"Into Thin Air"

A Case Study in Physiology

by
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Part I - Mt. Denali, Alaska, 17,660 Feet

The winded climbers slowly ascended the icy cliff in the near darkness of 4 a.m., carefully avoiding the steep crevasses that fell off sharply to either side. Several times each hour, Tom Benman, lead climber and expedition frontman, would call out "Everyone okay?" They had stopped replying long ago, too exhausted by the supreme effort of simply placing each foot in the proper direction. Three hours into a 12+ hour climbing day, the silence was permeated only by labored breathing and the crunch of ice under crampons.

Emily Norman, a Registered Nurse and the only woman on the six-person expedition team, was third in line, following her friend Mark McKinley, the least experienced climber of the group. For the last couple of days, Mark had been coughing heavily, and all morning had been slowing up, causing a backlog behind them and prompting several "everyone okay"'s from Tom. Knowing Mark's competitive spirit, Emily was hesitant to urge him to pick up the pace, and when he pulled up to rest on a protected ledge, Emily motioned to the other climbers to pass on by. Her head was pounding anyway, and she rationalized she could use the break.

"You okay?" Emily asked.

"Yeah....I just....can't seem to....catch my breath," gasped Mark.

"Just rest a minute. There's no rush, Mark. Take your time....slow, deep breaths."

Tom appeared from the upper trail. "What's up?"

"Mark's having a little trouble catching his breath." Emily was getting worried.

Tom looked sharply at her. "How much trouble?"

"Quite a bit, I think." Emily looked over at Mark, whose breathing didn't appear eased by the rest stop, and then back at Tom. "I think we should get him down to a lower altitude. Quickly."

Tom nodded. "I'll get the others."

Questions:

1. What types of physiological problems do humans encounter at high altitudes?
2. What symptoms did the climbers exhibit that might be related to altitude? Explain.
3. Compare the air at 18,000 feet (atmospheric pressure 280 mm Hg) to the air at sea level (760 mm Hg). What specific changes in the primary atmospheric gases (nitrogen, oxygen, carbon dioxide) might occur? Are they significant?
4. What is the specific pulmonary response to high altitude? [Assume you are considering a subject at rest.]
5. How will this response affect overall blood gases? What about oxygen loading and unloading from hemoglobin? Explain how you arrived at your conclusions.
6. After breathing at altitude for a few days, the body normally begins producing more 2,3-DPG. What is the significance of this change? How will it affect the pulmonary changes observed?

1) altitude sickness is the body's physiological reaction to the low oxygen levels that exist at high altitudes. This happens when you ascend too quickly or go from sea level to high altitudes in one day, and your body cannot get the oxygen it needs

2)
- Mark - short of breath, coughing heavily
- Emily - has a headache (a common symptom at altitude, hypoxia)

3)
recall that the "makeup" of the ambient air
- 21% oxygen
- 79% nitrogen
- <1% carbon dioxide

the density of the primary atmospheric gases change with altitude, but the composition stays the same. At sea level, the air that we breathe is at a pressure of 760mmHg, with the partial pressure of oxygen being 160mmHg (think of Dalton's law, 21% of 760mmHg). By the time the oxygen gets to the lung, we are down to about 14% (106.4mmHg) oxygen and an increase in the concentration of carbon dioxide at a pressure of 41.8mmHg. At 18000 feet, the partial pressure of oxygen is reduced to 58.8mmHg (21% of 280mmHg)

Image Credit: Climber descending the summit ridge, Mt. Denali, Alaska, 1999. Photograph by Scott Darsney, used with permission.
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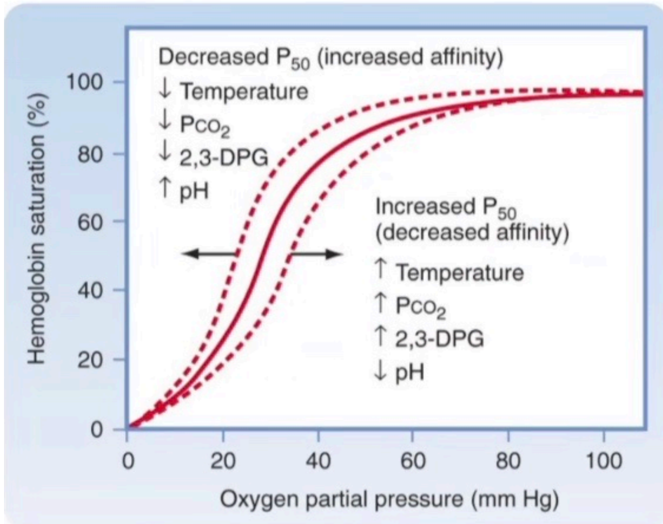
4)
This question is necessary to show that the altitude has an effect on breathing that is independent of any exercise. Students should correctly answer with "hyperventilation" which can lead to a discussion distinguishing hyperventilation and hyperpnea, and the causes for each.

