mismatch, mimicry, and extreme environments

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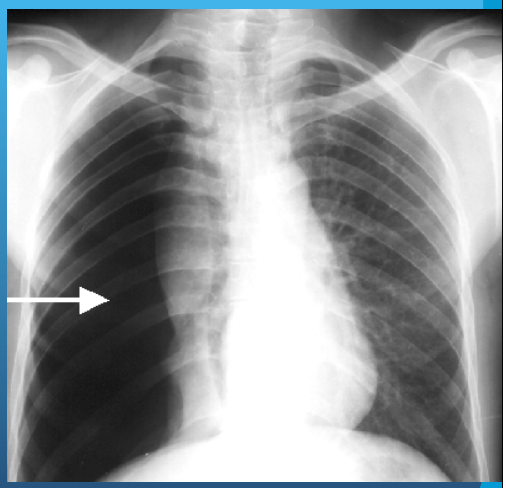
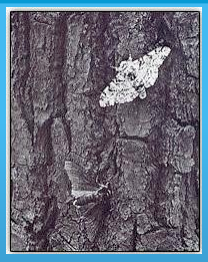
Pneumothorax

- POPS
- Divers: don't hold your breath!
- Lungs rupture at transpulmonic pressure of 80 mm Hg, 3.47 feet seawater



Goals of the talk



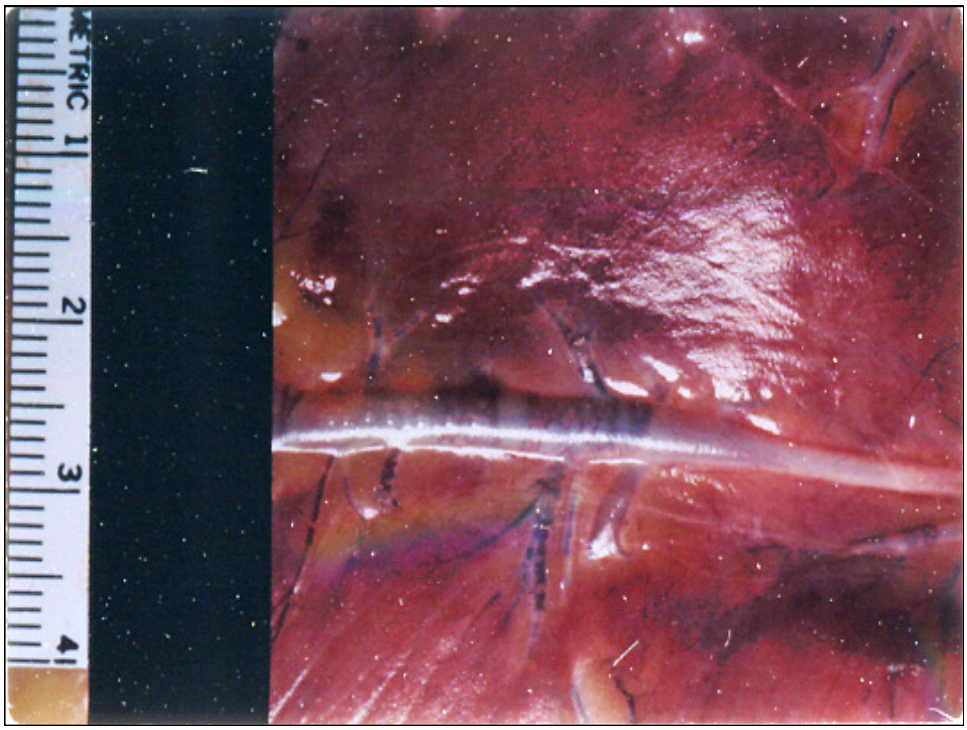
- Ask evolutionary question – why?
- Understand how evolution shaped mammalian physiology
- Recognize how new technologies expose humans to dangerous new environments – SCUBA and high altitude
- Environmental mismatching causes disease
- Understand how mimicry causes the body to misbehave

Spearfisherman

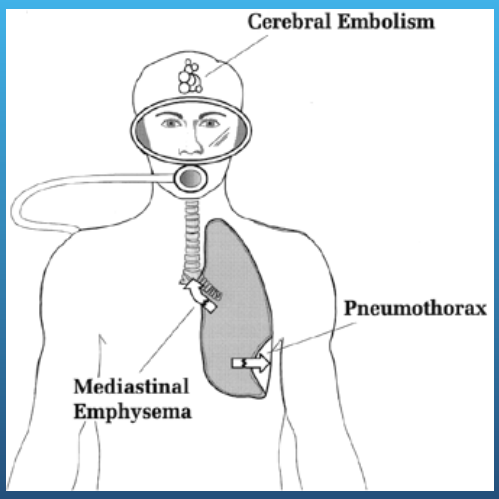
- 29 year old male diver
- Multiple dives - last dive to 85 feet
- Spearfishing without a buddy
- Witnessed rapid ascent
- Seizure as he hit the surface.

