

Hypoxic Drive: Myth, Fact, Fiction or Reality?

By John R. Goodman BS RRT

There has been much recent interest from people who post on copd-alerts and other patient oriented websites about something known as “Hypoxic Drive.” So bear with me for a few minutes while I sort of set the table for you. Let’s start with the word “Myth.” Myth comes from the Greek word *Mythos*, which means *story* or *word*. Myths have traditionally been tales believed to be true, usually sacred, set in the distant past, in other worlds with extra-human, in-human, or heroic characters. But the common denominator is they are rarely if ever “testable.”

What are some of the longest held myths or legends? A partial list might include vampires, dragons, Bigfoot, fortune telling, astrology, witches and voodoo. But, how do legends and myths begin, and just as importantly, how do they propagate? The scenarios usually runs something like this....Something happens in long ago history, over time the historical story becomes legend. Given time and repetition, the legend becomes a myth. And with even more time myths eventually become pseudo-history. And don’t forget there are always the hoaxes (some very good), fairy tales, and outright deceptions.

It is both unsettling and painful to quote Nazi minister of propaganda Joseph Goebbels, yet it was he who said back in 1937 that “If you tell a lie big enough, and keep on repeating it, people will eventually come to believe it.”

How about a modern example. In 1986 the book “Holy Blood and Holy Grail” was published. It was based on a deception, which was based on ancient myths. It merely suggested a theory, but the authors claim their theory was based on facts, which were not true. Jump forward to 2003, and the publication of “The Da Vinci Code.” It took the theories postulated in “Holy Blood and Holy Grail,” added another set of pseudo-historical possibilities, and then became a huge world-wide movie phenomena. This in effect continued to spread the mistruths and untestable theories. The result, however, is that when presented in a professional manner (as if it were peer reviewed) people accept it as both believable and truthful. The moment they accept it...they are fooled.

Need more proof? Let’s look at the ten top medical myths (by very large survey) that have been rigorously disproven by well designed, peer reviewed scientific studies. In order they are:

1. Sugar makes your kids hyperactive. (Nope, not even kids with ADHD.)
2. You lose most of your body heat through your head.
3. You should drink at least 8 glasses of water per day.
4. Chewing gum takes 7 years to pass through your system.
5. Cracking your knuckles will cause arthritis later in life.
6. Teething may cause a fever.
7. Back pain should be treated with bed rest.
8. Eating turkey makes you sleepy due to the Tryptophan.
9. Eating at night makes you fat.
10. It is harder to lose weight than gain weight.

When discussing the hypoxic drive theory, there are actually only 2 components we really need to discuss.

1. There truly *is* a normal hypoxic drive mechanism.
2. The “theory” relating hypoxic drive to COPD patients who have or are thought to have chronically elevated carbon dioxide levels.

Note to audience: Normally at this point of the article I would go into the beautiful anatomy and physiology of the peripheral chemoreceptors, their location, and the very small role they play in ventilation. Well, thank the dear Lord cause I am not. There are so many websites and blogs you can access if you want to know the cellular mechanisms. But why don’t we just stick to the story line for the purposes of this article.

We can say with 100% certainty that we really do have specialized chemoreceptors that really do respond to changes they sense in the blood flow passing by them. But, remember our definition of myth. The “theory” of hypoxic drive is very, very real and very, very testable. Hundreds of papers have been reported in the peer reviewed literature on the pure anatomy and physiology of hypoxic drive.

Even a cursory review of the literature will teach you a great deal about hypoxic drive itself. But trying to see who, where, or when the idea of giving high concentrations of oxygen to known CO₂ retainers could actually precipitate acute respiratory failure (ARF) is very murky and speculative at best. In fact, it is really tough to put our finger on exactly when or where this myth actually got started. It seems to have been mentioned for the first time by Dr. Alvin Barach back in 1938, but to the best of our combined research it seems to be associated most strongly with Dr’s Arnott and Dr. Campbell in 1960. The paper was printed in Lancet; a much respected peer reviewed British Medical Journal. The original paper was on “respiratory failure” and was also presented in many lecture halls around the world.

Here are a couple of quotes from the original paper. *“Owing to the insensitivity of the respiratory centre to carbon dioxide, the respiratory drive of such patients depends unduly on the hypoxic stimulus. Once this is corrected, ventilation becomes less and carbon dioxide retention increases....perhaps dangerously.”* Hello Hypoxic Drive theory!

Further *“Some people maintain that is alright to give high or uncontrolled O₂ if the patient does not underbreathe. Of course that is true, just as it is safe to pass on a blind curve if nothing is coming the other way.”* Hello, it’s dangerous to give these particular patients more than 2 liters of oxygen per minute. (As an interesting side note, when Dr. Campbell was a little older he and 3 colleagues published a paper in the British Medical Journal titled “Ability to distinguish whiskey from brandy.”) Ya gotta love that!

