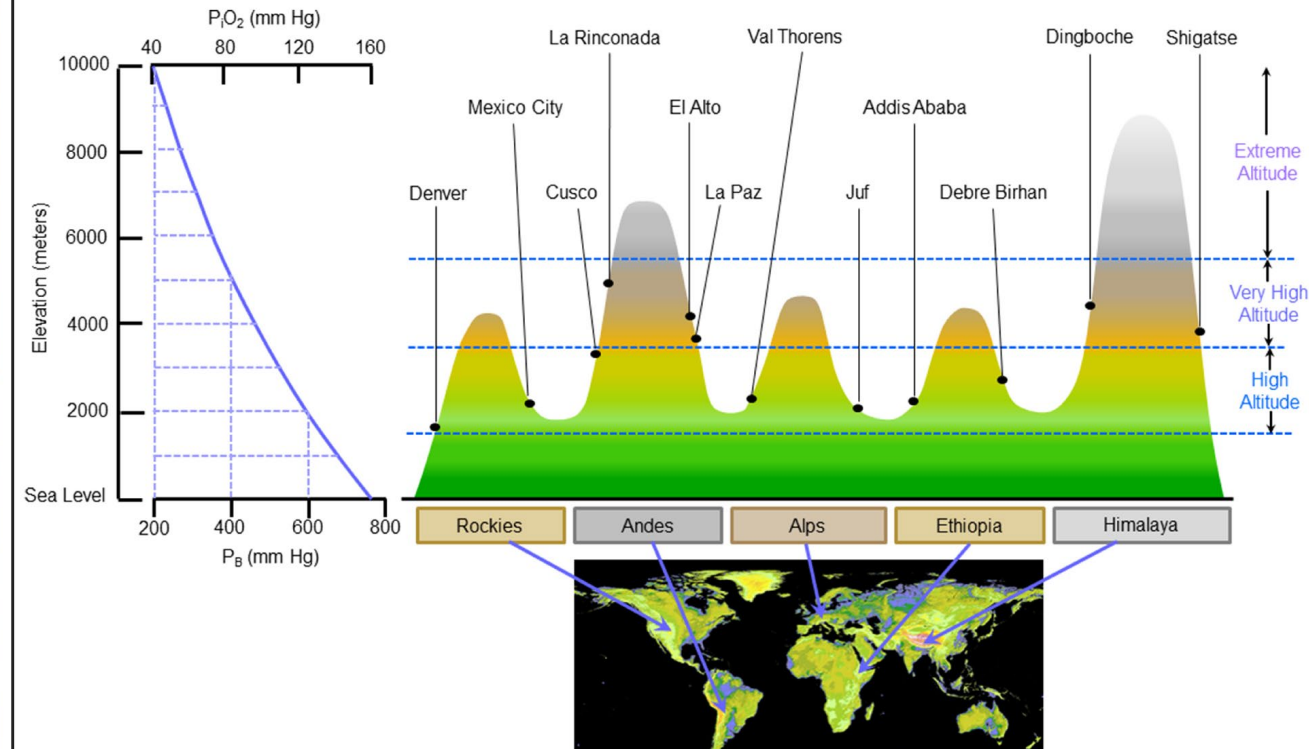


The Cardiovascular System at Altitude

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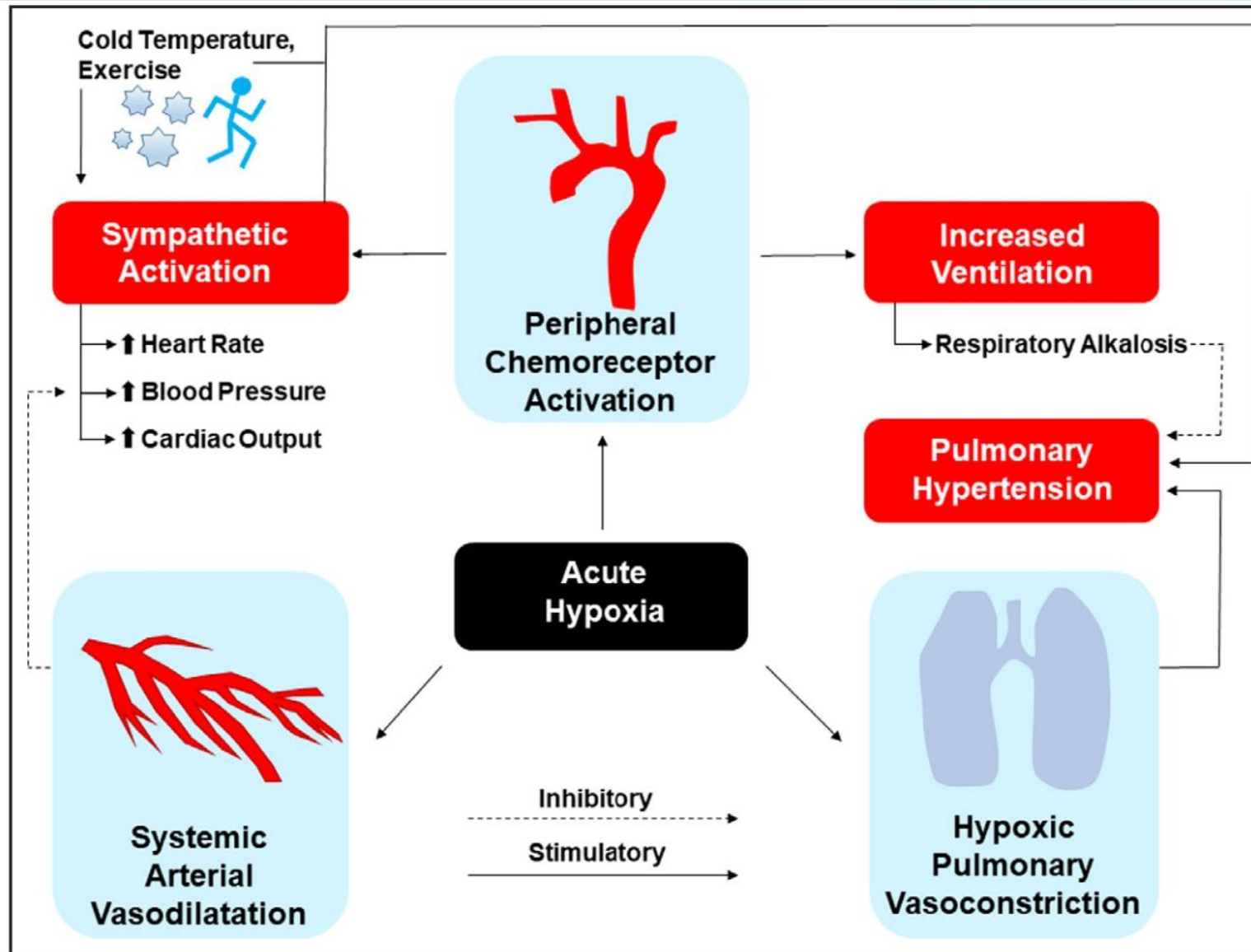
What Qualifies as High Altitude?

