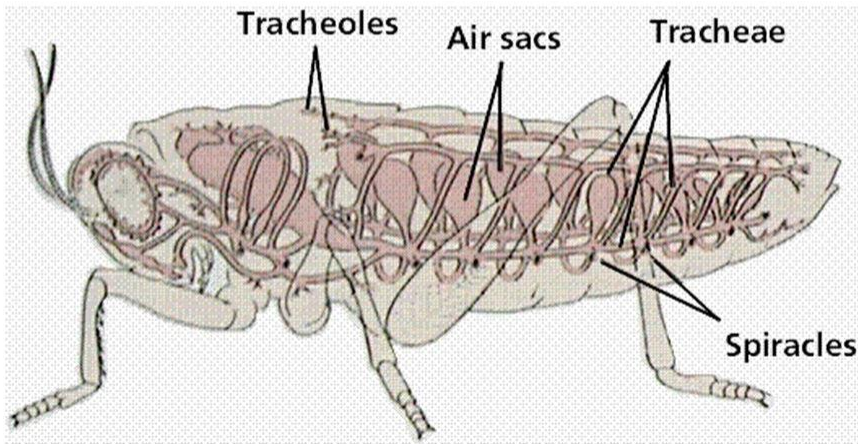




TIME FOR
RECAP

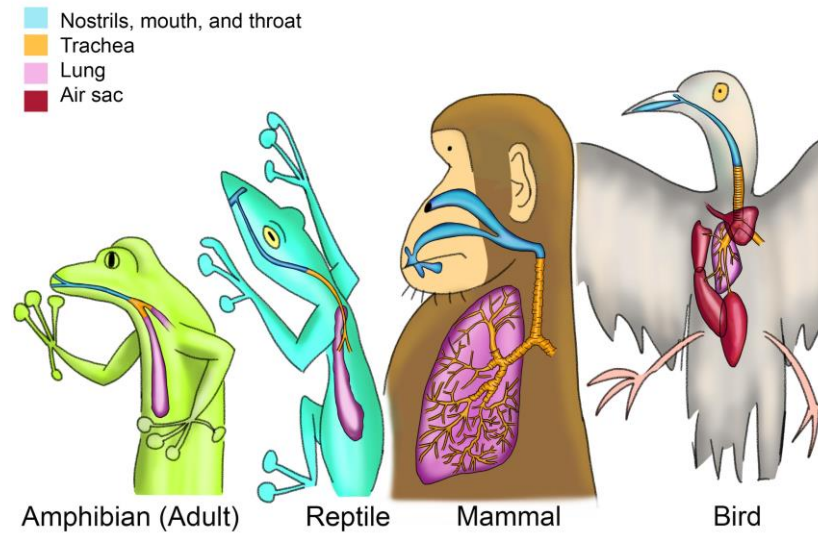


The Insect Gas Exchange System



Insects also use tracheae, which may be actively ventilated with air sacs and body movements.





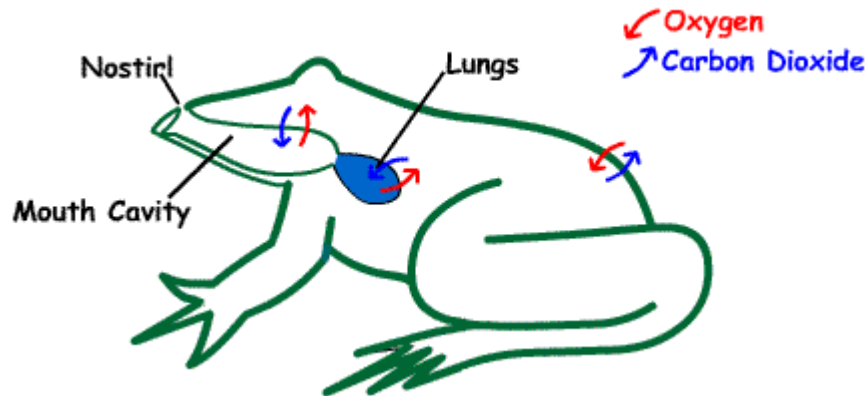
The first air-breathing vertebrates were bimodal or trimodal, with gills and air-breathing device(s)—skin and/or lungs.



Mangrove rivulus

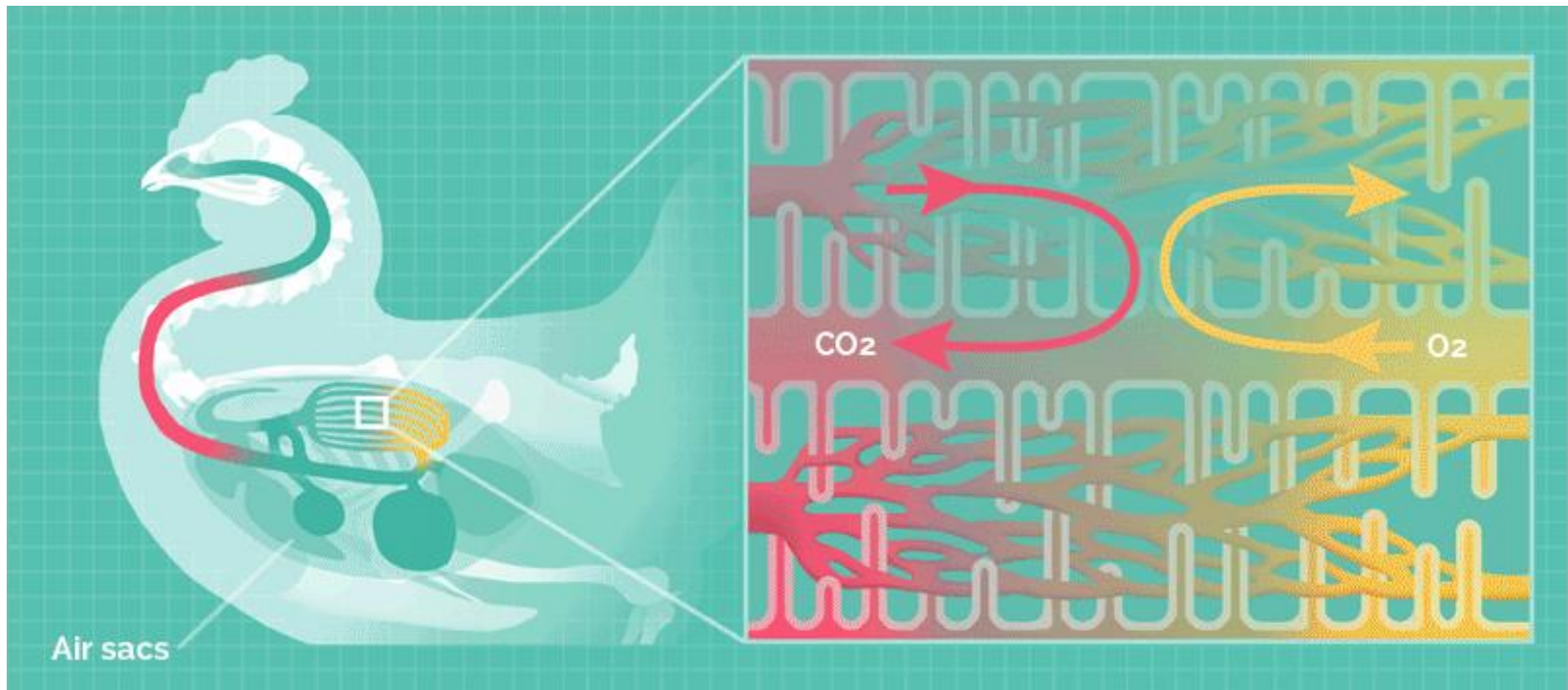
All lungs except those of birds and crocodilians have tidal ventilation.

