

Early History and Pioneers of Procedural Sedation and Analgesia

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Abstract: I present a brief early history of Procedural Sedation and Analgesia (PSA). I have highlighted the crucial milestones in the journey prior to the eventual progression to modern PSA as well as naming the outstanding pioneers who originally opened the field. I show how the seminal work started with the discovery of the anaesthetic and analgesic actions of nitrous oxide and progressed via nitrous oxide to intravenous conscious sedation and minimal sedation with nitrous oxide. Although the discovery and true pioneers of both anaesthesia and later PSA (Procedural sedation and analgesia) were dentists, physicians wrongly attribute both these discoveries to their own profession. I have emphasized the misconceptions regarding the actual pioneers of PSA, mainly because of incorrect and often selective citations and misinterpretations. These errors have led to confusion and have obfuscated the early history of PSA. They have also distorted scientific priorities and therefore the scientific record. The paper is an attempt to remove and correct such distortions and present the true record in the light of the verifiable historical facts.

Keywords: Procedural, analgesia, conscious sedation, minimal sedation, anxiolysis, dissociative, deep sedation, intravenous, correcting historical errors, scientific.

THE EARLY HISTORY AND PIONEERS OF PROCEDURAL SEDATION AND ANALGESIA

The story of 'Procedural Sedation and Analgesia' (PSA) starts as does the entire history of anaesthesia with nitrous oxide (N₂O) [1-3].

Few medical practitioners and more particularly anaesthesiologists [4-7] acknowledge the crucial pioneering and trailblazing role of dentists in these two fields. Nonetheless, the evidence points unerringly to the fact that they were the initial discoverers of both anaesthesia and PSA. In each case, members of the dental profession undertook the seminal work [2, 3, 8] Thus, dentists presented the boon of general anaesthesia to man [2, 3, 5, 6] and its later modification, PSA [8, 9].

TERMINOLOGY

Conscious Sedation has become equated with PSA but in fact conscious sedation is one of the phases/states in PSA.

PSA is therefore not the same as conscious sedation, because procedural sedation implies a continuum which includes 4 relatively distinct and defined states, that may nevertheless merge into each other, as they progress from a lighter to a deeper state and vice versa. These states, as we move from the lightest to the deepest level are listed below: [10]

1. Minimal sedation or anxiolysis;

2. Moderate sedation previously referred to as 'conscious sedation';
3. Dissociative sedation;
4. Deep Sedation.

From a practical standpoint, one must realise that a patient can stray from a lighter to a deeper state and even into anaesthesia if they are not monitored carefully, because the borderlines are by no means rigid. The boundary from 'deep sedation' to anaesthesia is passed when the subject lapses into unconsciousness and cannot be aroused by repeated painful stimuli [10].

However, whatever the grade of PSA or the definition thereof, there is no doubt which profession were the pioneers and trailblazers and did the seminal work on anxiolysis, moderate sedation and anaesthesia that eventually resulted in PSA, as we know it today.

NOTE ON THE HISTORY OF ANAESTHESIA AS RELATED TO PSA

On 10 December 1844, Horace Wells, a practicing dentist, [3, 11] witnessed the first public display of analgesia, while being entertained by Gardener Colton who was using N₂O for public entertainments [3, 12]. Unlike Davy, who experienced the analgesic actions of the gas himself, and recorded it in his book, [1] Wells realised the significance of his observation [5, 12, 13]. During the entertainment, and under the influence of the N₂O, one member of the audience danced about, hurting his legs enough to bleed [5, 12]. Wells established that the injured individual had felt nothing until the effects of the gas had disappeared [3, 5, 13].

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Consequently, Wells also took part in the first public demonstration of N₂O *analgesia*, but clearly without anaesthesia [12, 13]. The very next day, 11 December 1844, [3, 5, 12] he tested the validity of his observations, in the presence of witnesses, by having his own diseased wisdom tooth extracted, without pain, under the *anaesthetic* effects of the gas [3, 5, 12].