Altitude Zone, Height	Popular USA Destinations	Reduction in VO ₂ Max	Sea-level FIO ₂ Equivalent
Extreme Altitude: ≥5,500 m, 16400 ft	Denali Summit, AK: 6,190 m	47%	~0.09
	Mount Whitney, CA: 4,421 m	29%	~0.12
High Altitude: 3,000 m, 9840 ft	Mount Rainier, WA: 4,392 m	29%	~0.12
	Summit County, CO: 2,425 m	9%	~0.15
Moderate Altitude: 2,000 m, 6560 ft	Park City, UT: 2,134 m	6%	~0.16
	Lake Tahoe, CA: 1,901 m	4%	~0.16
Low Altitude: 500 m, 1640 ft	Denver, CO: 1,609 m	1%	~0.17
Sea-Level			



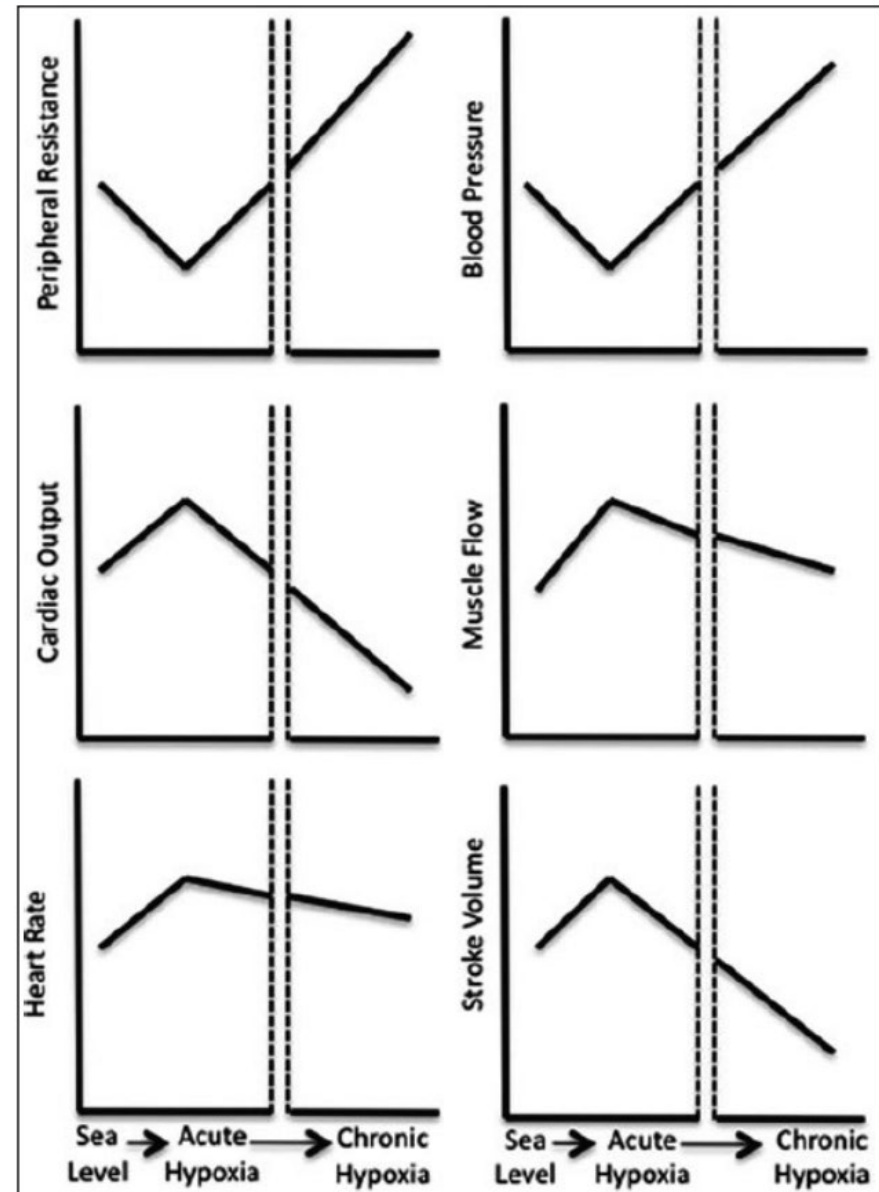
Globally, about 400 million people reside above 5000 ft.