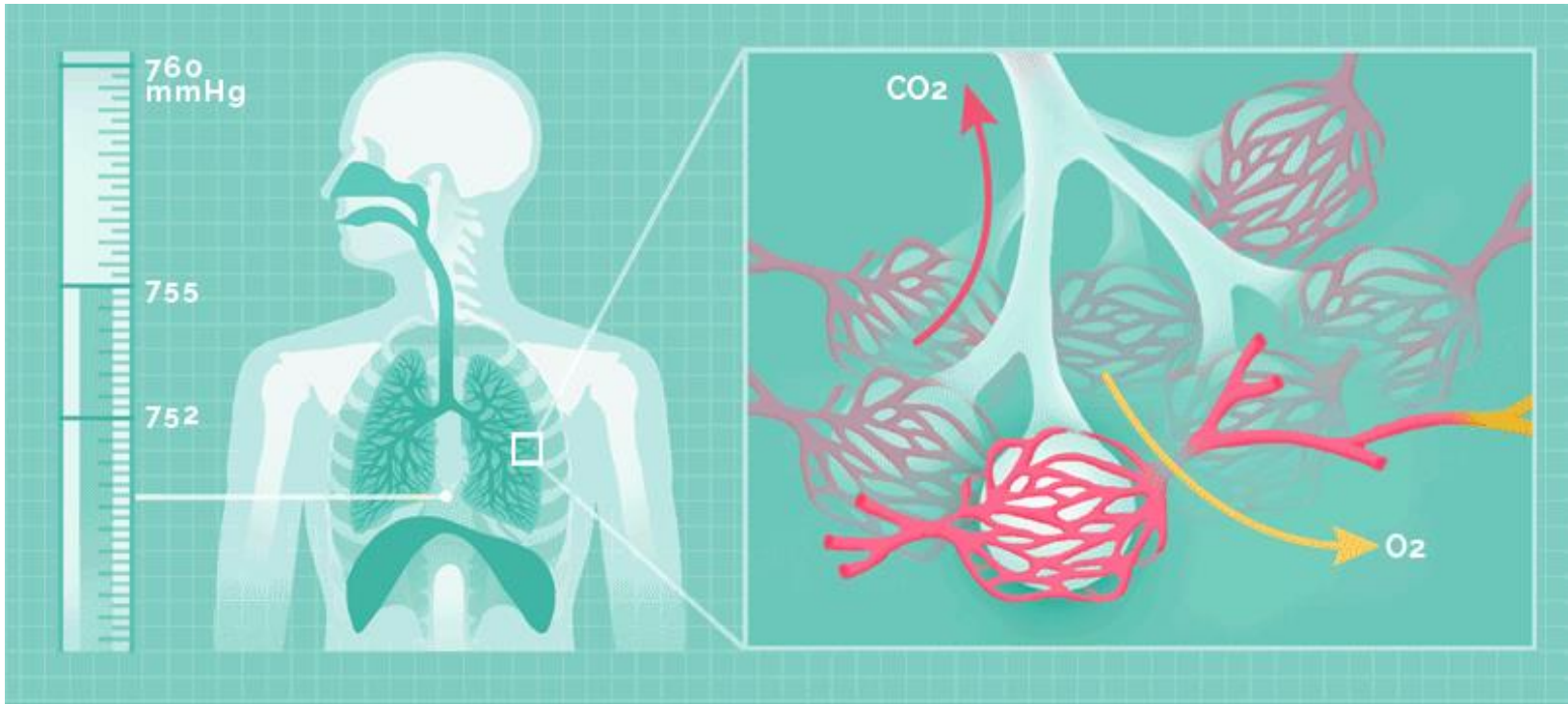
Frog lungs may be simple or moderately folded and are inflated by positive pressure.



Reptiles as well as birds and mammals have respiratory systems ranging from simple to elaborately folded, inflated by negative pressure.

Ventilation and gas exchange are separated in crocodilian and avian respiratory systems due to air sacs and parabronchi with air capillaries. Flow-through breathing due to air sacs, plus crosscurrent flow in the parabronchi, enhances gas exchange in crocodiles and birds.



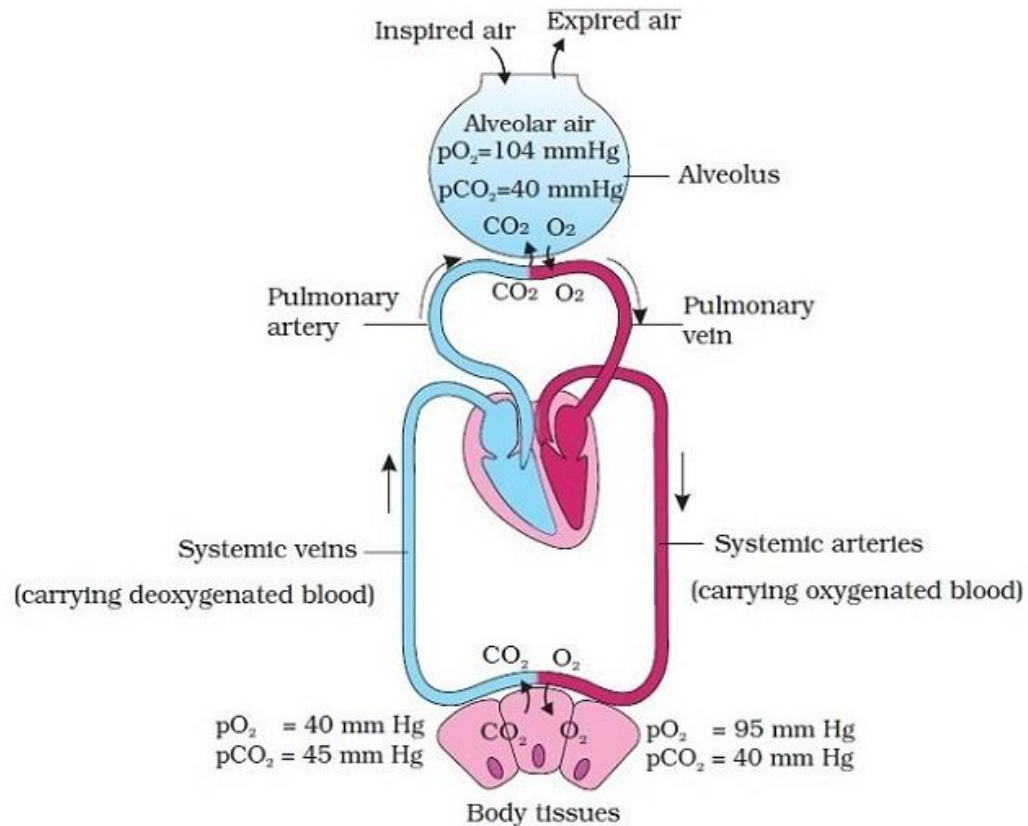


Mammalian airways terminate in alveoli, which are involved in both ventilation and gas exchange.

Mammalian lungs are inflated and deflated tidally by cyclical changes in intra-alveolar pressure generated indirectly by respiratory muscles (ribs, diaphragm).

