TIMELINE OF SOME SIGNIFICANT EVENTS IN THE EVOLUTION/HISTORY OF ANAESTHESIA ("Add-Ons" & Updates - Mar 2019)

YEAR	EVENT	PERSON / PLACE INVOLVED
c.280 BC	The importance of monitoring the pulse and its nature stressed (see 130)	Praxagoras of Alexandria. His pupil, Herophilus further developed the concept by using water clocks to monitor pulse rates. Herophilus also determined the existence of both motor and sensory nerves; Galen later explained the difference between motor and sensory nerves in his work *De Motu Musculorum*
130	Emphasis on the importance of monitoring/assessing the pulse (see c.280 BC)	Galen (Aelius or Claudius Galenius) of Pergamon. A Greek physician, surgeon and philosopher who worked in Rome. He regarded "sphygmology" (sphygmos is Greek for pulse) as the "*most important diagnostic……with strength, frequency, rhythm and character*". He also promoted the importance of body temperature and auscultation
1525	Ether used on animals (see 1275, 1540 & 1730)	Paracelsus. A description of his use of ether and its effects on domestic fowls appeared in the 1603 first edition of *Operum Medico-Chimicorum Sive Paradoxorum*
1804	Morphine isolated from opium (see 1831 & 1845)	Friedrich Sertürner, German apprentice pharmacist. It was initially named "morphium", after Morpheus, the Greek god of dreams. It was also called "principium somniferum" (the soporific principle) - a water-insoluble crystalline substance. This was produced in oral form as morphine acetate and was difficult and expensive to produce. The Frenchman, Gay-Lussac, in an editorial accompanying a French translation of Serturner's latest paper on the subject in 1817, proposed the name morphine instead of morphium
1831	Introduction of a cheap chemical process to isolate morphine hydrochloride and codeine hydrochloride from opium by an interaction with calcium chloride (see next entry)	Dr William Gregory, a medical graduate from University of Edinburgh. He later became a Professor of Chemistry at several institutions in Scotland after graduating in chemistry at the University of Giessen. This "muriate of morphia" was also known as "Gregory's salt" (see next entry)
1831	A cheap and easy method of producing morphine developed (see 1804 & 1845) (also see previous entry)	William Gregory's process was later further refined by Dr William Smith, a Scottish surgeon who only practised as an apothecary and who started to produce morphine as the hydrochloride. He later also developed methods for producing both ether and chloroform (see previous entry)
1832	Chloral discovered by chlorinating ethanol (by exposing absolute alcohol to chlorine gas , which resulted in hydrochloric acid and the oily aldehyde chloral) (see 1869 & 1874)	Professor (Baron) Justus Freiherr von Liebig - a German chemist in Gieben who is extremely famous for contributions to agriculture and biological chemistry (see 1833)
1836	The first subcutaneous "placement" of morphine (see 1845 & 1863)	G V Lafargue, a French physician. He inoculated his own arm with morphine paste in 13 sites hoping to produce a local effect but actually produced a systemic effect of profound drowsiness. He failed to recognize the potential benefits because he was focussed on looking for local effects
1841	Anaesthetic effects of sulphuric ether on humans first recognized	During an "ether frolics" party in Anderson, Georgia, USA, a medical student named Philip Abney Wilhite "administered ether to a young black boy, who became deeply anaesthetized, to the point that all present believed that he had been killed" (according to Wilson C Wilhite, a descendant of Philip Wilhite, writing in the Bulletin of Anesthesia History 2011). Philip Wilhite sent for a doctor but the boy had recovered by the time the doctor arrived. It is thought that Philip Wilhite told one of his teachers about the incident - the teacher was Dr Crawford Williamson Long! The historic Wilhite House still stands in Anderson.