Response to Lower Oxygen Levels



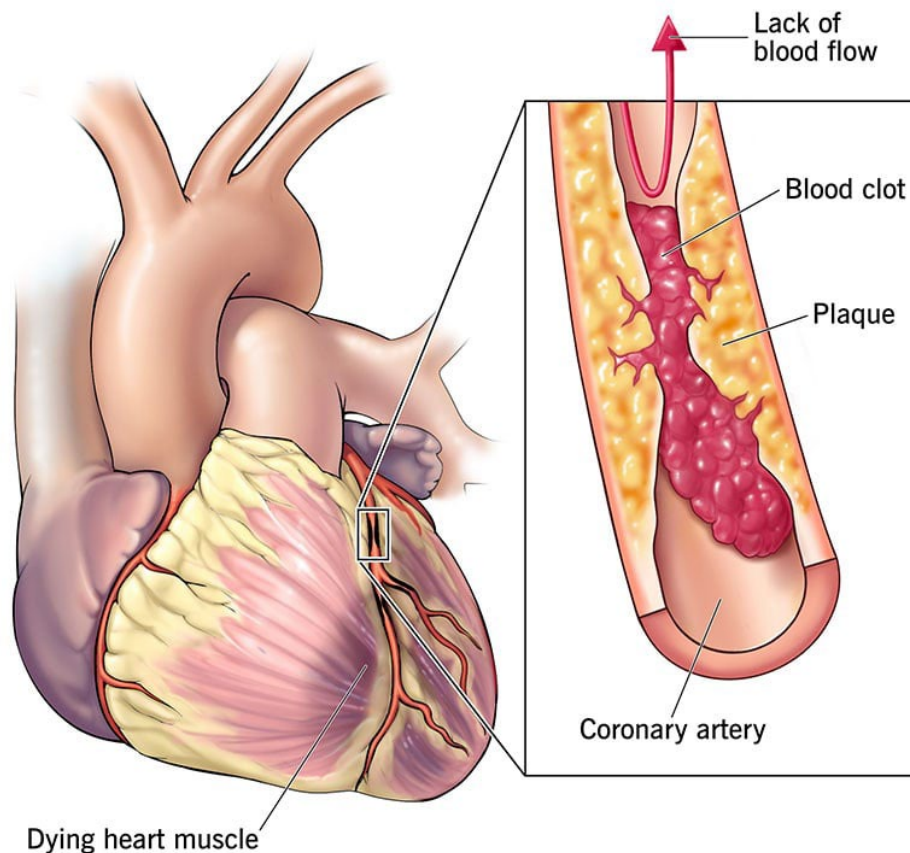
Acute vs Chronic Effects

- Acute = minutes to hours
- Chronic = days to weeks
- Blood pressure drops initially, but goes up over time
- Heart rate increases initially, but goes down over time
- Cardiac output (flow by the heart) increases initially, but drops over time



- Lower mortality from:
 - Cardiovascular diseases
 - Stroke
 - Cancer (esp. colon and lung cancer)
 - Alzheimer Disease
- Decreased rate of diabetes (in men) – 16% reduction
- Possibly increased life expectancy at moderate altitude vs sea level (difference may be negligible when you account for smoking and lung disease)
 - 1.2-3.6 years in men
 - 0.5-2.5 years in women
- However, there is a possibility that these effects are related to socio-economic factors and/or lifestyle behaviors

Heart Attack

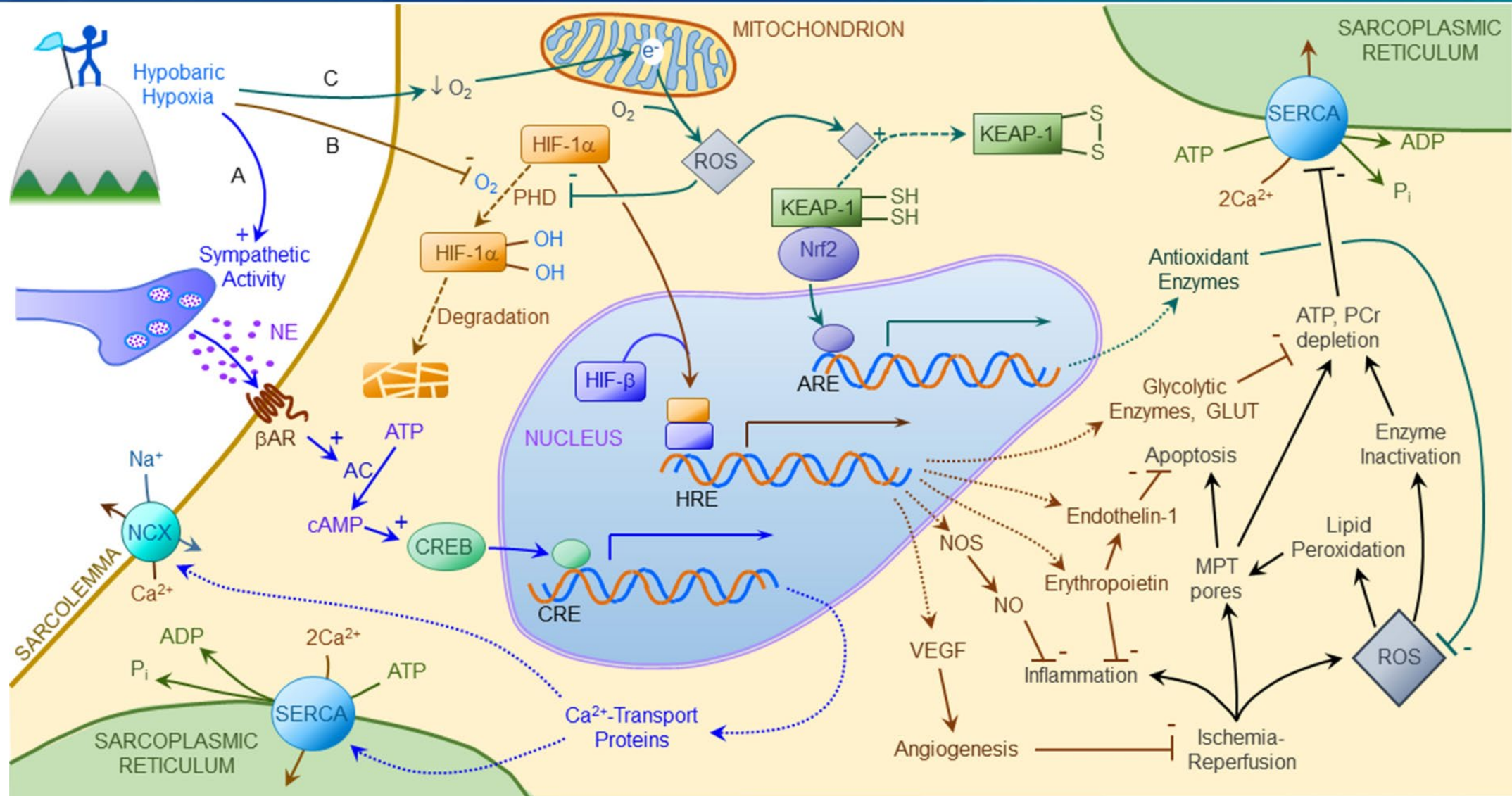


- Ischemic heart disease mortality for people at >1,000m was 4-14 per 10,000 people lower when compared to people within 100m of sea level.