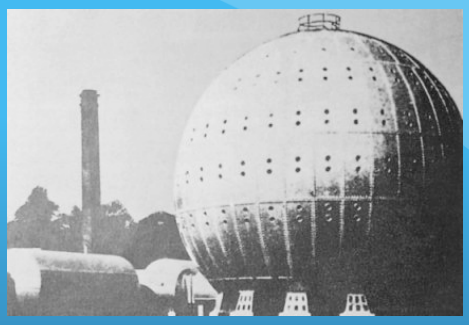
Cause of death

- Air embolism
- Immediate Onset



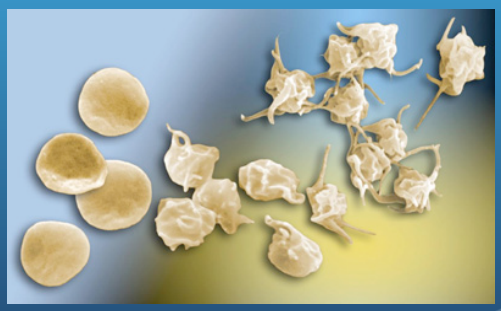
Gas Embolism





Bubbles activate platelets

- Lipids micelles, LDL cholesterol and plasma proteins change conformation at bubble-plasma interface
- Platelets adhere to these proteins



Thorsen T. el al. Undersea and Biomed Res. 1987; 14:45-59

Northern Elephant Seals

- Platelets lack sensitivity to epinephrine
- Platelets do not aggregate in response to agonists that activate platelets of terrestrial mammals
- Likely adaptation to diving stress

Field C. Thrombosis Res. 2001; 101(4):267-277

Immune Response to Bubbles

- Dogs without neutrophils -> avoided brain injury in Gas Embolism.
- Rabbits without complement -> did better!

Shastri KA. et al. Undersea Biomed Res. 1991; 18(3):157-165

Dutka et al. Stroke 1989;20:390-395

Ward CA et al. J Appl Physiol. 1987;62:1160-1166

Bubble response in Humans – resembles blood infection

- Systemic Inflammatory Response Syndrome: fever, low blood pressure, fast heart rate, lung injury
- Resulted from air embolism

Crit Care. 2003 Oct;7(5):R98-R100. Epub 2003 Aug 1

Human Blood Changes with Bubbles – resembles trauma!

- Drop in platelet count
- Increase in activated platelets
- Decrease in Antithrombin III
- Decreased clotting time
- Hemoconcentration
- Decrease in complement

Philip RB et al Aerospace Med. May 1972; 498-505

Similarity between Trauma and the Bends

- Normal symptom-free hyperbaric exposure and decompression induces changes similar to trauma
- Platelets, Lipids
- Plasma cortisol
- Creatine Phosphokinase

Martin KJ. Observations on hematologic and biochemical parameters in DCS. Abstract. Association Clinical Pathologists: 89th general meeting

So why are bubbles causing inflammation?

- Here is our ***why*** question.
- When else does air get into the body?
- (Trauma and Infection)

Trauma

1. Closed(simple) - Within skin
2. Open (compound) - Outside communication

And infection (the two often go together!)

- This is a diabetic who neglected a small wound on his foot

Most Often…

- Tissue and blood exposure to air means:
- 1) Bleeding…
- 2) Infection or infection prone state
- A signal that causes blood to clot and activates immune cells would save lives!

Novel Environment - Mismatch

- A mismatch of environments
- SCUBA is a mimic of trauma & infection!

Hyperbaric Oxygen eliminates mimic signal

- Mechanical: eliminates and shrinks bubbles
- Disrupts platelet binding to bubbles
- Inhibits immune cell activation
- Restores oxygen to tissues
- Happy caveman

High Altitude Mountaineering

- Does anybody belong at 26,000 feet?
- High altitude hypoxia
- Mimics pneumonia and acute lung injury!