1842	Diethyl ether first officially used on a human (1 lump from neck of Mr James M Venable) - first fee for anaesthesia & surgery was US$2.00 plus 25 cents to cover the cost of the ether (see previous entry)	Anaesthesia & surgery by pharmacist & physician Dr Crawford Williamson Long in Jefferson, Georgia. Operation performed on 30th of March 1842 but not reported in literature until 1849 in the Southern Medical and Surgical Journal and titled "An Account of the First Use of Sulfuric Ether by Inhalation as an Anaesthetic in Surgical Operations". A 2nd tumour was excised from the same patient by Long on the 6th of June 1842 using the benefit of ether. Long's 3rd, and final use of ether in 1842, was for the amputation of a toe from a black boy, who was "the property of Mrs S Hemphill". The Crawford W Long Museum was opened in Jefferson in 1957
1846	First private use by W T G Morton of diethyl ether: to extract a wisdom tooth (from patient Eben H Frost) September 30	William Thomas Green Morton in Boston - a dentist (after experimenting with ether on his goldfish, his pet terrier and himself). He used a handkerchief soaked in ether. A dentist colleague, Dr Hayden, held a lamp for Morton because it was night time
1846	Morton's famous glass ether inhaler provided	This was delivered to Morton by an instrument maker named Chamberlain on the morning of the historic public demonstration of 16th of October. Morton, when considering using a gas bag, took advice from his former teacher, Professor Charles Thomas Jackson (a polymath, chemist and geologist to whom also the invention of the telegraph is attributed), who had experience of "ether frolics" and who gave Morton a glass flask and tube to use and suggested "Burnett's" ether was the purest available

1846	First successful public demonstration of anaesthesia with diethyl ether (then called sulfuric ether): (to remove vascular lesion on neck of Mr Edward Gilbert Abbott by surgeon & founder of the "New England Journal of Medicine", John Collins Warren) October 16	William Thomas Green Morton (using Morton's Ether Inhaler) in the Bullfinch amphitheatre (subsequently named the "Ether Dome") of Massachusetts General Hospital, Boston. After performing the surgery, Warren uttered the famous words: "Gentlemen, this is no humbug". Morton tried to patent ether as "Letheon" in the USA but too many people new what "his" compound was for that move to be successful. Because of his involvement and advice to Morton, Charles Jackson negotiated a 10% cut of any profits that Morton might have obtained but also fought the patent attempt via the US Senate
1846	First ether anaesthetic for surgery in France	Administered on the 15th of December by Francis Willis Fisher, a doctor from Boston, Massachusetts. This was for the excision of a lip cancer in a 59 year-old man
1847	Recognition of the benefits of hand hygiene/washing/antiseptic technique (see 1894)	Dr Ignaz Philipp Semmelweis (later Professor) a Hungarian obstetrician. While working at the Vienna General Hospital, he noticed the long-standing difference in mortality (5-fold) from puerperal sepsis between 2 clinics: one run by nurses and another run by doctors who had earlier in the day been routinely working in the morgue. Semmelweis noticed a colleague had died from septicaemia after being pricked by a scalpel in the morgue and he put two and two together and assumed there was "something" being carried on the doctors' bare hands to the women in the clinic. He introduced hand washing in chlorinated lime solution for the doctors coming from the morgue - this reduced mortality from 11.4% to 1.3%. His theory and practice were not accepted by the profession until the work of others on germ theories much later in the century
1847	Ether probably first used in Scotland (Edinburgh)	Professor (later Sir) James Young Simpson who, after visiting Professor Robert Liston (*vide*) just after his first use of ether, used it to assist childbirth
1847	Chloroform first used clinically (November) (to relieve labour pains, which were thought by many to be punishment for & method of atonement for Original Sin!) (see 1831, 1851 & 1853)	Professor (later Sir) James Young Simpson of the University of Edinburgh (obstetrician & gynaecologist) - after experimenting on himself & some friends at the dinner table. The first woman to receive chloroform was Simpson's niece and she named the baby "Anaesthesia" ! It has also been reported that Simpson, at his own expense, gave Florence Nightingale 1,000 doses of chloroform to take to the Crimean War, which ran from 1853 to 1856
1847	Publication of John Snow's *On the Inhalation of the Vapour of Ether*	
1847	"Patient Controlled Analgesia" (PCA) first proposed (see 1967 & 1969)	William Morton, Boston dentist, advocated its use in labour when suggesting the woman herself should hold an ether-soaked sponge and breath on it when experiencing labour pains
1851	Florence Nightingale expresses her belief in the use of chloroform for anaesthesia (see 1847)	This followed her observation of an amputation. During her involvement in the Crimean War, in which she worked from 1854, she helped advocate the use of chloroform during surgery on wounded soldiers; this despite the expressed opposition (although not an order) from the Inspector General of Hospitals, Dr John Hall, who has been quoted as saying "*the smart of a knife is a powerful stimulant and it is much better to hear a man bawl lustily than to see him sink into a grave* " !
1853	First "hypodermic" (term coined by Dr Charles Hunter, a surgeon in London) injection using a proper glass syringe and hollow needle attached (see 1853 x2, 1858, 1863 & 1869)	Dr Alexander Wood in Edinburgh - he injected local morphine to treat a woman with neuralgia using the Ferguson-produced syringe that he had designed and commissioned (see previous entry). Despite noticing, but being annoyed by, the resulting somnolence of the patient, he, like Lafargue, got side-tracked by his intention of producing local effects. For his efforts, Wood has been referred to as the "father-in-lore" of local anaesthesia.
