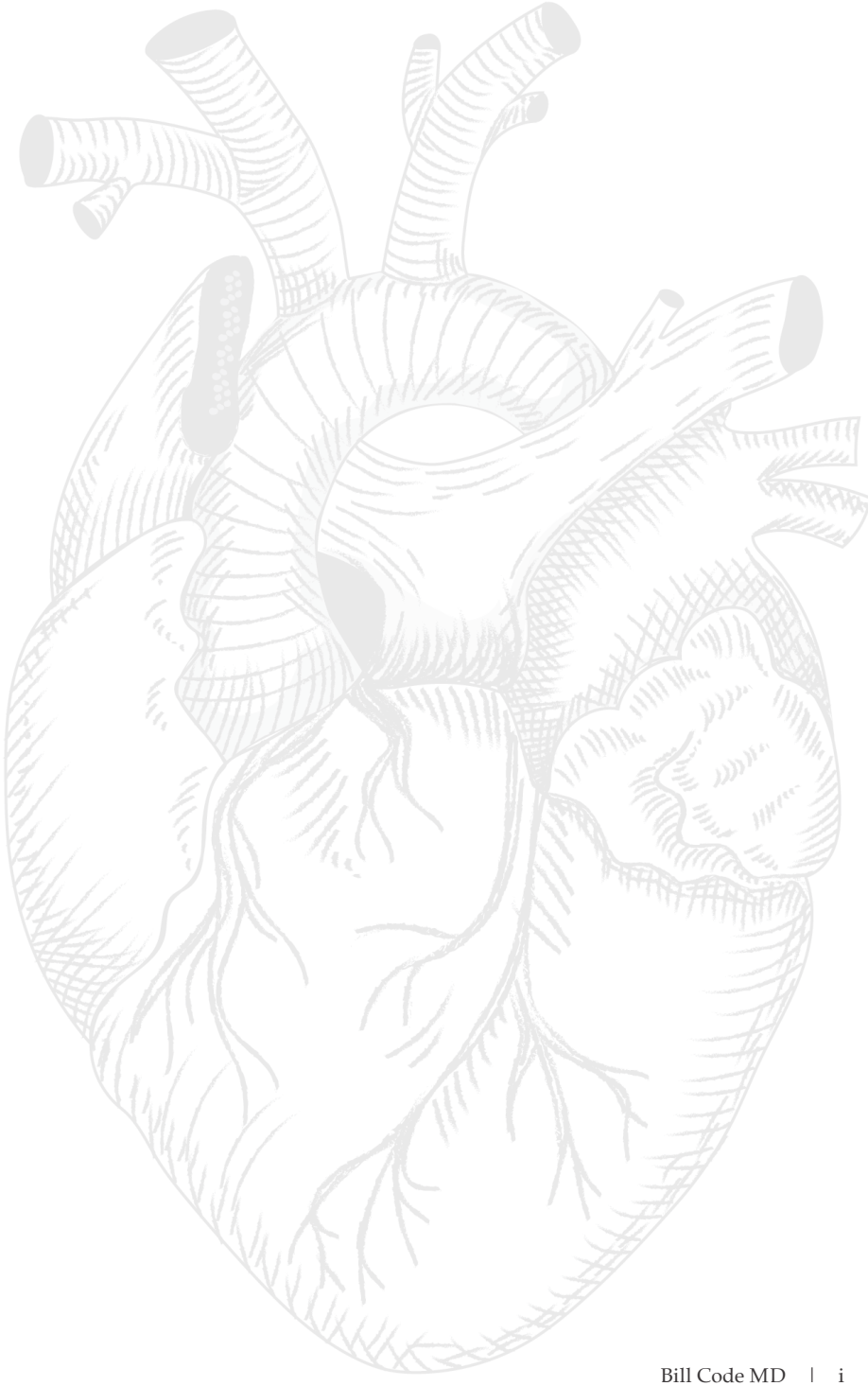

Solving the Heart Puzzle

An MD's Journey Through Oxygen, Omega-3s, and the Science of Healing

— Bill Code MD —

This book contains advice and information relating to healthcare. It is not intended to replace medical advice and should be used to supplement rather than replace regular care by your doctor. It is recommended that you seek your physician's advice before embarking on any medical program for treatment. All efforts have been made to assure the accuracy of the information contained in this book as of the date of publication. The publisher and the author disclaim liability for any medical outcomes that may occur as a result of applying the methods suggested in this book.