On Mont Blanc

- More than 15,000 feet.
- Climber becomes groggy and short of breath. Spends a night at the hut.
- In the am, he is no longer conscious and is foaming at the mouth.

We can change – a little bit

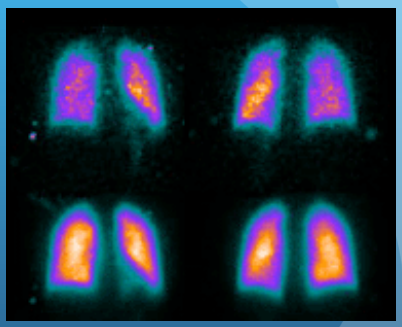
- Over time, we breathe faster at altitude
- We change our body chemistry
- We make more blood cells
- And if you go to Wheeler Peak your oxygen levels will be LOW!

High Altitude Pulmonary Edema

- This happens all the time at Taos ski valley!
- Lung vessels shrink, pressure goes up, fluid leaks
- Blood is 90% water: seeps out

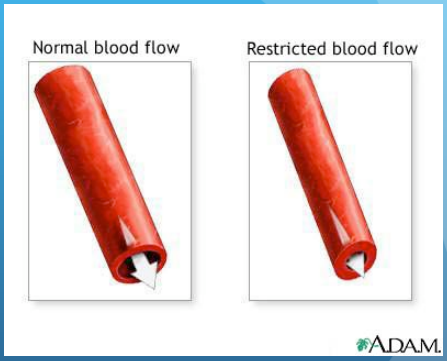
Pulmonary vasoconstriction

- Vasoconstriction happens in infected parts of the lung:
- Moves blood towards normal part of lung to maintain normal oxygen levels in arteries.
- Adaptive in Pneumonia



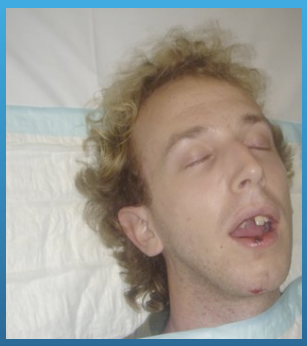
Hypoxic pulmonary vasoconstriction

- Bad at extreme altitude (Maladaptive)
- Fluid leaks out from high pressure in lung arteries
- Mismatch: In the lung, altitude hypoxia is a mimic of lung infection!



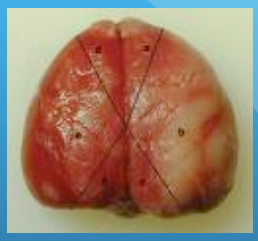
Our victim is also comatose

- Why?



Mountain Sickness

- Fluid leaks into the brain
  HACE
- Big Headache Mountain
  Himalayan peak where mountain sickness was first reported by Too Kin, a Chinese official in 37 BC



Low Oxygen causes inflammation

- Low oxygen screams danger to the immune system.
- Neutrophils cannot kill bacteria efficiently – cannot make hydrogen peroxide without oxygen
- Low oxygen makes immune system switch to a high-cost backup defense
- Backup defense causes widespread white blood cell activation: openings occur in vessels to let white blood cells (and fluid) out.

If low oxygen state occurs everywhere…

- Backup defense ends up damaging you.
- Then you end up with immune injury to vessels everywhere – wbcs stick to vessels, fluid leakage occurs.
- In the brain this causes swelling, headache and coma.

Mimicry in Acute Mountain Sickness

- AMS
- Hypoxia
- Hyperventilation with low CO2
- Fever
- Translocation of gut bacteria
- LPS in blood
- Sticky platelets, activated wbcs

- Sepsis
- Hypoxia
- Hyperventilation with low CO2
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How do we treat our victim?

- Descent
- Supplemental Oxygen
- Steroids – decrease inflammation
- Vasodilator to open up blood vessels in the lungs.

Acute Mountain Sickness Summary

- Mountain Sickness caused by low oxygen
- HAPE = vasoconstriction. Adaptive in lung diseases and maladaptive at extreme altitude (environmental mismatching)
- HACE = edema. AMS is a mimic of sepsis and induces backup defense.

New technology allows people to go to high places

- Supplemental oxygen, high tech fabrics and materials allow mountaineers to achieve altitudes incompatible with life
- Altitude illness mimics pneumonia in the lungs and sepsis in the brain and elsewhere.

New technology introduces bubbles to tissues

Bubbles mimic trauma and infection