1856	First direct monitoring of human arterial blood pressure (see 1733)	French surgeon Dr Jean Faivre. He measured both brachial and femoral pressures in a patient (an amputee) using a mercury manometer
1858	Systemic action of morphine first fully recognized and appreciated (see 1853 & 1863)	Dr Charles Hunter, a surgeon in London. Using Alexander Wood's technique of injection, he noted that the pain relief afforded by a remote injection was equivalent to that of a "local" injection. Hunter referred to his injection as "hypodermical" and Woods insisted on calling it "subcutaneous". A special committee from the Medical and Chirurgical Society then took 2 years to decide that systemic effects of morphine were of primary importance compared with local effects
1863	First recorded use of subcutaneous morphine injection for post-operative pain relief	Dr James Paget, Middlesex Hospital, England, administering ⅓ grain (= 20mg) to a patient who had had a leg amputated. He recommended doses of ¼ to ½ grain (= 15 to 30mg). His report implied this was not the first case to receive morphine this way

1864	Barbituric acid synthesized (see 1902 & 1932)	Adolf von Baeyer, Germany, by condensing urea with an apple ester, diethyl malonate thus forming malonylurea, also known as 6 hydroxy uracil. One theory is that the name, barbituric acid may have been suggested from the fact it was discovered on the feast of St Barbara - December 6. Another theory is that von Baeyer et al were celebrating the discovery/development in a hotel when an artilleryman, who was there celebrating the feast of Saint Barbara (the patron saint of gunners), suggested the combination name for the compound. It took 10 more years to discover its actual structure. It has no sedative properties. Von Baeyer became a Nobel prize-winner in 1905 for his life-long work in chemistry
1869	Chloral hydrate (formed by distilling chloral with sulphuric acid and then adding water) first described as an oral premedication (see 1832 & 1874)	Oscar Liebreich, a pharmacologist in Berlin. Its hypnotic effects had, earlier that decade, been experimented with in both animals and humans by the German chemist, pharmacologist and doctor, Rudolf Buchheim, together with his students - although without publication. It subsequently was combined in solution with alcohol to produce "knockout drops" and obtained notoriety when used by a Chicago bar owner by the name of Michael (Mickey) Finn who used to rob his patrons after putting them under its influence
1874	First successful human intravenous anaesthetic administered (see 1832 & 1869)	French surgeon Dr Pierre-Cyprien Oré. He had been using chloral hydrate to treat the convulsions of tetanus and strychnine poisoning from 1872 but in 1874, while sedating a tetanus case, he also undertook some minor surgery on the patient and realized its anaesthetic benefit
1885	First spinal anaesthetic given (accidental during attempted peridural (epidural) with cocaine on a dog) (see 1898)	Dr James Leonard Corning (neurologist in New York) who also coined the term "spinal anaesthesia" & was the first to describe post-dural puncture headache in patients. In the same year, Corning injected cocaine between the 11th & 12th vertebrae of a man suffering from "spinal weakness and seminal incontinence" but, as he did not obtain spinal fluid in his syringe, it has been speculated that he administered an epidural injection rather than a spinal. He did suggest that this method could be used instead of general anaesthesia
1890	Ether declared a poison by the English Government Chemist Department	This occurred after some members of the Department drank ether and reported that it did indeed make them feel intoxicated. This was done during an investigation into the then common practice of Irish folk who, having taken "the pledge" of abstinence from alcohol, would drink ether to obtain a similar feeling to that of alcoholic intoxication. This practice had also expanded due to the Government's then campaign to close down illicit stills
1899	Hedonal (methyl propyl carbinol urethane) discovered	H Dresser, Munich, by furthering ideas of Oswald Schmiedeberg, a pharmacologist in Strasburg, Germany, namely, to replace the ethyl group in ethylurethane with a heavier chain. Initially using it orally from 1901, Nikolas P Krawkow of the Military Medical Academy in St Petersburg, after animal experiments, first used it intravenously on a human in 1909 - an elderly man with a malignancy on his leg. It gained widespread usage but was last used about 1930
1902	First commercially marketed barbiturate - diethyl barbituric acid (Veronal) - subsequently called barbital (USA) and barbitone (UK) following the events of 1917 - refer (see 1864 & 1932)	Re-discovered (and patented) in Germany by Hermann Emil Fischer & Joseph Freiherr von Mering and marketed by 2 companies, Bayer Pharmaceuticals and E Merck in 1904 (see 1917). This compound had originally been produced in 1882 but was only fully investigated at this time