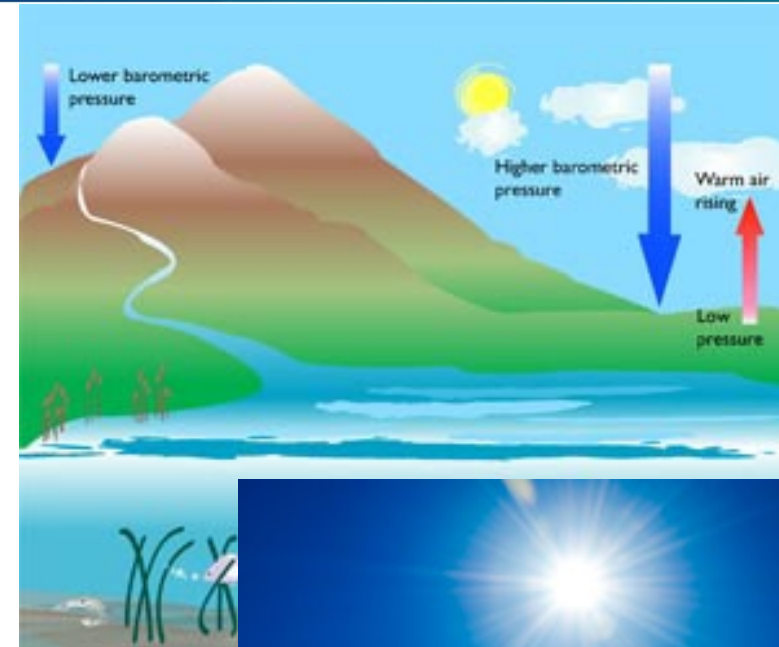


- Data has shown 20% lower mortality risk for subjects with an exercise capacity of 5-7 metabolic equivalents (METs) compared to those achieving below 5 METs.
- Living at higher elevation may promote relatively high fitness level since 5-7 METs are required even for slow uphill walking.

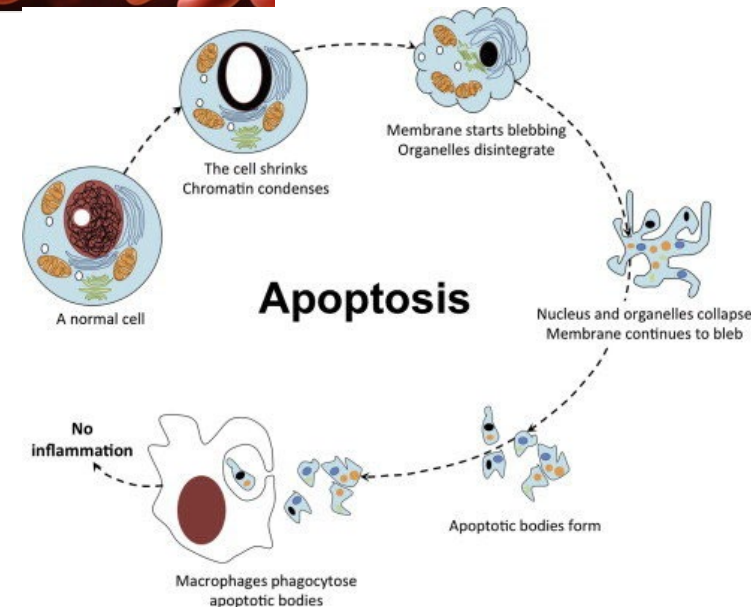
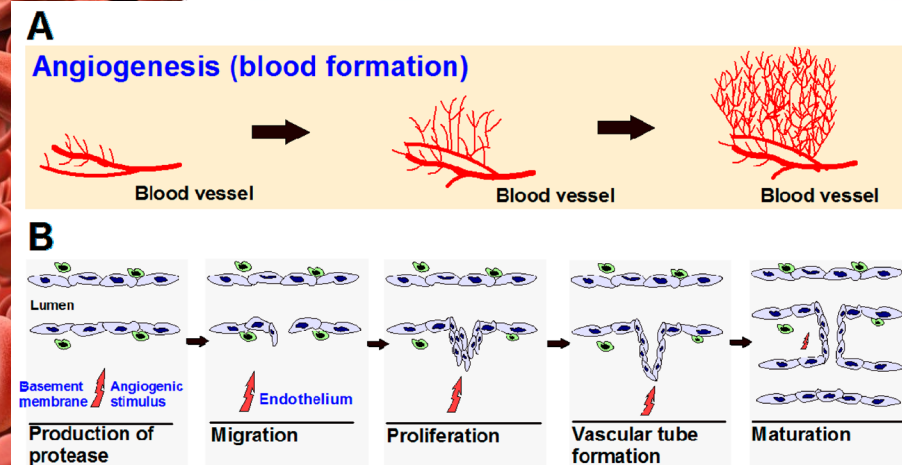
Cardioprotective Gene Expression



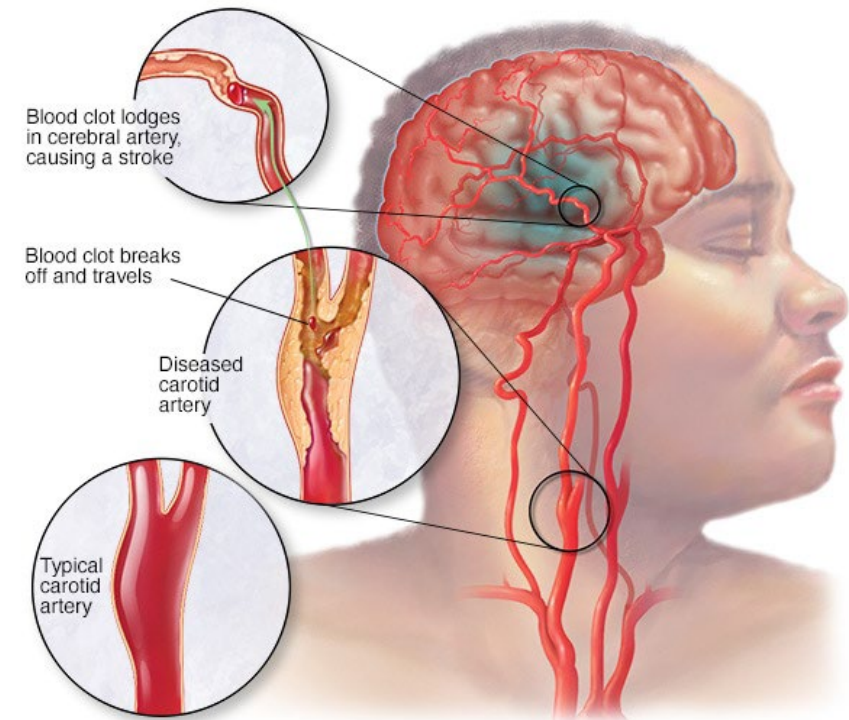
- Lower barometric pressure and resultant lower partial pressure of oxygen
- Increased ultraviolet and ionizing radiation
 - Improved synthesis of Vitamin D
 - Reduced clot formation
 - Lower parathyroid hormone
 - Lower insulin resistance
 - Decreased diabetes, hypertension, inflammation