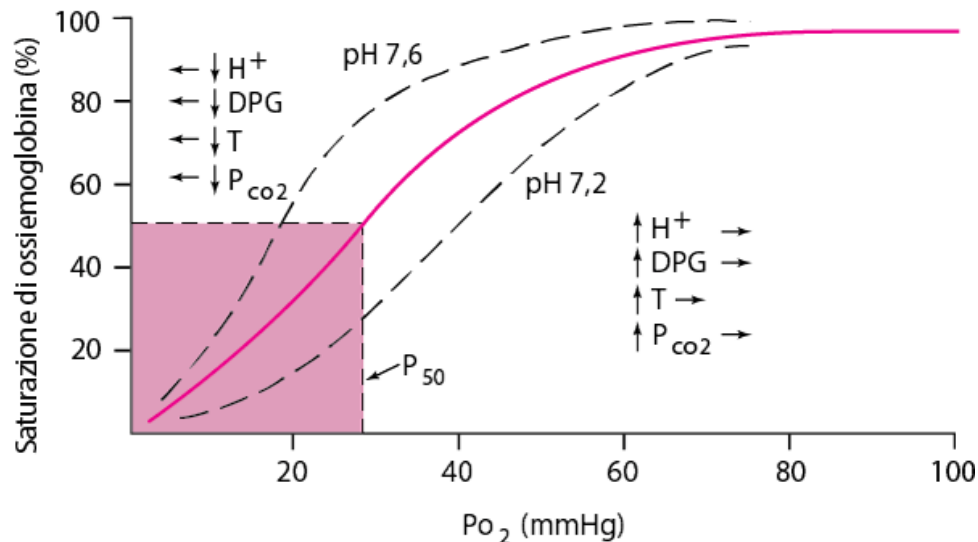
Lung air has a lower partial pressure of O₂ than does atmospheric air.

Gases move to/from alveoli to blood and blood to/from body cells down partial pressure gradients maintained by breathing and circulation to be in the proper directions.

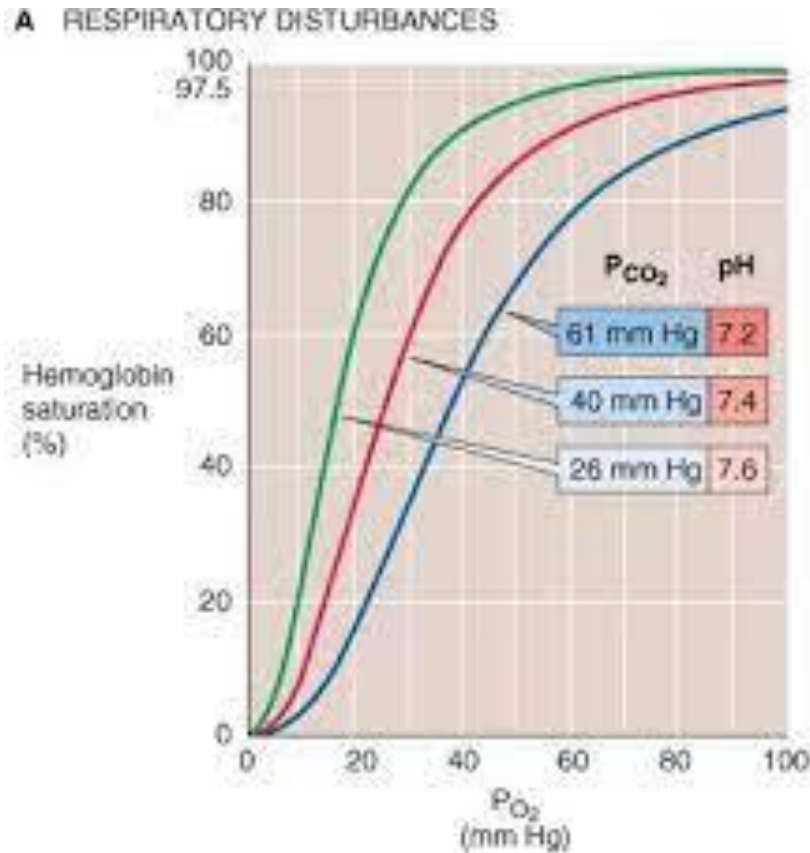


Most O₂ in many circulatory systems is transported bound to hemoglobins (Hb), hemocyanins, and other metal-containing respiratory pigments. These trap O₂, so they cannot contribute to *PO*₂, thus favoring gas diffusion. Most Hbs are tetramers of globin subunits each with an iron-containing heme group.

The *PO*₂ is the primary factor determining the percent hemoglobin saturation. O₂ binding by Hb follows a sigmoidal curve with a steep rise at intermediate *PO*₂ levels and a plateau at high levels. This arises from cooperativity, in which subunits switch between high and low-affinity states and affect their neighbors' states. At high *PO*₂ in the lungs, Hb is nearly 100% saturated. As it enters low-*PO*₂ tissues, cooperativity ensures proper release of O₂.



Acid (the Bohr effect), temperature, and certain organic phosphates enhance O₂ release. O₂ affinity, measured by P₅₀ values, has evolved to enhance gas delivery in different species.



The Deepest Diving Mammals

Blainville's
beaked
whale

1,599 m
5,246 ft



Baird's
beaked
whale

1,777 m
5,830 ft



Southern
elephant
seal

2,133 m
6,998 ft



Sperm
whale

2,250 m
7,382 ft



**Cuvier's
beaked
whale**

2,992 m
9,816 ft



Empire
State
Building



- ✓ Large Lung Capacity
- ✓ High Myoglobin Levels

Mirceta et al. Science 2013 doi: 10.1126/science.1234192.

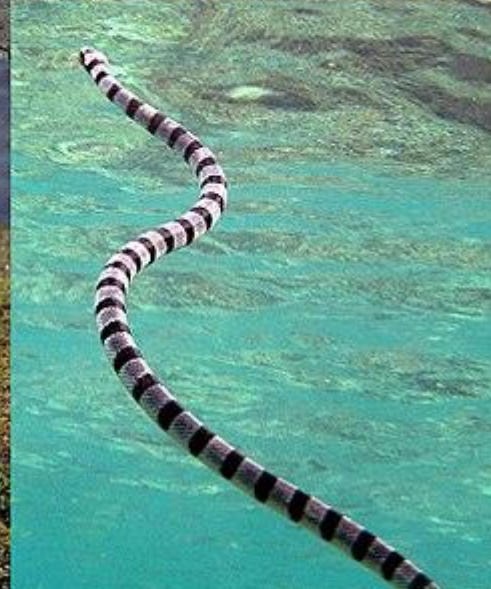
- ✓ Increased Blood Volume
- ✓ Low Heart Rate

Williams et al. Nat Comm 2015 <https://doi.org/10.1038/ncomms7055>

- ✓ Enhanced Gas Exchange
- ✓ Blood Shift



Adaptations for diving in reptiles



Some reptiles, such as sea turtles, crocodiles, and some species of snakes and lizards, have adapted to diving in order to forage for food, avoid predators, or regulate body temperature.

Decreased heart rate and oxygen consumption: When reptiles dive, they can decrease their heart rate and oxygen consumption to conserve oxygen and stay underwater for longer periods of time. This is achieved through physiological changes in the cardiovascular system, such as reduced blood flow to non-essential organs and an increase in blood volume.

Large lung capacity: Reptiles that dive have evolved to have larger lungs in relation to their body size, allowing them to take in more air and store more oxygen for longer dives.



Ability to slow metabolism: Some reptiles, such as sea turtles, can slow their metabolism while diving, reducing their need for oxygen and allowing them to stay underwater for extended periods.