- acute adaptation to high altitude and low oxygen supply is primarily by hyperventilation, which improves oxygen saturation Hyperventilation is an increased ventilation rate that is independent of the cellular oxygen needs and leads to abnormally low carbon dioxide levels and high (alkaline) blood pH.
- hyperpnea is an increased depth and rate of ventilation to meet an increased oxygen demand. This does not significantly alter blood oxygen or carbon dioxide levels, but merely increases the dwpth and rate of ventilation to meed the demand of the cells

5)

- hyperventilating decrease carbon dioxide levels --> increase in pH
- hyperventilating makes oxygen unloading from hemoglobin more difficult due to a decreased in P_{50}
- the oxygen-hemoglobin dissociation curve is shifted to the left with decreasing carbon dioxide



6) 2,3-Diphosphoglycerate (2,3-DPG) is a special intermediate of glycolysis in erythrocytes which is rapidly consumed under conditions of normal oxygen tension. However, when hypoxia is encountered in peripheral tissues, the concentration of 2,3-DPG can accumulate to significant levels within hours. At these concentrations, 2,3-DPG can bind to hemoglobin and reduce its affinity for oxygen, resulting in a right-ward shift of the oxygen-hemoglobin dissociation curve discussed in oxygen transport. This results in enhanced unloading of oxygen by hemoglobin and thus results in enhanced oxygen transport to tissues encountering long-term hypoxia

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Part II - Gasping for Air

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John, the assistant expedition leader and a seasoned alpinist, helped Tom guide Mark down the steep trail. Mark's breathing, increasingly labored with every passing moment, was loud enough to worry Emily and Pete, the expedition's final climber.

"Geez, do we sound like that?" gasped Pete. "I mean, I'm out of breath, too, but he sounds horrible!"

"No, we're not that bad. Remember, that's why we spent the prep month at 15,000 feet. Mark was with us, so he experienced the same physiological changes we did. This," Emily nodded at Mark, "is some sort of problem."

Questions:

1. What physiological changes is Emily referring to (above) that will occur when someone lives at altitude for an extended period?

2. How are these changes advantageous?

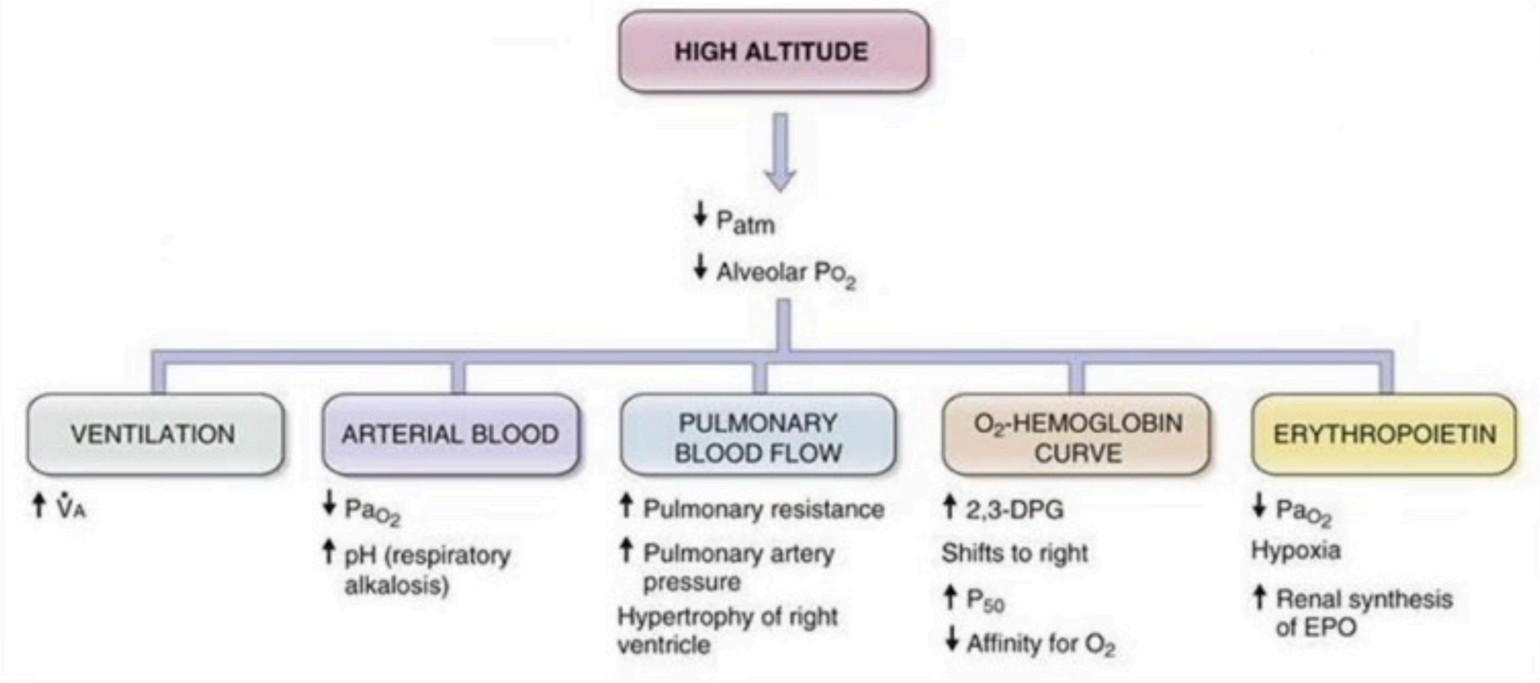
3. What is the specific physiological pathway that results in the changes described?

