundreds of cases reported by Bier and Donitz (1904) and Deetz in 1906 but numbers or ages are not specified. In 1909-10 Gray H. Tyrell from Great Ormond Street Hospital for Sick Children in London published three detailed papers of 100 cases each of spinal anesthesia in children. These papers occupied 14 ½ pages in the Lancet. Epidural and caudal anesthesia came later. In 1950 Curwen in Durban reported 99 caudals in neonates at a South African Congress.\(^4\) In the 1970s Schulte Steinberg passed soft catheters from the sacral canal to the thoracic region to provide epidural anesthesia in infants.\(^5\) This technique was developed further by Busoni in Florence, at a hospital where much of the surgery was done under caudal anesthesia, and by Bosenberg in Durban, where it helped to provide postoperative analgesia and overcome the deficiencies in nursing staff in their intensive care unit.\(^5\)

The introduction of bupivacaine was accompanied by a resurgence in interest in regional and local anesthesia in children in the 1960s and 70s.\(^4\) The first studies of blood levels in children following various routes of administration and doses were done starting in 1976.\(^6\)

Cardiac surgery began in the 1950s. Several palliative operations were developed because corrective surgery in babies under 10 kg only became feasible about 1969 when deep hypothermia (\(18^\circ\)c) and circulatory arrest became a viable option.\(^7\) Safety was enhanced by the addition of carbon dioxide to the oxygenator gas during cooling so that the corrected CO2 remained normal and the hemoglobin - oxygen dissociation curve moved to the right. This increased oxygen release to the tissues prior to circulatory arrest. As surgical skills improved the need for circulatory arrest declined.
In 1952 there was a disastrous epidemic of poliomyelitis in Copenhagen. Ibsen, a young anesthesiologist recently returned from the USA was consulted and found that the patients with impending respiratory failure had hypercarbia and retained secretions in their lungs. He advocated tracheostomy, regular suction and ventilation which was carried out mostly by medical and then dental students as well for a total of 167,000 hours (equivalent to 1000 weeks!) The mortality decreased from 85 to 25 %. This led to the development of ventilators and Intensive Care units.

The epidemic spread to Sweden in 1953 and in 1955 Goran Haglund opened the first pediatric intensive care unit in the world in Gotenburg. Hans Feychting opened a postoperative department in 1961, in Stockholm, which became the Intensive care unit in 1966. Prolonged nasotracheal intubation and where necessary, controlled ventilation (IPPR) were the main stimuli to early development of pediatric intensive care. Brandstater in Beirut reported several cases in 1962 and this report was followed by reports from Adelaide and Melbourne in Australia (1964), and Toronto (1965), all having started about 1963. Jackson Rees visited Australia in 1963 and returned to England via Toronto spreading the news while he went. The first patient in Melbourne was intubated having had failed tracheotomy removal. The tracheotomy was replaced by a nasotracheal tube which was successfully removed after five days. There were many problems to be solved and lessons to be learnt.

A tube passed through the nose bypassed the normal humidifying function of the nose. Consequently secretions in the airway dried and caused obstruction. Tom Allen described the death of the first case of tetanus which they tried to manage in this way in Adelaide in 1961. The next question was “should the gases be moistened with heated water vapor (humidified) or by nebulization where water was shattered into fine particles?” If these were too big they would not reach the distal airways or if too small they could flood the alveoli. Humidification seemed better but the water had to be heated so that it reached the nasotracheal tube at 34-35°C. Overheating had to be avoided by monitoring the temperature. Then tubing was devised which had a heating coil in it to maintain a constant temperature from the source to the patient at 34-35°C but this proved to be good for bacterial growth and infections occurred. Previously the water temperature was higher (50-60°C) which prevented bacterial growth (pasteurization). Many ideas were tried for fixing the tube so that accidental extubation did not occur. The development of subglottic stenosis was a consequence of using too large a tube. This could be avoided by having a slight leak around the tube when positive pressure was applied. What is taken for granted today was preceded by many problems which had to be solved fifty years ago.

It was not until about the 1980s that post-operative pain management generally began to improve. Before that premedication often included an injection of morphine, pethidine or omnopon with atropine or hyoscine as dying agents because ether produced secretions in the airway. Postoperatively morphine or pethidine were given, usually 4 hourly, intramuscularly. These were painful and often provided levels of analgesia below the pain threshold before the next dose was given. Oral premedication gradually supplanted the painful injections and intravenous infusions which gave a constant level of analgesia were introduced. These required more care and attention but were generally better for the patient.
The advent of the longer acting local anesthetic, bupivacaine, increased the use of caudal, epidural and nerve blocks for pain relief. Infusions helped to maintain steady states so Acute Pain Services developed when staff and funds became available. These were often a long, slow struggle to establish.

Sporadic chronic pain services existed but the increasing recognition of the importance of pain management generally led to development in this aspect as well. Much research and development has taken place on pain in the past 30 to 40 years so that it is now a separate specialty in more developed countries.

There are many less developed countries where lack of manpower, equipment and drugs are still a problem but there are many people trying to help these countries improve their situation. We should not forget that there are places away behind the developed world.

This is a brief outline of some anesthetic history with a bias showing how pediatric anesthesia emerged from the days of ether and chloroform towards more developed practice and care of children so that parents can now accompany them to the operating theatre and be with them in the recovery room. Chapters on the child in hospital did not appear in anesthetic textbooks until 1979 (Brown and Fisk)\(^{[12]}\). In fact there were few textbooks on pediatric anesthesia before that - Robert Smith (1963), Leigh and Belton (1954), Davenport (1967), Wilton (1965), Steward (1979).

It was notable 50 years ago that the superior attitude of senior surgeons changed and they began to express their appreciation of their anesthetic colleagues ability and help to make advances in Pediatric Surgery possible.
REFERENCES

* Curwen Ninety nine cases of caudal anaesthesia in neonates. (The author has a typed copy of this paper given to him by its author. It was presented to a South African meeting in 1950)