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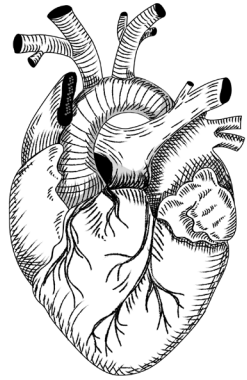


CHAPTER 10

Microcirculation

1. Microcirculation: *Where the Rubber Meets the Road*

The heart and the brain's vascular network are vast and dominated by small, tiny vessels. To understand disease and intervention it is more useful to focus on the microcirculation than on the few larger epicardial or intracranial arteries. The size comparison is critical. The macrocirculation is vessels of larger diameter: >500 microns or 0.5mm in size. Meanwhile, the microcirculation denotes arterioles and capillaries in the 2.0 to 200 Micron range. For comparison the human hair is roughly 50 to 100 microns. Ideally, we should visualize that most perfusion problems occur at these vessels that are hair sized or smaller, rather than at the few major conduits like the aorta, carotids and coronary vessels.

2. Poisseuille's Law

This law explains why small changes or narrowing is significant. Clinical intuition often underestimates the hemodynamic impact of minor luminal narrowing in small vessels.

Poisseuille's Law describes that the flow through a cylindrical tube is proportional to the 4th power of its radius. Therefore, if the radius is halved, then the flow falls to one sixteenth of the original. This is why even modest concentric narrowing from edema or swelling of the wall, or inflammatory thickening, can therefore cause considerable reductions in flow. The clinical implications of this are that even though it seems a minor problem of inflammation, it is not a mild problem because it can sharply reduce regional perfusion.

Certainly, this law is drilled into anesthesiology trainees when choosing IV or intravenous cannula size. For example, a 14 gauge may look like a garden hose to the anesthesiologist, but it is only modestly larger than a 22 gauge. However, the flow differences between these two are dramatic. This same principle applies to tiny arteries or arterioles and capillaries in the heart and the brain. Finally, even without obvious stenosis or narrowing on imaging, microvascular narrowing can generate substantial lack of oxygen or ischemic problems.