1)
- production of erythropoietin (EPO) and the subsequent increase in ematocrit

2)
- Polycythemia (increase in hematocrit) due to increase in EPO which is brought about by the release of erythropoietin, mainly from the kidney, in response to the low arterial Po_2
- This situmulates the bone marrow to produce more red blood cells to carry more oxygen

3)

- The renal and endocrine systems interact with the cardiovascular and respiratory systems in a homeostatic loop
- Get more red blood cells circulating so that the body would be able to cary more oxygen
- Adaptations allow us to compensate for the lack of oxygen at higher altitude



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Part III - Airlift

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Mark deteriorated rapidly and lost consciousness by the time the group reached the lower camp. The urgency of the situation strengthened the tired legs of the climbers, as Tom, John, and Pete carried Mark the final yards towards camp. Emily had run ahead to call for support help, and the group was told an airlift was on its way and would be there within the hour. The camp's medical tent had some basic supplies and a resident paramedic, and he and Emily went to work stabilizing Mark with oxygen and a Gammow bag (a pressurization bag).

90 Minutes Later, Denali Valley Hospital

"We have a 28-year-old white male, unresponsive, no prior history of pulmonary disease, who became unconscious around 15,000 feet after hiking to 17,000 feet earlier today. His friends say he was having severe breathing difficulty prior to losing consciousness...."

As the paramedic droned on, Emily looked around for the nearest phone so she could locate Mark's family in case this was as serious as it looked.

Questions:

1. How would the oxygen and Gammow bag help Mark?
2. If you were a member of the medical team examining Mark, what types of tests would you run? Why? [Try to focus on what types of things you would like to measure, whether or not you know of a possible test for them.]
3. What types of results do you expect to find? Explain your reasoning.

1)
- Gammow bag is portable hyperbaric chamber used for the treatment of acute mountain sickness (AMS). By increasing air pressure around Mark, the Gammow Bag simulates descent of as much as 7000 feet, thus relieving AMS symptoms.
- Supplemental oxygen will help Mark's body get enough oxygen to alleviate his symptoms

2)
- neurological test; to look for high-altitude cerebral edema (brain swelling)
- lung function; to look for high-altitude pulmonary edema (fluid from blood vessels leak into the lungs)
  - these are serious and fatal complications of altitude sickness
- heart rate and blood pressure
- blood test; to assess blood gases and assess kidney function

3)

- we expect Mark to:
  - have an increased heart rate and blood pressure to compensate for the high altitude
  - decreased blood oxygen levels
  - increased hematocrit
  - decreased lung function
  - incomplete renal compensation

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Part IV - Mark's Medical Data

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The following tables summarize the findings of the Denali Valley Hospital Medical Team:

BLOOD LEVELS

	MARK'S	NORMAL
Arterial Oxygen	52 Torr	80-100 Torr
Arterial Carbon Dioxide	30 Torr	35-45 Torr
Arterial pH	7.23	7.38-7.44
Hematocrit	58%	42-52%
Arterial glucose	102 mg/100ml	60-110 mg/100ml
Urea Nitrogen (BUN)	12 M	7-14 M
Creatinine	1.1 mg/100ml	1-1.5 mg/100ml
Potassium	4.0 meq/L	3.5-5.0 meq/L
Sodium	145 meq/L	136-145 meq/L
Bicarbonate	18 meq/L	20-24 meq/L
Chloride	100 meq/L	98-106 meq/L

No prescription medications or other pharmacological agents were found.