1907	Open-drop ether first used in England	Dr H Bellamy Gardner, an anaesthetist at Charing Cross Hospital. He developed his wire-framed mask, covered with layers of gauze, to enable the administration. Open-drop ether had already started to be used in the United States around 1900
1909	Intravenous ether & chloroform first administered to produce general anaesthesia	Dr Ludwig Burkhardt, a surgeon in Würzburg, Germany. He used 4% solutions; initially using chloroform and later ether. The technique became widespread but ceased around the 1930s
1920	Somnifene (mixture of salts of diethylbarbituratic and diallylbarbituratic acids) synthesized	Tomas Alday Redonnet, a Spanish pharmacologist. Marketed by Hoffmann-La Roche & Co. Initially used for oral sedation by Liebemann in Zurich. First used clinically intravenously in 1921 by Bardet and Bardet (father & son) on a labour ward case. First used for surgery in 1924 by Fredet and Perlis. In the first half of the 20th Century it became the most widely used sedative/anaesthetic agent for "Deep Sleep" therapy
1925	The glass electrode for the measurement of blood pH developed (key words: blood gas analysis)	Phyllis Margaret Tookey Kerridge, chemist, physiologist and (later) physician, London. Hers was miniature and a refinement of existing pH electrodes. She also included platinum in the glass, which provided much greater electrical signals than previous models. The concept of glass as an electrode was built on the paper published by Max Cremer in 1906 showing that there existed an electrical potential between acidic and alkaline solutions when separated by a glass membrane. Cremer's work was furthered by several workers, particularly Wilhelm Giese, H L F von Helmholtz, Fritz Haber and Zygmunt Klemensievics in the intervening years
1932	Hexobarbitone (Evipan) produced (see 1864 & 1902)	Developed by chemists Helmuth Weese & Scharpff in Germany. Produced by Bayer. This was the first rapidly-acting intravenous anaesthetic drug. Became very popular and had been used over 10 million times by the end of World War II

1941	Introduction of the ASA's physical status/risk classification. This was modified in 1963 with the deletion of Classes 5 & 6, which were substituted by the single E for emergency (further modifications - see 2014)	The American Society of Anesthesiologists established a committee of 3 doctors (Meyer Saklad, Emery Rovenstine and Ivan Taylor) to classify "operative risk". Having decided they could not do that specifically - "*No attempt should be made to prognosticate the effect of a surgical procedure upon a patient of a given Physical State* " (Saklad), the trio developed a system based on the physical status of the patient at the time of surgery, viz: **Class 1** - No organic pathology or patients in whom the pathological process is localized and does not cause any systemic disturbance or abnormality; **Class 2** - A moderate but definite systemic disturbance, caused either by the condition that is to be treated or surgical intervention or which is caused by other existing pathological processes, forms this group; **Class 3** - Severe systemic disturbance from any cause or causes. It is not possible to state an absolute measure of severity, as this is a matter of clinical judgment; **Class 4** - Extreme systemic disorders which have already become an eminent threat to life regardless of the type of treatment. Because of their duration or nature there has already been damage to the organism that is irreversible. This class is intended to include only patients that are in an extremely poor physical state. There may not be much occasion to use this classification, but it should serve a purpose in separating the patient in very poor condition from others; **Class 5** - Emergencies that would otherwise be graded in Class 1 or Class 2; **Class 6** - Emergencies that would otherwise be graded in Class 3 or Class 4
1942	Nalorphine (N-allylnormorphine - first effective narcotic antagonist) synthesized (see 1914 - Pohl) (also see 1960)	Weijland and Erickson, Burroughs Wellcome. Marketed in 1952 as "*Lethidrone*"
1945	The British Association of Operating Theatre Technicians was formed on December 13	Stan Warner (from University College Hospital), David Crowley (from the Brompton Hospital) were the prime movers following a suggestion from Dr (later Sir) Ivan Magill who knew them both from work and was very impressed by their standards. These men, together with many others, had been trained by the army in WWII. The first formal training course for technicians began in 1947 at St Thomas' Hospital. It should be noted that, with the advent of anaesthesia 100 years before, surgical "holders" were no longer required and many of them became assistants to anaesthetists; this Association can be said to have formalized the relationship of anaesthetic assistant.