In 1848, the Parisian Medical Society in France attributed the discovery of anaesthesia to Wells, although he died before receiving the news [3, 12].

His priority was later acknowledged posthumously, by the American Dental Association in 1864, and the American Medical Association in 1870 as the 'discoverer of practical anesthesia (sic)' [3].

In spite of the incontrovertible attribution for the discovery to Wells, based on carefully researched historical data, the medical profession still wrongly acknowledges William Morton, as the discoverer of anaesthesia [2, 4, 14]. At the time, Morton was a dentist and former partner of Wells [2, 12]. The incorrect attribution is common, despite the fact that Wells' demonstration of anaesthesia, with nitrous oxide in December 1844, [12] was witnessed by a number of people, almost two years year prior to Morton's ether demonstration in 1846 [4, 12, 14]. Perhaps the reason for this obduracy, in the face of contrary facts, is that Morton later became a physician [3, 14, 15].

My purpose in outlining this aspect of the development of PSA is twofold to:

1. emphasise the inextricable relationship between the early historical development of PSA and its link to N₂O;
2. demonstrate how the historical record of scientific priority can be distorted by selective and incorrect attributions. The history of PSA is a case in point.

DEVELOPMENT OF PSA

Stanislav Klikovitch

The next significant pioneer of PSA was a physician, Stanislav Klikovitch. He was born in Vilno (now called Vilnius), which at the time was part of Russian occupied Poland. He enters the picture almost 40 years after Wells' discovery of Anaesthesia, when most practioners were using 100% N₂O only as an anaesthetic [12]. In 1881, he was awarded an MD in St Petersburg for a thesis describing his experience with

using N₂O therapeutically [16]. Klikovitch introduced the concept of using the analgesic actions of N₂O, while the patient retained consciousness. He was also one of the first people, since Davy, to study the gas systematically [1, 16]. He began his therapeutic experiments after demonstrating its safety in animal experiments. Among his clinical discoveries was the use of the gas to treat cardiac angina pain as well as acute asthma. He also employed its analgesic effects during cervical polypectomy [16]. Interestingly, the beneficial therapeutic actions of the gas for treating asthma was repeated, years later by 2 independent workers [16].

However, his most enduring contribution was to its use in obstetrics. He was the first researcher to clearly distinguish between the anaesthetic and analgesic (non-anaesthetic) actions of N₂O and showed the gas' safety and usefulness during parturition [16, 17]. Klikovitch also outlined the most effective method of applying N₂O during childbirth [16, 17]. Nonetheless, as already discussed, at the time Klikovitch worked, nitrous oxide was used mainly for its anaesthetic actions. Indeed, even in obstetrics, the use was not widely adopted until after the development of suitable delivery equipment [17].

The development of appropriate delivery systems for N₂O and O₂ began in 1902 [15] or 1903 [12], with Charles Teeter (a dentist) [12, 15, 18]. This was followed in 1910 by Heidbrink [12, 15, 18] (also a dentist) and McKesson, a physician working independently [12]. However, the obstetrics use of the gases only really took off after 1911 when Guedel, [17] developed equipment that allowed self-administration of N₂O and O₂ [17].

INTRAVENOUS SEDATION

Niels Bjorn Jorgensen

Even today, many members of the medical and dental profession are unaware that surgical anaesthesia, and as a result of it, the advances in modern surgery were due to the inventive mind of a dentist Horace Wells [5-7, 12, 13, 19, 20]. They seem even less aware of the work done by another dentist in the field of intravenous sedation [19].

The towering figure in the story of intravenous sedation was Neils Bjorn Jorgensen, also a dentist. It followed his quest to make dental patients feel as comfortable and pain-free as possible, during operative procedures [7, 8, 15, 19, 20].