Efficient swimming: Many diving reptiles have streamlined bodies and powerful flippers or limbs that allow them to swim efficiently underwater, conserving energy and oxygen.

Ability to tolerate high levels of carbon dioxide: When reptiles dive, they accumulate carbon dioxide in their bodies as they consume oxygen and produce carbon dioxide. Some species have evolved to tolerate high levels of carbon dioxide, allowing them to stay underwater for longer periods of time without surfacing.

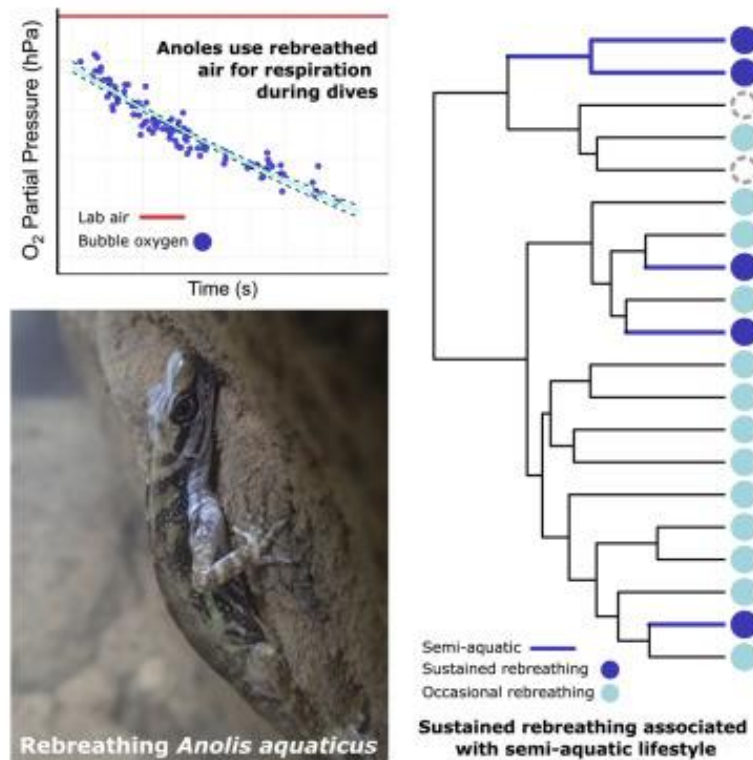
Overall, the adaptations for diving in reptiles are diverse and often complex, reflecting the variety of ecological niches that these animals inhabit.

Hold the scuba

Underwater "rebreathing" in *Anolis* lizards

Videos recorded by:
Chris Boccia, Lindsey Swierk, and D. Luke Mahler

- Anolis lizards can respire underwater by “rebreathing” exhaled air
- Many anole species occasionally rebreathe, but aquatic specialists do so routinely
- Phylogenetic analyses suggest regular rebreathing is adaptive in diving anoles



To Breathe or not to Breathe: Adaptations of Deep Diving Marine Iguanas



Marine iguanas are able to hold their breath for long periods of time due to their efficient respiratory system.

- ✓ Their lungs are smaller in size compared to other reptiles, but they have more alveoli, which allows for more efficient gas exchange.
- ✓ Their large cloacal opening helps to expel carbon dioxide quickly.

How does a crocodile breathe underwater?

When a crocodile submerges in water, the glottis automatically closes to prevent water from entering the lungs. The muscles around the lungs also contract to prevent them from collapsing.

Their lungs can act as an oxygen-storage area. Moreover, the movement and pressure of a crocodile's beating heart can help pump or mix the air in the lungs, further supporting their breath-holding abilities.

Oxygen is then obtained through the thin skin membrane in their throat called the buccopharyngeal mucosa, which absorbs oxygen directly from the water.

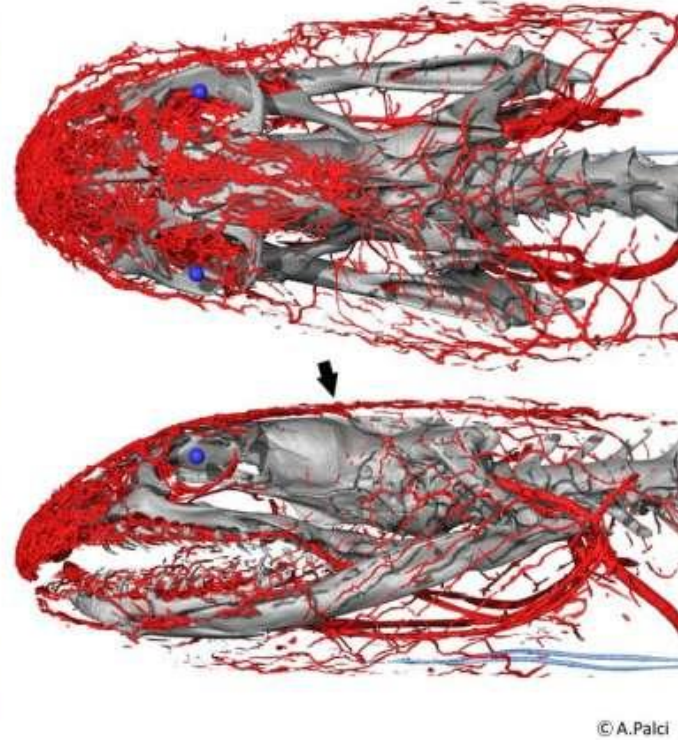
When a crocodile does resurface to breathe, it rapidly exhales and inhales air, which allows it to replenish its oxygen supply quickly.



Tropical sea snake uses its head to 'breathe'

The highly venomous blue-banded sea snakes, which live in tropical waters of Southeast Asia, are found on coral reefs and warm coastal waters.

Sea snakes must surface regularly to breathe but are among the most completely aquatic of all air-breathing vertebrates.



During submersion, the blue-banded sea snake (*Hydrophis cyanocinctus*) is now thought to use an extensive vascular network across the top of its head to absorb oxygen from the surrounding water.



Adaptations for diving in birds

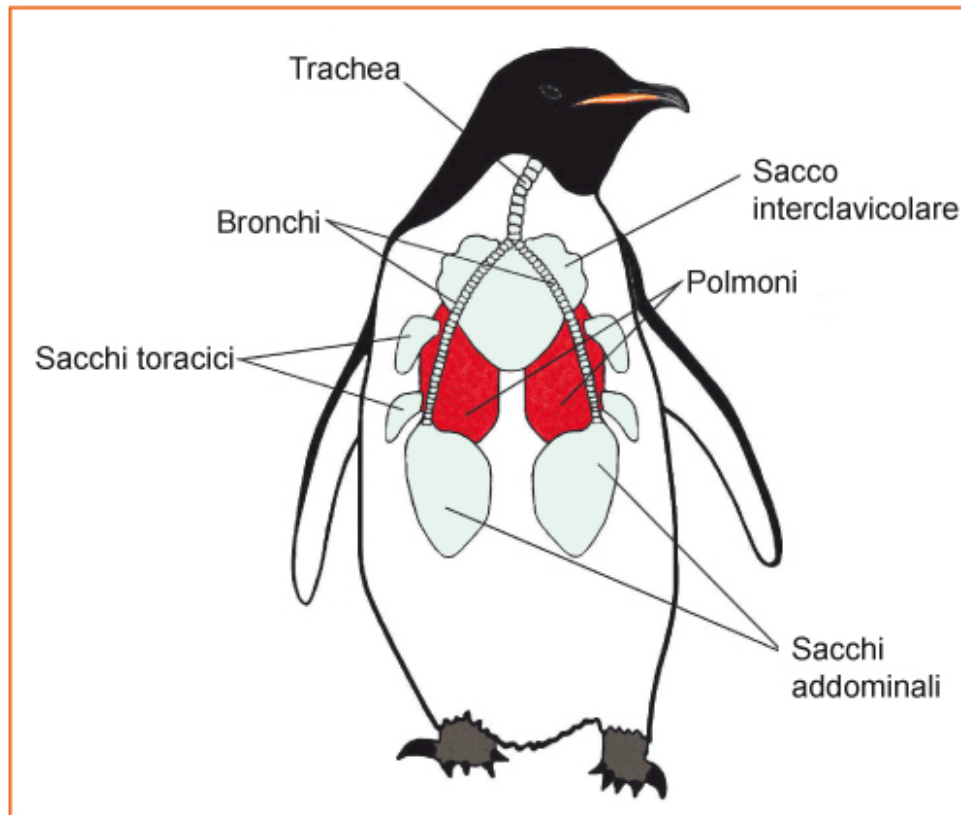
Birds have evolved a range of adaptations for diving, allowing them to hunt for food and evade predators in aquatic environments. Some of the most important adaptations for diving in birds include:

- **Streamlined body:** Many diving birds have a streamlined body shape, which reduces drag and makes it easier for them to move through water. Examples of birds with a streamlined body include penguins, cormorants, and loons.
- **Waterproof feathers:** Many diving birds have feathers that are specially adapted to repel water and keep the bird dry. The feathers have a special structure that traps air, creating a layer of insulation between the bird's skin and the water. This helps to keep the bird warm and dry, even when diving in cold water.

Adaptations for diving in birds

- **Large lungs:** Diving birds often have larger lungs than other birds, allowing them to take in more oxygen during each breath. This helps them to stay underwater for longer periods of time.
- **Flexible neck:** Many diving birds, such as cormorants, have a flexible neck that allows them to move their head and neck in different directions while swimming underwater.
- **Webbed feet:** Many diving birds have webbed feet, which helps them to swim more efficiently. The webbing between their toes creates a larger surface area to push against the water, allowing them to move faster and more easily.
- **Dense bones:** Diving birds often have denser bones than other birds, which helps them to stay submerged in water. The extra weight of the denser bones helps to counteract the buoyancy of the water and allows the bird to dive deeper.

Gli uccelli più adatti alla vita acquatica sono i pinguini



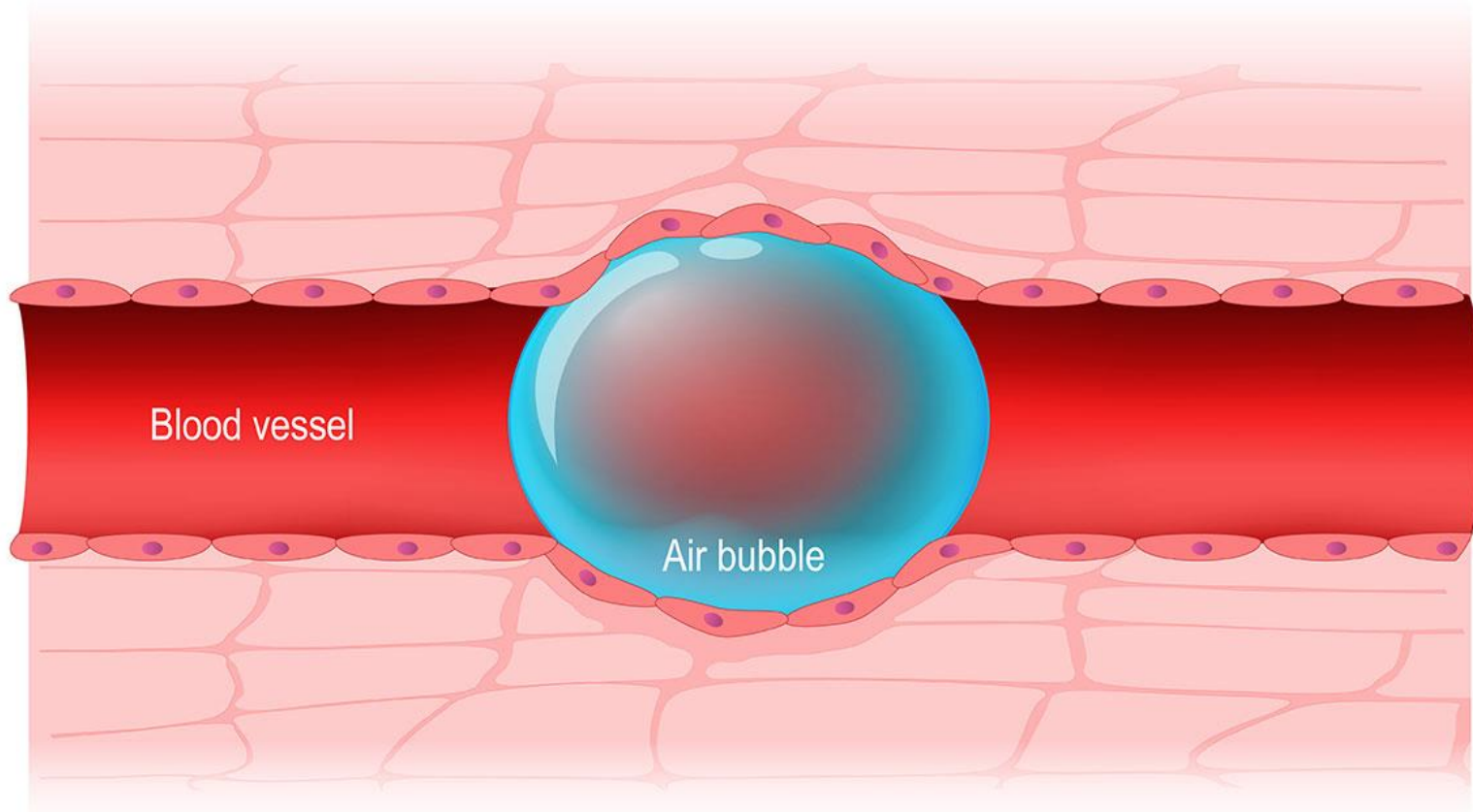
■ **FIGURA 9.42** L'apparato respiratorio del pinguino consiste di sacchi aerei, che fungono da serbatoio di aria, e di parabronchi (veri polmoni). La compressione e il rilasciamento dei sacchi aerei, secondo un ciclo ben determinato, consente in una prima fase di portare aria ai polmoni per gli scambi e in una seconda fase di eliminare l'aria reflua dai polmoni.

.....