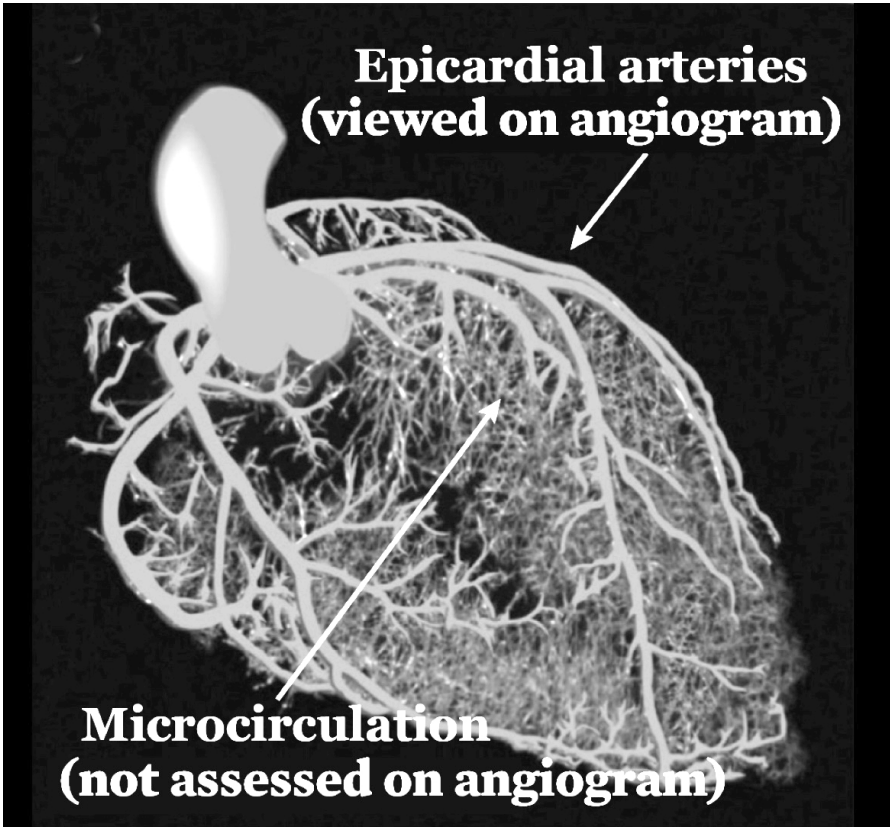


Figure 6: Microcirculation and Coronary Vessels.

3. Oxygen and Cognitive Function

Oxygen delivery appears to be a rate limiting factor for cognitive performance. This includes memory and learning even in healthy young individuals. This can become clinically obvious in people with a neurological vulnerability. This would include multiple sclerosis, post concussive symptoms or other brain insults. These people often report substantial improvement in cognitive cognition and resilience to sensory overload when oxygenation is optimized. "Resilience to interference" here refers to the ability to tolerate noise, light, motion, and other environmental stimuli without overwhelming fatigue or symptom exacerbation.

To illustrate this, I want to describe a clinician who with long standing MS had severe sensitivity to sound, light, and minor physical jolts during travel. He later discovered that improving oxygenation with either hyperbaric oxygenation or at home extra oxygen with a concentrator could markedly reduce these sensitivities. In addition, it allowed him sustained cognitive work for example writing a large reference heavy book. Although this is anecdotal such experiences are consistent with experimental data showing that increased brain oxygenation can improve both learning curves and reduce vulnerability to outside interference.

Short term high flow oxygen experiments have suggested that even brief exposures to high concentrations of oxygen such as 70 to 80% oxygen via non rebreather mask, can confer measurable cognitive benefits lasting hours. Clinically, longer and repeated exposures such as 30 minutes twice a day may yield more robust and persistent improvements for these chronic conditions.

4. Altitude, Oxygen Conditioning and Room Air is Not Fixed

Room air is not really a fixed reality. Both altitude and inspired oxygen fractions can shape effective oxygen delivery. It is well recognized that approximately 140 million people live at altitudes greater than one mile (1600 meters). In cities like Mexico City and Denver and even higher Andean cities in Bolivia folks must manage chronic altitude hypoxia.

Oxygen conditioning is a term used when people adapt their high altitude urban settings by enriching the room air to 26 to 28% oxygen. The rule of thumb is that for each 1% increase in inspired oxygen it will permit a comfortable tolerance of an additional 330 meters or 1000 feet of altitude. Therefore, enriching to 26% oxygen at one mile will approximate the same as occurs at sea level for oxygen availability.

And a practical example of this oxygen conditioning occurs in hotels in high altitude tourist hubs. This includes Cusco which is at the gateway to Machu Picchu where they sometimes offer oxygen enriched hotel rooms of 28%. Booking such rooms can prevent or mitigate altitude sickness in susceptible travelers. However, it is difficult to predict who will become symptomatic and require these special rooms. Individuals who bring their own oxygen concentrators can further reduce their own risk. This is what I did successfully visiting Machu Picchu several years ago.

Another important consideration is the barometric pressure where you are currently living. Even modest differences in barometric pressure at or near sea level for example a range of 980 to 1030 hectopascals can translate into roughly a 10% difference in available oxygen. Sensitive patients such as those with chronic headaches or lung disease may often feel these changes. It is reasonable and prudent personal practice to monitor barometric trends and correlate them with your symptom flares.

Simply look at your phone weather app!

5. Hyperbaric Oxygenation: *From Diving Medicine to Neurology*

Hyperbaric oxygenation (HBO) was developed primarily in diving and military medicine for decompression sickness called the bends or gas embolism. Multi place hyperbaric chambers are typically situated at a major naval and military center. The chambers are now underutilized as diving has become safer and deep exploration uses submarines, cameras, and robotics.