In 1923, Jorgensen began his mission by using ethyl alcohol successfully in adults [15, 21]. At the time, and the way he used it, ethanol was possibly the only relatively safe, reliable oral sedative agent available [15]. In 1945, he became the first person in the world to use a cocktail of pharmacological agents for intravenous sedation [15, 19]. The Jorgensen (or Loma Linda University) intravenous sedative technique consisted of careful titrating intravenous pentobarbital, followed by scopolamine and meperidine to produce a relaxed compliant pain-free patient [15, 20, 22]

Like the invention of general anaesthesia, few regard dentists as the pioneers in this field. Indeed, in two recent papers on PSA, [23, 24] Jorgensen and dentistry are completely ignored, and in one of these papers, we are led to believe that intravenous sedation was first used for PSA, only in the 1980's [23]. That intravenous PSA has been adopted in the field of the anaesthesiologist is not in dispute, however, this is a long way from the palpably false belief that PSA was introduced by anaesthetists. Only in the NICE Guidelines for sedation, in 2010, is dentistry acknowledged as follows [25] 'We are especially grateful to our dentists who have been pioneers in this field...'

The facts show indisputably, that Jorgensen is the true father of intravenous PSA in both medicine and dentistry [15, 19].

Of course, with the development of other intravenous agents, other pharmacological agents have been added to the armamentarium of those using the intravenous route for PSA [23, 25].

It is therefore fair to say that Jorgensen, a dentist, is truly the father of procedural intravenous sedation in dentistry and medicine [8, 7, 15, 19].

NITROUS OXIDE SEDATION

As we have seen, a physician Klikovitch, was the first to recognise the anxiolytic potential of nitrous oxide, at levels consistent with consciousness [16, 17] Nonetheless, he only fairly systematically studied its anxiolytic and analgesic applications in obstetrics and gynaecology, without realising its potential as a safe, easily utilisable anxiolytic for other surgical applications [16].

Harry Langa

Once again, it was a dentist, Harry Langa, more than anyone else, who introduced N₂O and O₂ minimal

sedation for use in dentistry. He is therefore indirectly responsible, [15, 26] for its later use in other applications in medicine [27]. In 1937, Langa started using low-dose subanaesthetic nitrous oxide mixed with high concentrations of oxygen, to produce conscious sedation [28]. From 1949 onwards, [28] Langa introduced a high-quality training course in conscious sedation with nitrous oxide, which he termed relative analgesia [15]. Langa noted that one of the major obstacles to introducing the use of analgesic nitrous oxide to dentists was ignorance. They were filled with the frightening stories of the dangers of 100% N₂O as previously used in dentistry, including fatalities [12, 15, 28, 29] And they were aware that for these reasons it was no longer used as an anaesthetic in dentistry. Clearly, they were unaware of the fundamental differences between the properties of analgesic N₂O when diluted with high concentrations of O₂, used as an anxiolytic and analgesic, and the anaesthetic properties of N₂O at 100% [28]. The reader may be interested to know that from 1980, and for 30 years thereafter, I struggled in the face of a hostile criticism from dentists, physicians and anaesthesiologists, to reintroduce minimal sedation with N₂O and O₂ to South Africa. Their criticism was usually based on the same erroneous premise that earlier opposed Langa - that it was dangerous. Indeed, the same criticism had been levelled in Europe and North America in my efforts to get physicians to use minimal sedation for treating acute substance abuse withdrawal states, [30] despite its safety, efficacy and rapidity of action [31].

In 1962, the American Dental Society of Anesthesiology held a series of courses which were attended by dentists from 43 dental schools [15]. By 1976, Langa had trained 6000 dentists at various American dental schools, to safely use N₂O and O₂ for PSA [15, 32]. In 1968, his work on nitrous oxide resulted in publication of his classic book (Relative Analgesia in Dental Practice: Inhalation Analgesia and Sedation with Nitrous Oxide), [9] which by 1976 had reached a second edition [33]. This was the first textbook devoted specifically to the subject of PSA. It was also, for many years, the most comprehensive guide dealing with PSA using N₂O and O₂ [15]. It still remains the most extensive and detailed textbook on the subject of N₂O and O₂ for PSA.

