Sarah Alger: Welcome to Proto, a new podcast that explores the frontiers of medicine. I'm Sarah Alger.

Jason Anthony: And I'm Jason Anthony. This week, we're doing a deep dive into a fascinating chapter in medical history. The creation and uses of nitrous oxide or laughing gas.

Mike Jay: His idea was that he was going to produce and synthesize all the known gases and see if they had any therapeutic applications.

Sarah Alger: That's author Mike Jay, and he's talking about Humphrey Davy, who about 200 years ago, took a job with a so-called Pneumatic Institution, where scientists created and experimented with new gases. Their clinical trials involved, local doctors, neighbors and friends.

Mike Jay: Davy instituted a series of experiments where these people would come around in the evening and they'd inhale nitrous oxide from a green silk bag and they try and describe the experience.

Jason Anthony: The discovery of nitrous oxide would change not only the course of pain treatment, but also literature, popular entertainment and the limits of what was acceptable in a scientific publication.

Sarah Alger: Coming up on this episode of the Proto Podcast brought to you by Massachusetts General Hospital.

Jason Anthony: The history of medicine is in some sense, the history of pain. Pain is still the main reason that a patient makes an unscheduled visit to a physician or a hospital, and pain has always been a primary driver in the search for new cures and treatments.

Sarah Alger: The quest to manage pain is still ongoing. In an era when record numbers of people have become addicted to opiate painkillers, many research teams today are looking for new non-addictive alternatives, a topic we'll cover in Proto's January issue.

Jason Anthony: One of the first major breakthroughs in pain treatment happened not far from where we're sitting at the Ether Dome of Massachusetts General Hospital, right there in 1846, a patient senses were dulled enough to perform painless surgery for the first time in history.

Sarah Alger: But that act would not have been possible without earlier experiments and painkillers. And one of the most remarkable of those was nitrous oxide, laughing gas. The first lung full of nitrous oxide gas was inhaled in 1799. The subject Humphrey Davy described the experience as "A highly pleasurable thrilling in the chest and extremities." Mike Jay has written about the curious journey of nitrous oxide in his book, The Atmosphere of Heaven. He has also recently written the introduction to Oh Excellent Air Bag, a new collection of historical writings about the drug from the first 125 years of its existence. Thank you for joining us.

Mike Jay: It's a pleasure to be here.

Sarah Alger: I wondered if we could start with the discovery of nitrous oxide in 1799 and if you could introduce us to the three key players, maybe you could start with Thomas Beddoes.

Mike Jay: This was an era where there weren't many chemical remedies and medicine, but Thomas Beddoes was convinced that synthesizing new chemicals and in particular new gases, there were all kinds of medical breakthroughs to be made. So, he set up something called the Pneumatic Institution, which was probably the first example of what we would now call a medical research laboratory. He hired Humphrey Davy who was a young untrained but absolutely brilliant chemist, and almost immediately Humphrey Davy synthesized nitrous oxide and inhaled it and discovered it had an odd sweet taste. It seemed to be quite easy to inhale, it didn't seem toxic or as if it was going to kill him. He carried on inhaling and then produced the description of the experience that you started with.

Sarah Alger: And I understand one of the key players as well was one Samuel Taylor Coleridge. How does he fit into this?

Mike Jay: Once Humphrey Davy had discovered that nitrous oxide had these remarkable properties, he discovers that it made you feel very, very good and it also had these stimulating effects on the imagination. Once he discovered that, then he became interested to describe this new state of consciousness that turned out to be very hard to describe. So, he engaged the assistance of a lot of his friends who included young romantic poets, Robert Southey and Samuel Taylor Coleridge. Davy instituted a series of experiments where these people would come round in the evening and they'd inhale nitrous oxide from a green silk bag, and they try and describe the experience. So, he was interested in finding people who could describe eloquently what was going on, which was in a way very much what the young romantic poets were trying to do. They were also trying to create and construct a language of feeling, a way of talking about emotional states that hadn't been talked about before.

So, Southey and Coleridge, along with the young doctor Roget of Roget's Thesaurus fame and various other people who contributed descriptions of nitrous oxide. But Samuel Taylor Coleridge provided something particular. He'd just come back from Germany and he was one of the very first people in Britain to be exposed to the new German philosophy of Immanuel Kant and the idea that it might actually be the realm of the imagination, the realm of the mind that was the real world and the material world was just an emanation of it rather than the other way round. And in Humphrey Davy's climactic experiment with nitrous oxide in which he takes an enormous amount of it. He shuts himself in a box that has nitrous oxide pumped into it for about an hour and gets as high as he can possibly get. Davy emerges with the statement that nothing exists, but thoughts

Sarah Alger: I'd like to read just one line from your introduction. "The laboratory became a philosophical theater in which the boundaries between experimenter and subject spectator and performer were blurred to fascinating effect, and the experiment took on a life of its own." Now, that's certainly very different from medical research today. Was that extremely different for its own time period as well?

Mike Jay: It was certainly a very freewheeling experiment which left the medical ambit behind. Davy in particular really enjoyed taking nitrous oxide and whenever anybody else took it, he'd usually take some to keep them company and then he got into particularly on nice summer evenings when the full moon was up, he'd inflate a bag with nitrous oxide and take it out of the laboratory, up into the Hills overlooking the Avon Gorge in Bristol and with his large gas bag in one hand and his notebook and the other he'd sip away and write poetry and compose chemical formula.

Sarah Alger: And it takes an interesting turn after that and it ends up being used in side shows where a lecture would basically give nitrous to someone on stage. Can you tell us about that?