So if you were Lt. Columbo, how would you sum up the case so far? Columbo might look at things like this...A clinical association was made between high oxygen concentrations and increasing carbon dioxide levels. For the sake of this article, it probably doesn’t matter who was the first to make this association because, once the association was made a theory had to be

constructed to fit the facts. Sounds like it may be the beginning of a myth to me. This is especially true in medicine where there is almost an imperative to come up with an explanation.

I'd be the first to say that things are so very different today compared to the early 1960's. For example, simple oximetry was non-existent except for purely research purposes, the home oxygen industry was not even invented yet. There was a very widespread belief that any oxygen for patients with COPD was harmful, and as a result many physicians tolerated much lower saturations for their patients. There are cases where the patient's saturations were allowed to get down into the 20's and 30's with no one thinking that's pretty darn low.

So, an entire generation of physicians, respiratory therapists (including me when taught in college) nurses, first responders, and others were taught about hypoxic drive, and the myth associated with it. Over time, it is so easy to see how the myth, grew, propagated, and spread. Fortunately, since so very few other clinicians were seeing much clinical evidence of hypoxic drive, some of them began to look into it more rigorously. Credit for the first in a LONG series of papers de-bunking the myth usually goes to Dr's. Aubier, Murciano, and Fournier. In their paper published in the Am. Rev. of Resp. Dis. in 1980. Their paper was titled "Effects of the administration of oxygen on ventilation and blood gases in patients with COPD during ARF." They did find some evidence that in the 22 patients they studied some of the patients had a transient increase in their carbon dioxide level, but it had returned almost all the way to baseline (93%) after about 15 minutes. But, in real life, those 15 minutes may seem a lot longer. Could this have led to the "I've seen it happen" conclusion?

I could at this point summarize the entire article, but trust me; this very well designed study *should* have been the beginning of the hypoxic drive theory. In the time it took to go from the Madonna era to Lady Gaga, scores of papers have been written effectively exposing the myth of hypoxic drive. So, why won't the theory die! Even here, we can only speculate. Sometimes we may sign our name to something due to devotion to another physician or institution. It may be classic turf battles, professional pride, and even economics. Heck, they only stopped bloodletting about 100 years ago, and we won't even talk about leeches.

I firmly believe that it will take something like a **mini-medical paradigm shift** to bring the hypoxic myth down. The term "paradigm shift" was first defined in a book titled "The Structure of Scientific Revolution" written by Thomas Kuhn in 1962. He defined it as "A change in one way of thinking to another. A transformation." He described it as a revolution that did not just happen, but rather it had to be driven by agents of change. Who better to be agents of change than patients themselves? It was just under 500 years ago that Copernicus proved the sun was the center of the universe. No one ever thought the old Ptolemaic theory would ever be replaced, but it was. Copernicus, with a little help from his friends, proved scientifically that his theory was correct.

In summary, most myths and legends have some basis in fact. History is replete with examples of this phenomenon. While it is theoretically possible for a patient's hypoxic drive to be knocked out, in real clinical practice, it is so rare as to be virtually never seen. Don't believe me, as your pulmonologist or respiratory therapist how many COPD patients in their entire careers they have ever had a patient suffer from the hypoxic drive myth. I celebrate my 45th year as a

respiratory therapist this year, and in all that time I *have never, ever* seen a patient slow down or stop breathing when their oxygen has been judiciously administered.

If you think about it, oxygen is the only drug that may be administered without a prescription for flow rate. When does this happen you ask, every time a first responder, EMT, or paramedic finds a patient down. Quoting the father of oxygen therapy in the home, Dr. Tom Petty (and it doesn't get much better than that) from his book "Adventures of an Oxyphile" "Unfortunately, quite a few physicians believe or fear that oxygen use will cause retention of carbon dioxide. This is generally not true. The majority of patients using only a little supplementary oxygen just to correct the oxygen deficiency state, a saturation above 90% but not greater than 96% will have no bearing on carbon dioxide level."

It bothers me sometimes to think that the patient must in this case have to teach the teacher. Although I have no proof, I'm betting the hypoxic drive theory is still being taught from early in medical school, and at each step along the educational path for pulmonary (and other) physicians. Likewise, I suspect even some of my teaching colleagues in Respiratory Therapy programs have not yet become the agent of change. So I don't know how many more generations of clinicians and patients are going to have to push this elephant up the hill. But like a paradigm shift...we have to start somewhere and sometime. As for me...I will continue to follow Goodman's 1st maxim which is "follow any set of tubing long enough...and you'll always find a patient."