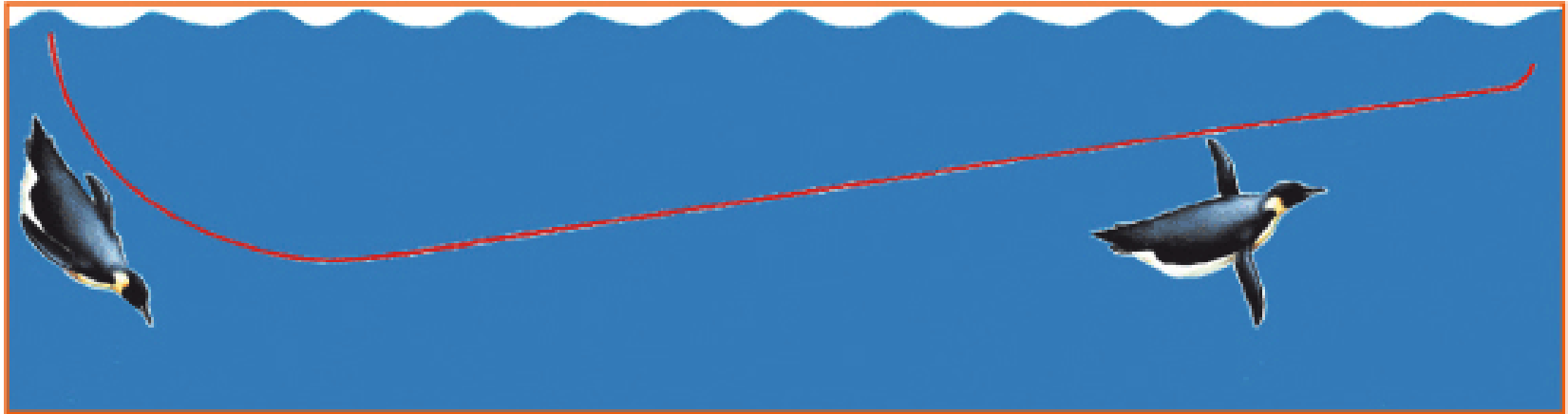


DIVE ON IN!

AIR EMBOLISM



How Penguins Avoid the Bends?



▣ **FIGURA 9.43** Quando un pinguino torna verso la superficie dopo un'immersione a discrete profondità, nuota lentamente in posizione obliqua. Si ritiene che questo comportamento favorisca la compartimentazione dell'azoto negli spazi lontani dai parabronchi in modo da evitare la formazione di emboli gassosi (sindrome da decompressione).

.....

Diving birds however, and birds in general, have very rigid lungs and surrounding structures which cannot collapse as marine mammals do. It does help when ascending to the surface. Penguins will use their natural buoyancy to spend less energy coming back up to the surface.

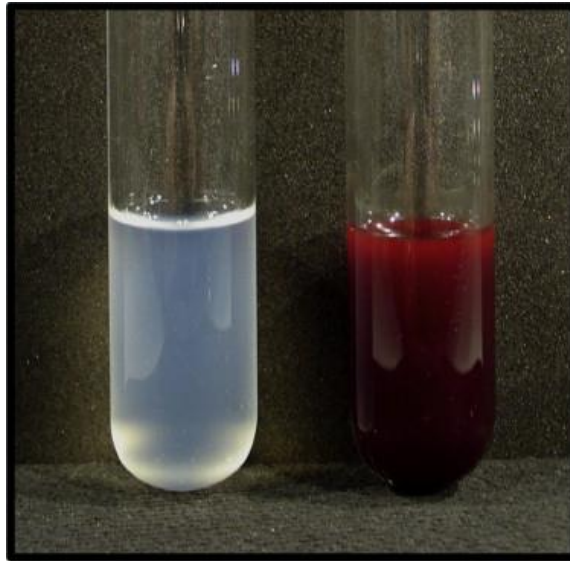
Penguin lungs have a unique structure with small, stiff air sacs that are less likely to rupture under pressure. They also have a greater number of capillaries surrounding the air sacs, which allows for more efficient gas exchange during diving.

Penguins have a **specialized hemoglobin** molecule in their blood that helps to bind and transport oxygen even at low levels. This allows them to extract more oxygen from the air they breathe, which reduces the need for large volumes of air and minimizes the risk of air embolism.



Antarctic icefish

Antarctic icefish (Chaenichthyidae) are noted for having a low metabolic rate and sluggish lifestyle. They are unique among vertebrates in that they completely lack erythrocytes and hemoglobin.



Genome analysis shows that they have completely lost the β -globin gene, whereas the α -globin gene is still present but mutated into a transcriptionally inactive pseudogene.

Di Prisco et al. Gene 2022 doi: 10.1016/s0378-1119(02)00691-1.

Sidell & O'Brien J Exp Biol 2006 doi: 10.1242/jeb.02091.

Icefish are ectotherms with body temperatures essentially equal to that of the environment. A lack of hemoglobin in this species represents an adaptation to a stable environmental condition of cold (-2°C) as well as water with a relatively high O_2 content.

In the low ambient temperatures, the viscosity of the blood is increased. Elimination of red blood cells helps to offset the decrease in blood flow.

Cardiac output is also remarkably elevated in icefish, which helps ensure that sufficient quantities of O_2 can be taken up at the gill and delivered to the tissues despite a low arterial–venous O_2 difference.

Relative heart size and blood volume are also increased in these animals.

The increased cardiac output is maintained by an increase in stroke volume and not heart rate, which is a relatively slow 14 beats per minute. Peripheral resistance to blood flow is also reduced in icefish, which ensures that the work actually performed by the heart is kept to a minimum despite the large volume of blood being pumped.

Di Prisco et al. Gene 2022 doi: 10.1016/s0378-1119(02)00691-1.

Sidell & O'Brien J Exp Biol 2006 doi: 10.1242/jeb.02091.

Compared to most fishes, the gill area of icefish is reduced and the secondary lamellae are thick.

Gas exchange does occur across the gills, although up to 40% of their O₂ requirement can be obtained through the skin. An increased density of capillaries in the skin ensures adequate gas exchange.

Many fish in the Southern Ocean, including icefishes, produce antifreeze proteins to prevent ice crystals from forming in their blood when ocean temperatures drop below the freezing point of fresh water.