- Hypoxia-inducible factor (HIF-1) pathways may reduce cardiovascular mortality (key regulator of multiple systems)
 - Forming new red blood cells (erythropoiesis)
 - Forming new blood vessels (angiogenesis)
 - Getting rid of sick cells (apoptosis)
 - Increased metabolism



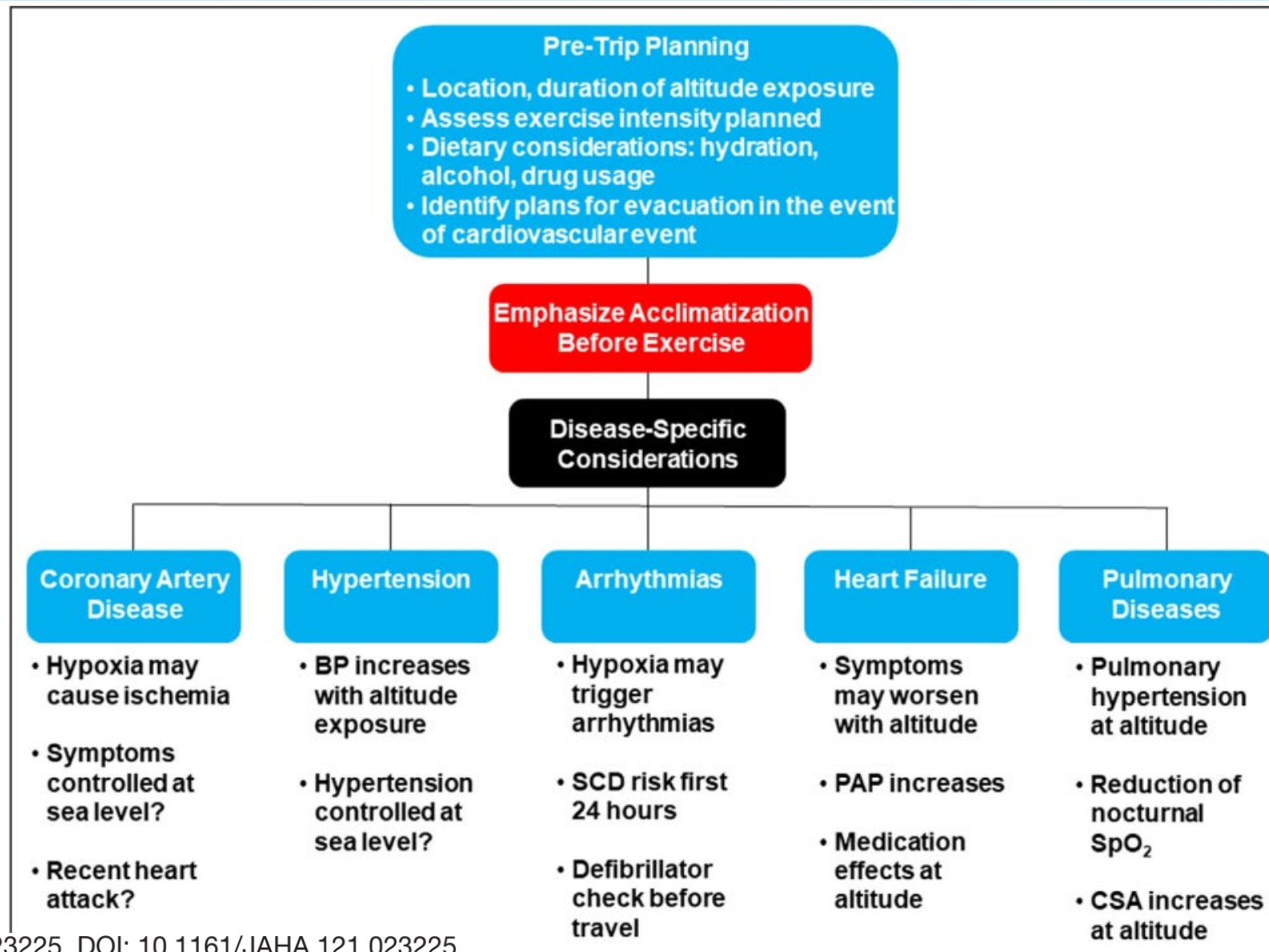
- Body adapts due to intermittent low oxygen stress
- Production of nitric oxide (NO) increased
 - Improves vasodilatation
- Pre-conditioning allows for protection against more severe and prolonged low oxygen events
 - Cardioprotective
 - Neuroprotective
 - Vasoprotective



- Higher mortality from:
 - COPD
 - Lower respiratory illnesses
- While higher altitude may be protective against development of some diseases, it could increase mortality when disease progresses.
- With chronic lung disease, higher altitude may exacerbate low blood oxygen levels and elevated blood pressure in the lungs (pulmonary hypertension).