1950	The Engstrom ventilator patented	Dr Carl Gunnar Engstrom, a Swedish physician. The polio outbreak spurred his efforts, especially to relieve students and residents who were hand-ventilating patients for 24 hours non-stop. It was introduced into clinical practice in 1951. It produced both positive and negative pressures on the lungs
1953	The first publication to mention the metabolism of inhalational anaesthetics in humans (Specific acknowledgement is made to a paper, *A Kuhnian Revolution in Anaesthetics* , by Dr David Zuck, a Past President of the History of Anaesthesia Society, discussing Kuhnian paradigm shifts in anaesthesia)	A monograph titled "*Trichlorethylene Anaesthesia*" by Gordon Ostlere. Although a study had been done in Oxford by Joan Powell in 1945, using dogs and later humans, had noted trichloroacetic acid in the blood after exposure to Trilene (now referred to as trichloroethylene), and was quoted in the journal *Anaesthesia* in 1950 by P J Helliwell & A M Hutton in their article also titled "*Trichlorethylene Anaesthesia* ", no one had previously addressed the possibility of volatile/inhalational anaesthetic agents being metabolized by the body. Perhaps this was because of a mis-assumption represented by the words of John Snow when talking about ether: "*An appearance is met that would be truly alarming, if we did not know that it was only due to an agent which is flying away every moment in the breath, to leave the patient, in a few minutes, without any permanent trace of its having been there* "
1954	The PCO_2 electrode for measurement in blood developed (carbon dioxide)	Richard W Stow and Barbara F Randall, physiologists at Ohio State University. This differed from an electrode described by Gesell, McGinty and Bean at the University of Michigan in 1926 that they developed to measure only gases, not liquids. Stow's electrode, which was the first 'membrane electrode' invented, had a rubber membrane that was permeable to CO_2 and that separated a wet pH and reference electrode from the blood. Dr John W Severinghaus further developed Stow's electrode with a stabilizing bicarbonate solution. The development of this electrode made previous "bubble" methods, the Van Slyke interpolation methods (one of which includes using the Henderson-Hassellbach equation) and the Poul B Astrup method obsolete
1954	The O_2 electrode invented (oxygen)	Professor (of chemistry) Leland C Clark, Ohio. Having invented the bubble oxygenator for cardiac surgery, his paper was refused by a journal editor because there was no way of measuring the oxygen in the outflow - so Clark invented the electrode (also see 1962)
1962	The first glucose biosensor developed	Professor Leland C Clark and Champ Lyons in Alabama. The basis of this invention came from Clark's invention of the oxygen electrode (see 1954)

1962	First formal guidelines established for intensive care units (ICU) (then called respiratory units) (see 1952)	These were drawn up during a symposium on respiratory units at the First European Congress on Anaesthesiology, which was held in Vienna. Suggestions included that units should be: established in major hospitals (so other disciplines could be involved in treatment when required); 10 beds per million population; no more than 100 miles apart for transport purposes; staffed by specially trained nurses and doctors; staffed 24 hours
1967	A form of "Patient Controlled Analgesia" (PCA) with opioids for post-operative pain relief first reported (see 1847, 1967 & 1969)	Dr Philip H Schezer, while working in New York. His system allowed the patient to press a button that alerted a nurse to deliver a small intravenous dose of either morphine or pethidine. He also contributed to the development of the heart-lung bypass machine while working with Dr Michael DeBakey at Baylor University and he advocated the use of acupuncture in palliative medicine
1969	Actual "Patient Controlled Analgesia" (PCA) with opioids first reported (see 1847 & 1967)	Dr James S Scott, University of Leeds, England, reported having used the technique since 1964 for women in labour. Pethidine was the drug used
1979	Epidural morphine for post-operative pain relief popularized (see 1901)	Dr M Behar et al, New York. He reported in the Lancet
2014	The American Society of Anesthesiologists' House of Delegates approved the latest changes to its classification of a patient's pre-operative physical status. The modifier "E" for emergency was retained as a separate entity. The Australian Society of Anaesthetists adopted the basis of this system in 1987 (refer) but then subsequently added modifiers and classifications to account for the extremes of age (less than 12 months or 70 years or older), services delivered after-hours and services provided to patients having surgery in the prone position, or being morbidly obese, or being in the third trimester of pregnancy (see 1941)	**Class 1 (P1):** A normal healthy patient; **Class 2 (P2):** A patient with a mild systemic disease; **Class 3 (P3):** A patient with a severe systemic disease that is not life-threatening; **Class 4 (P4):** A patient with a severe systemic disease that is a constant threat to life; **Class 5 (P5):** A moribund patient who is not expected to survive more than 24 hours without the operation; **Class 6 (P6):** A declared brain-dead patient whose organs are being removed with the intention of transplanting them into another patient