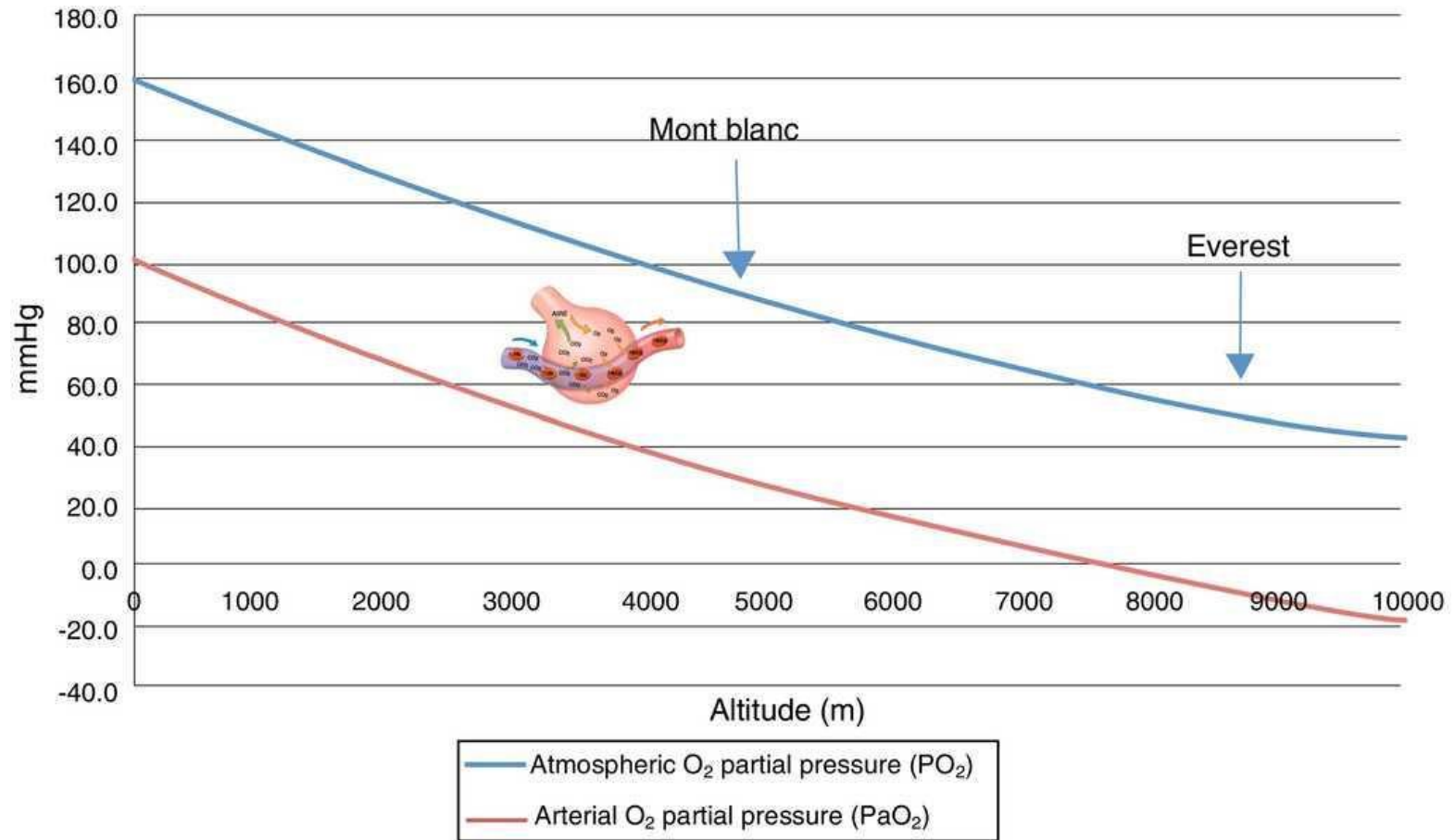


Structure of the Tenebrio molitor beta-helical antifreeze protein

Di Prisco et al. Gene 2022 doi: 10.1016/s0378-1119(02)00691-1.

Sidell & O'Brien J Exp Biol 2006 doi: 10.1242/jeb.02091.

Adaptations of vertebrates to high altitudes



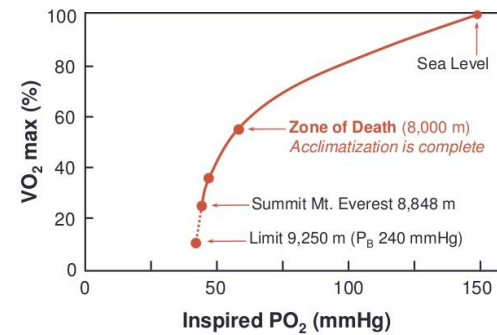
High Altitude Definitions

Elevation (meters*)	Altitude	Pressure (mmHg)	PIO ₂ (mmHg)	Effects
0-500	Sea level	760-743	159-155	Normal
500-2,000	Low	743-604	155-126	Minor impairment in performance
2,000-3,000	Moderate	604-537	126-112	Altitude illness appears; acclimatization is increasingly important
3,000-5,500	High	537-394	112-82	Considerable decline in performance; altitude illness and acclimatization are clinically important
>5,500	Extreme	<394	<82	Prolonged exposure leads to progressive deterioration (Zone of Death 8,000 m)

*1 meter= 3.28 feet

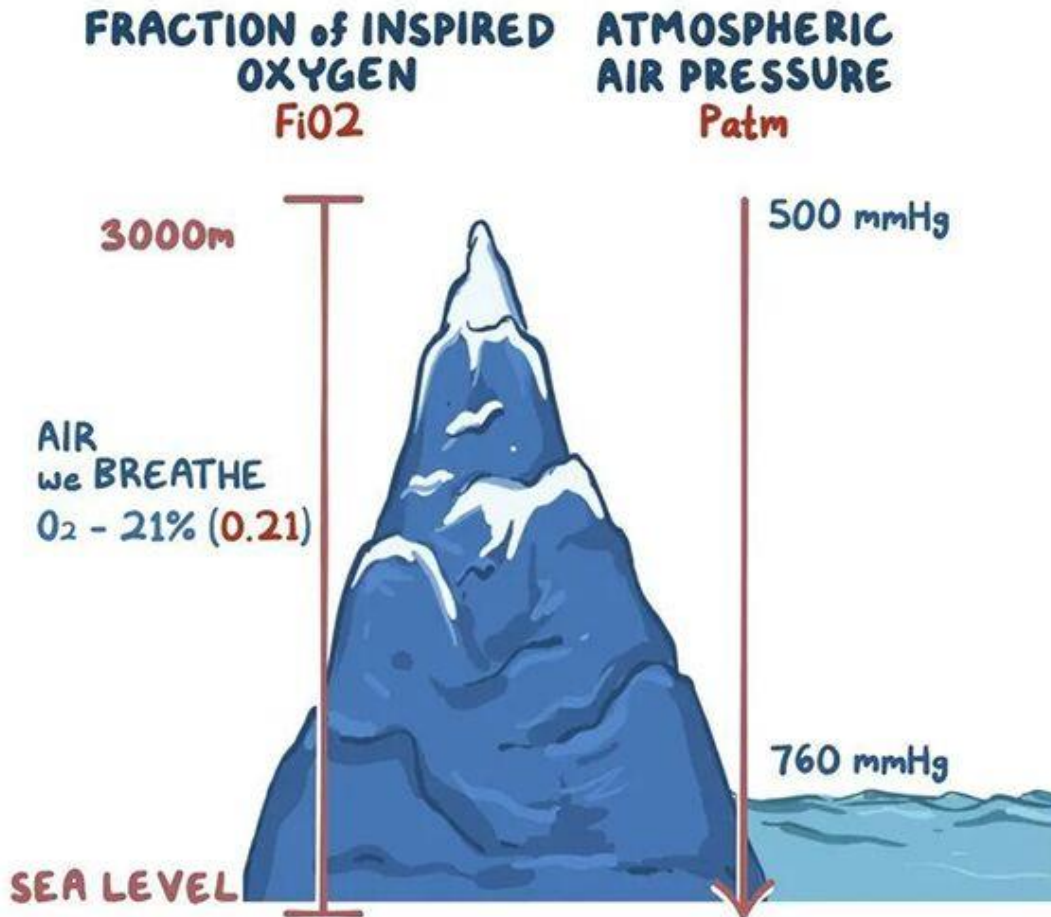
High Altitude

- Hypoxia limits exercise capacity



American Medical Expedition to Everest (AMREE 1981)