- Risk of Chronic Mountain Sickness (generally >3,000m)
 - Progressive loss of ventilatory rate
 - Low oxygen levels
 - Increased red blood cell counts
 - Results in high blood pressure in the lungs
 - Can lead to congestive heart failure
- Possible increased risk of heart rhythm issues

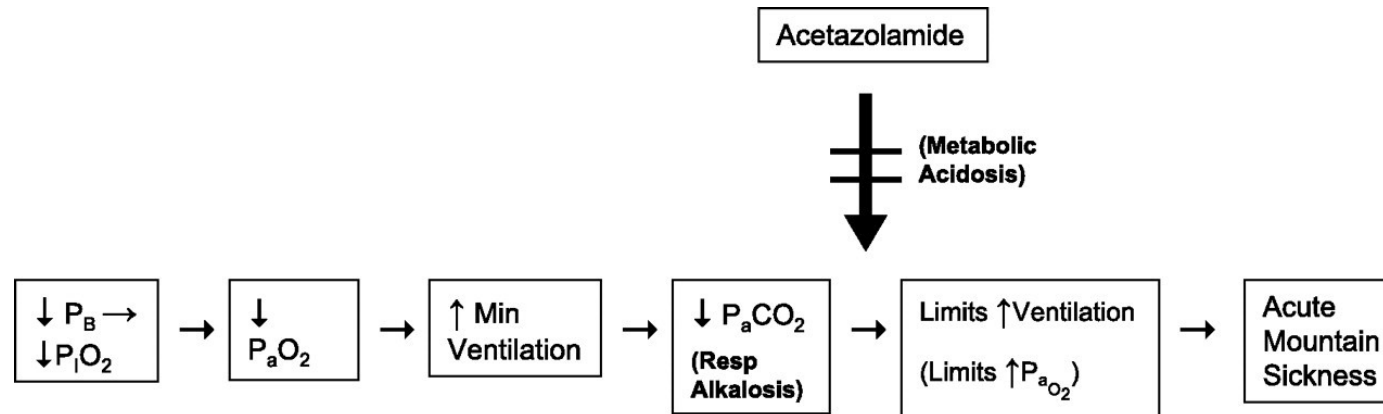




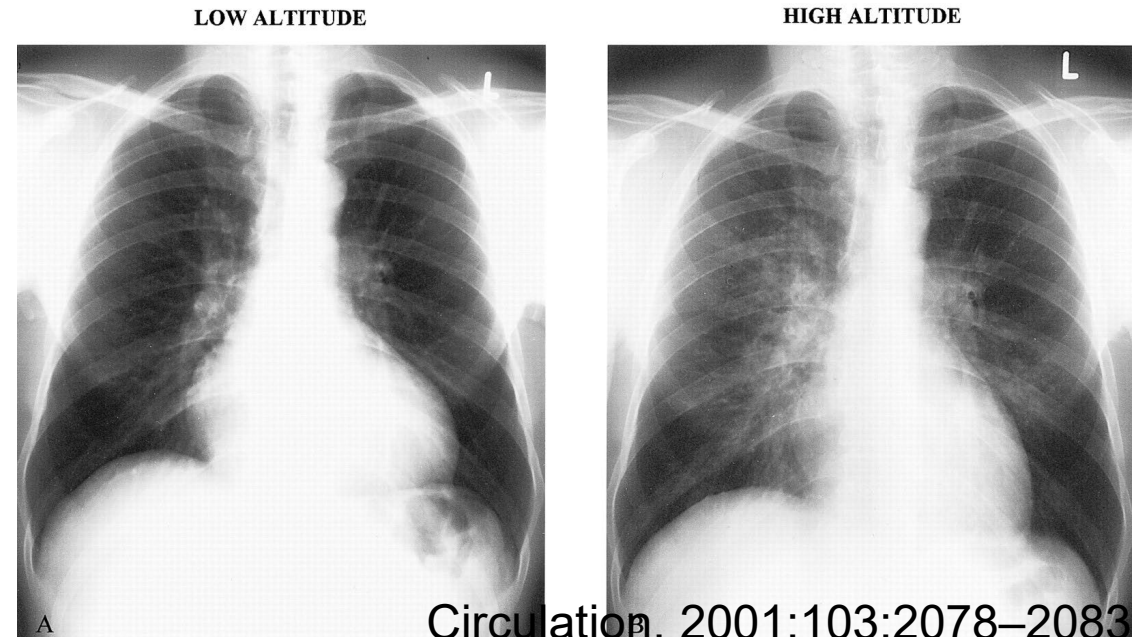
- Time to allow body to get used to higher altitude environment.
- Increased ventilation, oxygenation, and perfusion to the brain.
- Ideally 5 days before strenuous exertion at altitude.
- Data that even one day of acclimatization results in a 6-fold decrease in the risk of sudden cardiac death in the mountains.

- Acute Mountain Sickness (AMS)
 - Nausea, lack of appetite, vomiting, dizziness, fatigue
 - Increased risk with increased age
 - Usually resolves within first few days
 - Can progress to life-threatening diseases in rare cases

- Acute Mountain Sickness (AMS)
 - Symptoms are sometimes treated with a diuretic (acetazolamide)
 - Can discuss possible prophylactic use of acetazolamide with physician prior to high altitude activities in at risk individuals



- High-altitude pulmonary edema (HAPE)
 - Usually within 4 days of travel to high elevation
 - Can have rapid onset
 - Symptoms of fluid on the lungs (shortness of breath, fatigue, cough, low oxygen levels)
 - Requires descent to lower elevation
 - Supplemental oxygen
 - May require medications to treat
 - Avoidance of activity
 - Can carry 50% mortality untreated