Mike Jay: The phenomena of nitrous oxide raised all kinds of fascinating fundamental questions, how could a gas that as far as anyone knew didn't exist in nature had just been synthesized in the laboratory, how could that produce these extraordinary effects on consciousness? What did that say about the origin of thoughts and emotions and feelings? These were all fascinating philosophical questions, but they were questions that were beyond the reach of medical science at that time. So, the effect of Davy's work was really to bring it into this world first of all touring lecture theaters or scientific marvels, and then eventually nitrous oxide shows took their place alongside things like hypnotism and magic shows. That was a long way from what the Pneumatic Institution had in mind, but turned out to be the conduit by which nitrous oxide would make its great medical breakthrough.

Jason Anthony: So, let's quickly list the ways that this is not the way that science is conducted in 2016. First off, the way that Humphrey Davy puts himself right in the middle of the experiment, right?

Sarah Alger: Exactly right, and he enlists all of his friends as well, which is clearly not how science works now.

Jason Anthony: And he also puts poetry into his academic paper. He has the insights of Samuel Taylor Coleridge, this father of the romantic poetry movement in England, who's famous for work such as The Rime of the Ancient Mariner and Kubla Khan. He has all of these philosophical insights of his own and these go into this paper that would just become the toast of its day. I don't think that we see that in 2016 anymore.

Sarah Alger: I don't think so. Certainly not in the same paper. What followed after Davy was the primacy of science and peer review and all of that thing. There's the return to understanding and appreciating the humanities with science, but not together in the way that he did.

Jason Anthony: Makes me think of William Carlos Williams writing those beautiful poems as a physician on his prescription pad, and wondering if those would ever... they were lives that he kept separate, but wondering whether... we have so many physician poets and researcher posts, wondering whether those could ever live in the same documents in the way that they did.

Sarah Alger: It calls to mind for me the whole notion of narrative medicine, where you have the formal patient's chart and then you have the physician with more interpretive notes about the patient.

Jason Anthony: Absolutely.

Sarah Alger: But, but I can't foresee that something like this would pass peer review ever again.

Jason Anthony: Probably not.

Sarah Alger: In Humphrey Davy scientific paper published in 1799, he writes of nitrous oxide, "It appears capable of destroying physical pain, it may probably be used with advantage in surgical operations." But in fact, this application of nitrous oxide would not come into use for decades. My conversation with author Mike Jay continues with a story of how laughing gas went from philosophical curiosity to the important medical anesthetic still in use today.

Mike Jay: Davy noticed that when he inhaled nitrous oxide, he became much less sensitive to pain. He'd injured himself without noticing it, but the doses that he was taking, a lung full of nitrous oxide is a great deal less than an anesthetic dose. It didn't make people comatose, it made them more often laugh and giggle and shout and caper around the room and recite poetry. So, he registered the possibility of it being an anesthetic, but it was only really buried in the footnotes of his text.

Sarah Alger: And so now, can you tell us how Horace Wells enters the picture?

Mike Jay: There was a nitric oxide sideshow being run by a temperance preacher called Gardner Quincy Colton, who was using nitrous oxide in a very interesting way. As part of his temperance lectures. Horace Wells was a dentist who attended it and he noted at one point that somebody inhaled a bag of nitrous oxide and then stumbled around and while they were intoxicated by it hit their shin quite badly against a table but didn't notice the pain until later. Horace Wells as a dentist was very aware that one of the limiting factors on his business was that people avoided dental procedures because of the pain.

So, he started to wonder whether it might be possible to give nitrous oxides to people before they had their dental procedures. He had a tooth that needed to be extracted, he hadn't quite plucked up the courage to entrust that to one of his colleagues. So, he asked Colton to give him a bag of nitrous oxide to inhale and he then had his tooth extracted painlessly, and he came out rather like Humphrey Davy with a wonderful prophetic announcement, announcing a new era in tooth pulling, and people immediately said to him, "Somebody could make a great deal of money out of this." And Wells said, "No, let it be as free as the air that we breathe."

Sarah Alger: So, to circle back to Humphrey Davy, whatever became of him.

Mike Jay: Well, Humphrey Davy was launched onto a glittering career by nitrous oxide. He was head hunted from the Pneumatic Institution and brought to London where he gave lectures on respiration and demonstrations of nitrous oxide. At the same time, he was working on the Voltaic pile, which was the first cell battery, which enabled them to do electrolysis and to separate out all elements that hadn't been separated before. So, he then discovered potassium, calcium, magnesium, sodium, chlorine, incredible list of elements. He was very ambitious. He left his nitrous oxide experiments behind him and he became eventually the president of the Royal Society and the great romantic hero of that generation of British scientists. But, nitrous oxide was really an important part of his origin story as he became this great public figure, everybody remembered how he'd started and he'd started by fearlessly inhaling nitrous oxide, boldly going where no one had gone before and leading by example.

Sarah Alger: Mike Jay, this has been fascinating. Thank you so much.

Jason Anthony: If you'd like to learn more about the curious history of laughing gas, you can find our guests, Mike Jay's work in the anthology Oh Excellent Air Bag. That's available from public domain review.

Sarah Alger: We hope that you'll join us for the next Proto Podcast. You can find us on iTunes, Stitcher or wherever you get your podcasts, and at protomag.com where you can sign up for a free subscription to our print magazine. I'm Sarah Alger

Jason Anthony: I'm Jason Anthony. And Until next time, thanks for listening to the Proto Podcast.