PULMONARY FUNCTION TESTS

Inspired Oxygen Tension	147 Torr	150 Torr
Vapor Pressure	45 Torr	47 Torr
Alveolar Oxygen	110 Torr	98-104 Torr
RQ	0.66	0.78-0.82 Torr
Tidal Volume	0.4 L	0.5 L

HEART RATE: 88 bpm (normal: 60-90 bpm)

BLOOD PRESSURE: 105/60 (normal: 110-120/60-80 mm Hg)

Questions:

1. Are the results as you expected? What values agree/disagree with your predictions?
2. Which lab values appear to represent the most serious problem Mark is having? Is his situation life-threatening?
3. Compare the results of Alveolar Oxygen Tension to Arterial Oxygen levels. What might cause this type of discrepancy?
4. Overall, what do these findings tell you about possible diagnoses for Mark's condition?

1)

- Yes we expected;
  - that mark had decreased lung functioning as he was having difficulty breathing
  - low blood oxygen levels because Mark was at a high altitude, had difficulty breathing and lost consciousness
  - elevated hematocrit levels as he was at a high altitude

2)

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HEART RATE: 88 bpm (normal: 60-90 bpm)

BLOOD PRESSURE: 105/60 (normal: 110-120/60-80 mm Hg)

No prescription medications or other pharmacological agents were found.

- arterial oxygen --> mark is suffering from pulmonary edema

3)

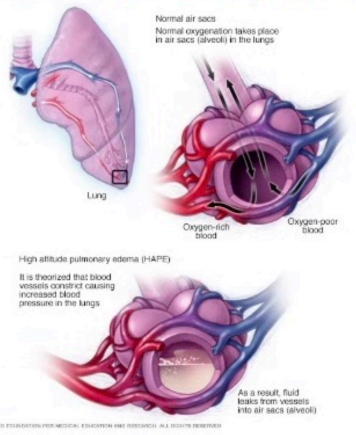
$$P_{AO_2} = P_{IO_2} - P_{ACO_2}/R$$

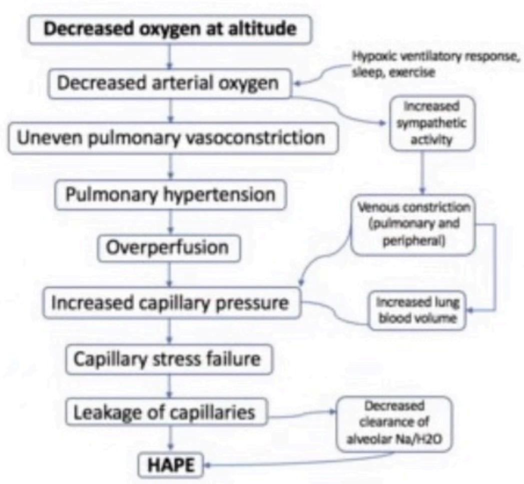
P_{AO_2} is the alveolar partial pressure of oxygen
P_{IO_2} is the inspired pressure of oxygen
P_{ACO_2} is the alveolar partial pressure of carbon dioxide (≈ partial pressure of arterial CO_2)
R is the respiratory quotient (=CO_2 production/O_2 consumption; ≈0.8)

- alveolar oxygen tension largely determines the partial pressure of arterial oxygen. This is because the partial pressure of oxygen in the alveoli largely equilibrates with that in capillary blood by the end of the pulmonary capillaries When the oxygen tension in the initial pulmonary capillary blood is lower, the alveolar-capillary oxygen tension gradient is widened which in turn enhances the rate of oxygen diffusion into the capillaries
- Mark has low arterial oxygen levels, high alveolar oxygen tension, and a low respiratory quotient.
  - the high alveolar oxygen tension is likely due to Mark's lungs trying to increase oxygen intake
  - respiratory quotient is a ratio between the amount of carbon dioxide produced in metabolism and oxygen used; Mark's R is low, indicating Mark's body isn't properly metabolizing fuel and moving towards an anaerobic (oxygenless) metabolism

4)

- Mark is suffering from pulmonary edema





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Part V - "Mark This..."

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Denali Valley Hospital, 8 pm

"Well, Mark, you gave us quite a scare!" Emily smiled down at him.

"I gave *myself* quite a scare... from what I remember at least. Most of it's pretty fuzzy. I just remember thinking that the acclimating didn't do much good! But I guess no amount of training can help with pulmonary edema."

"Nope," said Emily. "This sort of thing comes out of the blue. And it's virtually impossible to predict who will develop it. HAPE (High Altitude Pulmonary Edema) is a rare occurrence, but it can be quite serious."

"The doctors told me I'm susceptible to recurrence. Is that true?"

"Yes, unfortunately. You need to be careful about your climbing from now on."

1. what are the sequence of events that might lead to the development of HAPE?