Things to Monitor - Hypertension

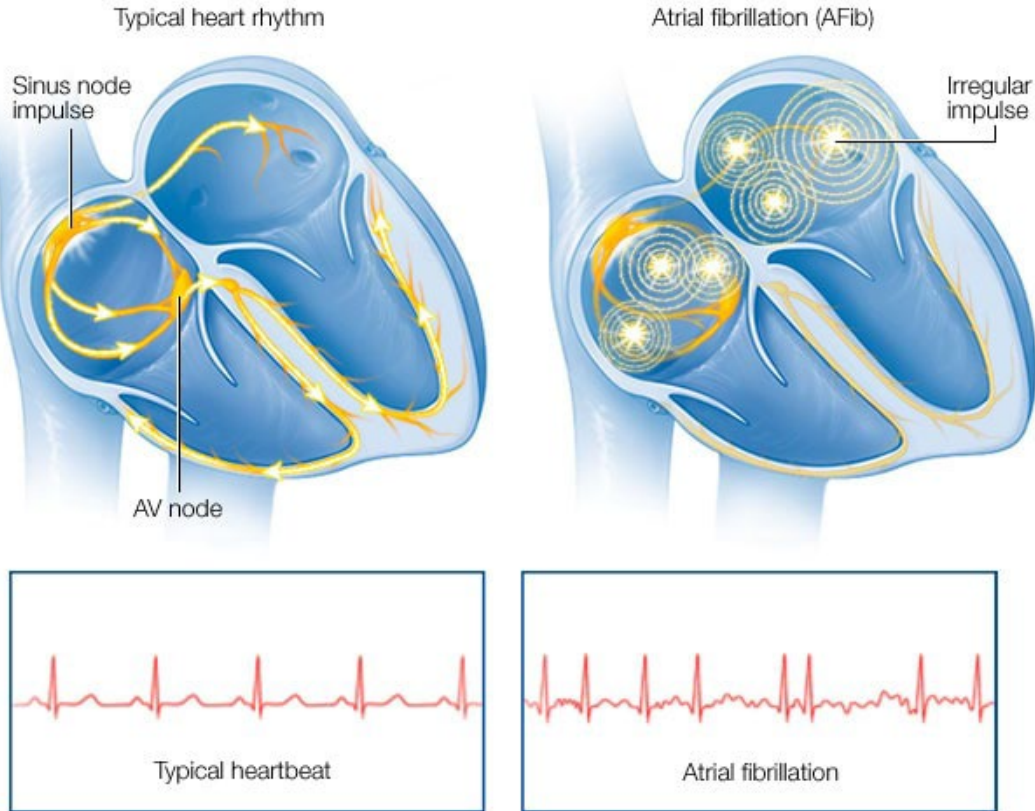
Table 3 Clinical and therapeutic recommendations for hypertensive patients planning to go to high altitude

Patients	Recommendations	Class of evidence	Level of evidence	Ref
Patients with moderate–severe hypertension and hypertensive patients with moderate–high cardiovascular risk	Check BP values before and during HA sojourn.	Ila	B	7,8,3
Well-controlled hypertensive patients/mild hypertensive patients	May reach very HA (>4000 m) with adequate medical therapy.	I	C	8,35
Uncontrolled/severe hypertensive patients	Avoid HA exposure in order to prevent risk of organ damage.	I	C	36S
Therapy				
	Angiotensin II receptor blockade (tested with Telmisartan) lowers BP in healthy subjects up to 3400 m	I	B	35
	Acetazolamide administration lowers BP at HA while improving SaO ₂ and mountain sickness symptoms	I	B	9
	Combination of nifedipine/telmisartan effectively lowers BP in hypertensive patients at an altitude of 3300 m	I	B	36
	Nebivolol effectively controls HA-induced BP increase and preserves nocturnal BP dipping. Selective beta-1 adrenergic receptors blockade is associated with a lesser impairment of exercise performance when compared with the administration of non-selective beta-blockers	I	C	13
	When moderate–severe hypertensive patients and hypertensive patients at moderate–high cardiovascular risk plan exposure to HA, adequate modification of their antihypertensive therapy should be considered in co-operation with their physician	Ila	C	

- Blood pressure may worsen at high altitude
 - Increased sympathetic tone
 - Orthostatic symptoms may worsen
- Medications targeting renin-angiotensin-aldosterone system may be less effective
- Beta-blockers may be more effective

The strength of these recommendations is to be weighted in the light of the limited evidence available. BP, blood pressure; HA, high altitude.

Things to Monitor – Atrial Fibrillation



- Heart rate increases with altitude.
- Those with heart rhythm issues may have worsening.
- May require adjusting medications to maintain heart rate control.
- Patients may also have recurrence of heart rhythm issues at higher elevations, which may require coming back down to lower elevations for management.

- Adults with coronary disease may have onset of symptoms at lower levels of exertion.
- A subset of patients may benefit from stress test at lower elevation prior to attempting to exert at higher elevation to guide medical therapy.
- May be increased risk of sudden cardiac death at higher altitude.
- Avoid traveling to altitude shortly after coronary event.





- Dutch study looked at people who were at least 6 months out from revascularization for acute heart attack.
- Compared with healthy controls.
- Stress test at sea level and at 4,200m after 10-day acclimatization.
- Both patients and healthy controls had similar decrease in exercise capacity and max heart rate.
- Suggests that patients with coronary disease can tolerate exercise at high altitude.

- However, adaptations to higher altitude may increase risk of heart attack
- Paradoxical vasoconstriction in arteries with atherosclerosis
- Low oxygen in air leads body to increase concentration of red blood cells relative to overall blood volume
- Benefit is increased oxygen carrying capacity
 - Blood doping for athletes
- Risk is that blood becomes thicker and may clot more easily
- Platelet activation may also occur



Mountaineer Conrad Anker after heart attack while climbing in Nepal.

Things to Monitor – Coronary Disease

ROOM AIR



NORMAL CORONARY VESSELS

n = 12, 50 7 yrs
Evaluation for chest pain.



CORONARY ATHEROSCLEROSIS

Zadeh Atherosclerosis 2008

(FIO₂ = 0.10 ~5,500m)



- Example of coronary arteries demonstrating paradoxical vasoconstriction

- Cardiac events more likely to affect older, unfit men.
- Usually within the first few days of altitude exposure.
- If an event occurs far from advanced medical care, outcome may be poor.