The basic concept is that HBO involves breathing nearly 100% oxygen at elevated ambient pressures. This is commonly done at 1.5 to 2.0 atmospheres absolute (ATA). This greatly increases dissolved oxygen in plasma, permitting high oxygen delivery even when hemoglobin is fully saturated. There is no reason to exceed 2.0 ATA or atmospheres of pressure when working to heal the brain or the heart.

The classic indications for hyperbaric oxygenation include decompression sickness, gas embolism whether created by physicians or a blast, or explosion. It is also used in certain aggressive necrotizing infections and problem wounds. The neurologic field has been slower to incorporate HBO despite reasonable studies or pathophysiological plausibility suggesting that their patients might benefit.

The safety considerations of HBO are very minimal when protocols are followed. The main risk in unconscious or non-cooperative patients is the barotrauma from inability to equalize middle ear pressure. This can be solved by a small needle puncture of the eardrum or tympanic membrane

when necessary. The other consideration is claustrophobia and the extremely rare oxygen toxicity seizures. Seizures are now felt to be due to vessel constriction and secondary low glucose when occurring inside chambers well above 2.0 ATA. Fire risk in the chamber is of minimal practical concern if the regular guidelines of what to take into the chamber are carefully followed.

6. Non rebreather Masks and High Flow Oxygen at Home

A non rebreather mask is a simple, powerful tool for increasing the inspired oxygen fraction well above that achievable with a simple nasal cannula. The design includes a face mask with side exhalation ports. A reservoir bag is attached beneath the mask. There is a one-way valve at the top of the reservoir bag. The oxygen enters from a supply tube usually from an oxygen concentrator.

The mechanism of operation is that during exhalation, the valve closes. Exhaled gas leaves from the mask edges or side ports, but not into the reservoir bag. Then fresh oxygen continues to fill the reservoir bag while the patient breathes out or exhales. During inspiration, the patient draws from both the supply line of oxygen and the reservoir bag. Therefore, the individual can achieve inspired oxygen fractions potentially approaching 100% but more commonly 70 to 80%, depending on the mask fit and flow rates.

The practical consideration is that when you combine a non rebreather mask with a home oxygen concentrator, it can deliver high fractions of inspired oxygen without requiring compressed gas cylinders. The flow meter of the oxygen concentrator typically includes alarms. Therefore, if the flow meter is set above safe continuous delivery thresholds, the flow must be turned down slightly or the machine will alarm. When you turn down the flow you will likely need to turn the machine off briefly to allow the alarm to reset.
See figure on page 80.

7. The Hyperoxia: *Hypoxia Paradox and HIF-1*

The "hyperoxia–hypoxia paradox" describes how intermittent hyperoxia can trigger cellular pathways normally associated with hypoxia upon return to normoxia. Central to this phenomenon is the hypoxia inducible factor 1 (HIF-1).

HIF-1 basics — Especially in the Heart:

- HIF-1 is a transcription factor that becomes stabilized and activated in low oxygen conditions or in certain reduction and oxidation environments.
- It regulates over 100 genes involved in survival under reduced oxygen, including those related to angiogenesis (growth new tiny blood vessels), erythropoiesis (increased new red blood cells), glycolysis (sugar fermentation) and cell survival.

Neuroprotective and Regenerative Roles—Especially in the Brain

- Increased HIF-1 expression is both neuroprotective and pro regenerative
- Enhances hippocampal memory and long term potentiation (nerve functioning) in research models.
- Supports neuroregeneration after stroke and even spinal cord injury.
- Facilitates angiogenesis and arteriogenesis in ischemic regions.

Angiogenesis and Collateral Formation

HIF-1 upregulates vascular endothelial growth factor (VEGF) and placental growth factor (PlGF), key mediators of new vessel formation. Clinically important downstream effects include:

- Angiogenesis: budding of new capillaries within hypoxic regions.
- Arteriogenesis: growth and remodeling of collateral arteries of the microcirculation around stenotic (narrowed) segments.

A significant subset of the population can develop robust collateral circulation and fare better in coronary or cerebrovascular disease crises.