It is ironic that physicians have taken almost complete possession of these discoveries and seemed have forgotten, or conveniently ignored, the seminal role taken by the dental profession in the field of PSA

Table 1: Main Milestones in the History of Procedural Sedation and Analgesia

Date	Pioneer, Profession & Event	Event & Investigator/s
1800	Scientist, Humphry Davy publishes his monograph on N ₂ O	Davy's details his research on N ₂ O and its chemistry and effects on animals and man including its psychotropic actions (euphoria, analgesia) and other properties [1]
10 December 1844	Dentist, Horace Wells realises significance of N ₂ O conscious analgesia	Wells, attends, witnesses & realises the significance N ₂ O analgesia at a public demonstration [3, 5, 12, 13]
11 December 1844	Wells introduces anaesthesia to man	First surgical procedure (tooth extraction) under anaesthesia is independently witnessed [3, 5, 12]
October 1846	Dentist, William Morton introduces ether anaesthesia	Morton (later qualifying as a physician) gives first public demonstration of ether anaesthesia (almost 2 years after Wells' demonstration of N ₂ O anaesthesia) [11, 12, 19]
1848	Wells acknowledged discoverer of anaesthesia	Parisian Medical Society (France) [3, 5, 12]
1864	Wells acknowledged discoverer of anaesthesia	American Dental Association [3]
1870	Wells acknowledged discoverer of anaesthesia	American Medical Association [3]
1881	Physician, Stanislav Kliekovich first to use N ₂ O's non-anaesthetic actions (for anxiolytic & analgesic properties)	Kliekovich, obtains an MD Thesis for the use of N ₂ O in medicine, obstetrics and gynaecology and various medical conditions (asthma and coronary heart disease) [16]
1902 or 1903	Dentist, Charles Teeter develops first practical delivery system for N ₂ O & O ₂ anaesthesia	Teeter, develops practical equipment for delivery of N ₂ O & O ₂ [12, 15, 18]
1910	Dentist, JA Heidbrink & physician, El McKesson improve Teeter's equipment	Heidbrink & El McKesson modifies Teeter's earlier design [12, 15]
1911	Physician, AE Guedel develops self-administration system for N ₂ O & O ₂	Guedel's self-administration system for N ₂ O & O ₂ heralds the wider use of N ₂ O & O ₂ for obstetrics [17]
1923	Dentist, Neils Jorgensen begins using Ethyl alcohol for PSA	Jorgensen uses oral ethyl alcohol for PSA [15, 21]
1937	Dentist, Harry Langa introduces PSA with N ₂ O & O ₂ for surgical applications	Langa introduces PSA with N ₂ O & O ₂ for operative procedures (in his dental practice) pointing the way for it's use for other medical procedures [27, 28]
1945	Dentist, Jorgensen introduces intravenous PSA, using drug cocktail	Jorgensen is the first practitioner to use an I.V. cocktail (pentobarbital, scopolamine, meperidine) for PSA [15, 19, 20, 22]
1949 onward	Langa introduces first quality training courses for PSA	Langa introduces high quality training for PSA [28]
1968	Langa publishes first textbook on PSA	Harry Langa writes comprehensive textbook on PSA using N ₂ O & O ₂ [9]
1980	PSA for Anaesthetic practice	PSA becomes accepted as a discipline for Anaesthetic practice [23]

Only the key events are listed, corroborative research can be found within the main text.

[19]. 'This seems to confirm the truth of what Winston Churchill was purported to have said, "History is written by the victors."' [19].

CONFLICT OF INTEREST

Since 2003 Prof Gillman have been the medical adviser to Sedatek, a company that sells conscious sedation equipment. I have no shareholding in Sedatek.

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