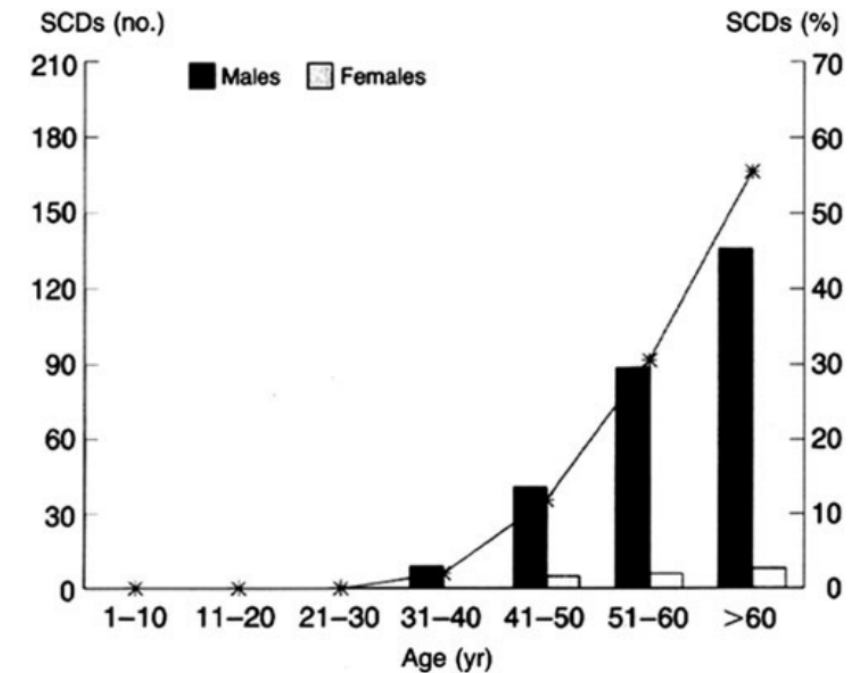


FIG. 5. Data from Burtscher et al. 1993 showing the relationship between number of sudden cardiac deaths (SCDs) in the Austrian Alps (left axis, solid bars for males and females), and the % of the total number of SCDs (right axis, solid line) as a function of 10 year age groupings (horizontal axis). Figure reproduced with permission from Burtscher et al., 1993.

Table 2 Recommendation for ischaemic patients ascending to high altitude

Patient risk class	Recommendations
General recommendations for all cardiovascular patients	<p>Patients should continue pre-existing medications at HA. All therapy changes, especially dual anti-antiplatelet therapy after drug-eluting stent implantation, must be discussed with a doctor before enacting. Individuals who do not engage in physical exertion at low altitude should not engage in physical activity at HA.</p> <p>Acetazolamide administration seems to reduce the risk of subendocardial ischaemia at HA in healthy subjects, and thus use of acetazolamide for AMS prevention might be helpful. No data are available, however, in patients with CAD.</p>
After AMI/CABG	Patients should wait at least 6 months after uncomplicated ACS episode as well as after revascularization before HA exposure.
After stenting	Patients should wait at least 6–12 months after coronary stenting before HA exposure.
Low risk (CCS 0-I)	May safely ascend to HA, up to 4200 m asl, and practice light-to-moderate physical exertion.
Moderate risk CAD (CCS II-III)	May carefully ascend up to 2500 m, but physical exercise heavier than light is contraindicated.
High risk (CCS IV)	Should not ascend to HA.

- European Guidelines (we do not have specific altitude guidelines from the American College of Cardiology)

Things to Monitor – Heart Failure

- More difficulty tolerating activity at altitude.
- Elevated HR, increased BP, increased lung fluid content, and decreased heart function can all be problematic in setting of known heart failure.
- Medications for heart failure may also inhibit some compensatory mechanisms for dealing with altitude.
- Diuretics may increase the risk of volume depletion.

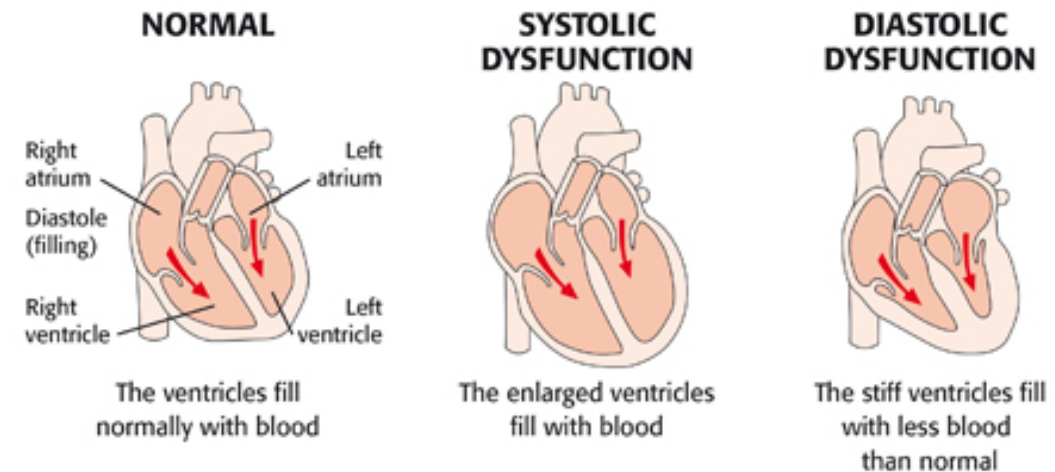


Table I Recommendations for heart failure patients going to high altitude

HF severity level	Recommendations
All HF patients	Carefully evaluate HF co-morbidities (e.g. pulmonary hypertension, anaemia, sleep apnoea) Carefully evaluate HF drugs (in particular diuretics, potassium supplementation, and β blockers). Whenever possible, β 1 selective should be preferred to non-selective beta-blockers Slow ascent is recommended. Although we do not have precise data on advisable ascent rate, it is prudent not to exceed that recommended for healthy travellers (300–500 m/day when above 2500 m)
Stable NYHA I-II patients	May safely reach high altitude up to 3500 m Once at altitude, not heavier than moderate physical activity is recommended
Stable NYHA III patients	May safely reach high altitude up to 3000 m, if needed Once at altitude, not heavier than light physical activity is recommended
Unstable/NYHA IV patients	Avoid high altitude exposure

- European Guidelines (we do not have specific altitude guidelines from the American College of Cardiology)

Key Points

- Living at altitude may be quite beneficial to your cardiovascular health
- Some of the benefit may derive from healthy behaviors, so keep those up
 - Exercise routinely
 - Control weight



Key Points

- Take care when you have visitors from low altitude
 - Older friends and family
 - Those with pre-existing conditions
- Encourage good hydration
- Avoid excessive alcohol
- Plan on time for acclimatization for visitors before embarking on heavy exertion and moving to higher altitude



- Monitor for signs or symptoms suggestive of issues related to altitude.
- Have a low threshold to move friends and family (or yourself) back to lower elevation if they are experiencing significant symptoms.
- Have a plan in place for emergency treatment, and plan for the fact that emergency evacuation can be difficult from the backcountry.
- Take friends and family to the hospital for significant symptoms.
 - It is not uncommon for us to see patients from out of state presenting with heart attack, heart failure, loss of consciousness, heart rhythm issues, etc.
 - Keep in mind that adverse effects of altitude can happen to anyone.

Thank you!



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