Mitochondrial Biogenesis

- Intermittent hyperoxia can promote mitochondrial biogenesis, increasing both mitochondrial number and function, both in heart cells and in neurons. This is critical for patients with fatigue syndromes (e.g., MS associated fatigue, chronic fatigue states) where mitochondrial dysfunction is suspected. Periodic "oxygen bumps" such as 30 minutes once or twice daily appear to support mitochondrial health over time.

8. Oxygenation at Home: *Toward a New Clinical Frontier*

The availability of compact oxygen concentrators since roughly the 1980s has opened the door to oxygenation at home. This can be used as a deliberate healing strategy and not just as a palliative support in cases of advanced lung disease. The equipment required is a portable suitcase sized concentrator with standard flow meters and alarms. Ideally it is combined with non rebreather masks for high fraction oxygen sessions of 30 to 60 minutes. There is an optimal integration with the existing CPAP systems via low-cost adapters, T-piece, fitted inline and available from respiratory technicians. Then, during the night, oxygen at 1 to 2 liters per minute can flow through this T-piece.

For practical use, it is best to set the flow just below the top of the concentrator's recommended range to avoid alarms. I suggest the use of 30 minutes in the morning and in the evening as time limited sessions in stable patients with either heart, cognitive or neurological symptoms.

This self-care model is now an emerging model in where one could take primary responsibility for ongoing oxygen based interventions at home. The client is then supported by a knowledgeable person which can be integrative practitioners, neurologists interested in oxygen therapies, or anesthesiologists who are familiar with gas laws. I suggest this is an exciting new frontier which is particularly useful in those with microcirculation concerns or problems.

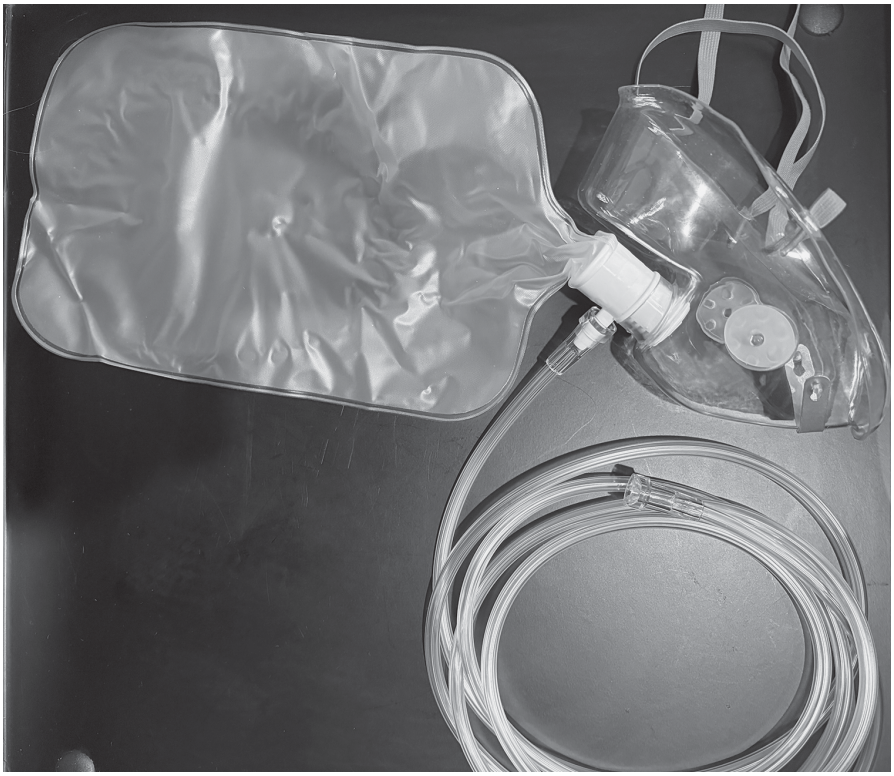
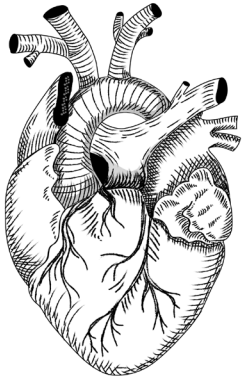


Figure 7: Non-rebreather mask (NRB).



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Any errors you note in this book are my responsibility. Please forgive me and let me know for the next printing.