Altitude Sickness



PROBLEM IS NOT PROPORTIONALLY LESS OXYGEN at HIGH ALTITUDES

PROBLEM IS

↓↓ PRESSURE

↳ SAME PROPORTION RESULTS in a SMALLER FiO2



↑↑ ALTITUDE

↳ ↓O2 →



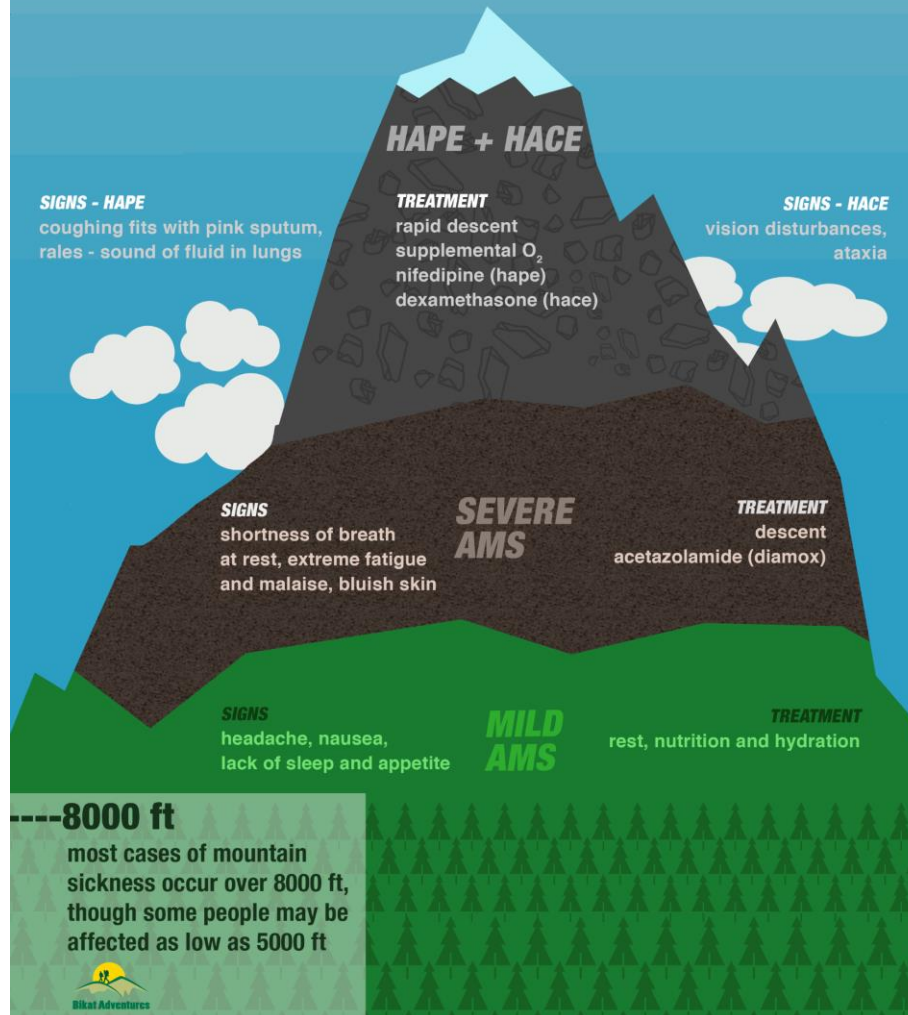
BODY makes PHYSIOLOGICAL CHANGES

- * KEEP TISSUES OXYGENATED
- * EVEN at ↓↓ ATMOSPHERIC PRESSURES
- * IF THIS FAILS

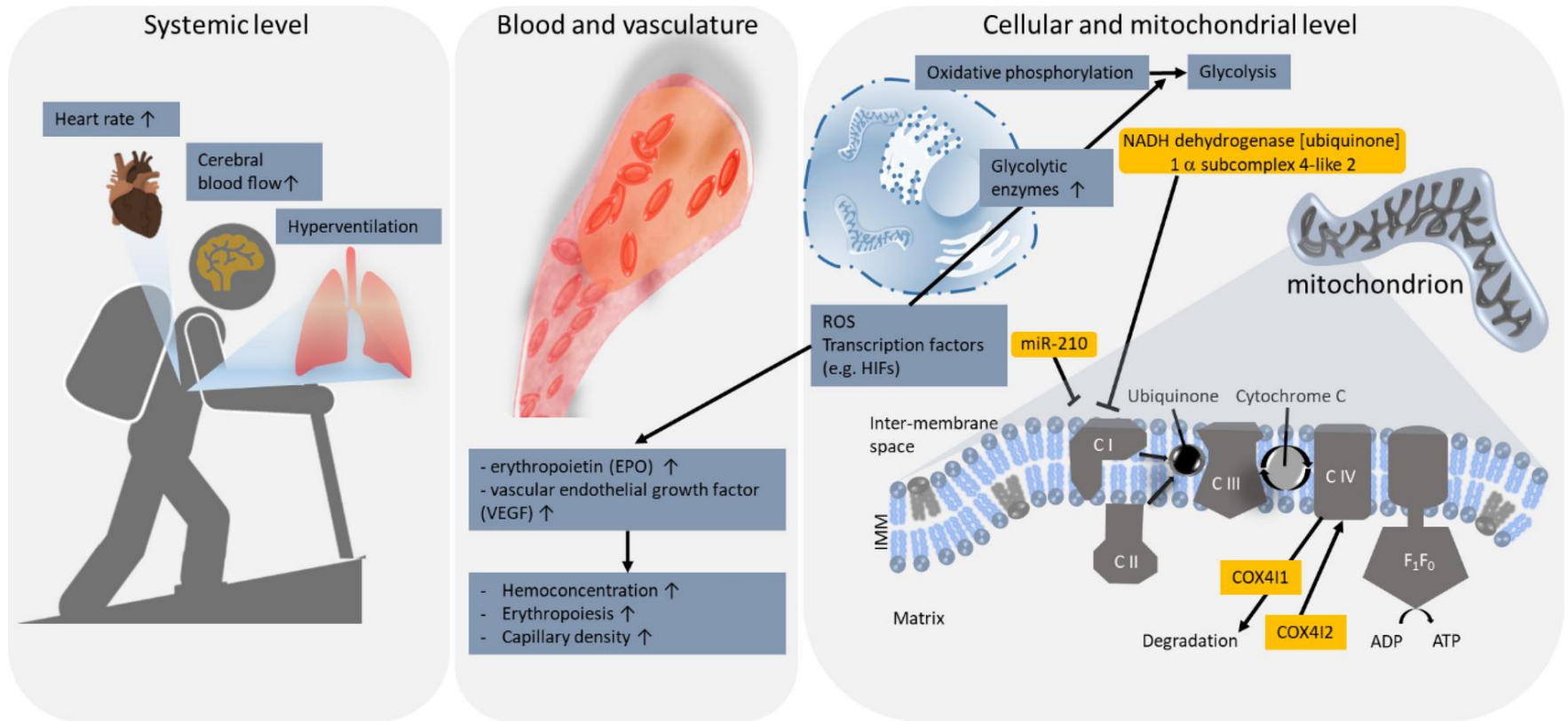
↳ **ALTITUDE SICKNESS**

MOUNTAIN SICKNESS

this chart serves as a quick reference for the signs of and treatments for various forms of mountain sickness. note that no treatment method is a replacement for proper acclimatisation processes and all treatments apart from rapid descent only buy you time to get to a lower altitude.



Acclimatization



Durante questo periodo la mancanza di ossigeno nel sangue induce principalmente la produzione di un ormone, l'Eritropoietina (EPO), il quale promuove lo sviluppo di nuovi globuli rossi, aumentando pertanto la capacità dell'organismo di prelevare ossigeno dall'aria.

When an air breather accustomed to low altitude travels to high altitude, or a water breather accustomed to well-oxygenated waters encounters hypoxic water, internal hypoxia ensues from low oxygen availability.

The body's initial reaction is an increase in ventilation and circulation, but over prolonged time at high altitude, acclimatization changes occur, including:

1. an increase in red blood cell numbers triggered by the hormone EPO from the kidney
2. angiogenesis, the growth of new capillaries triggered by the paracrine vascular endothelial growth factor (VEGF)

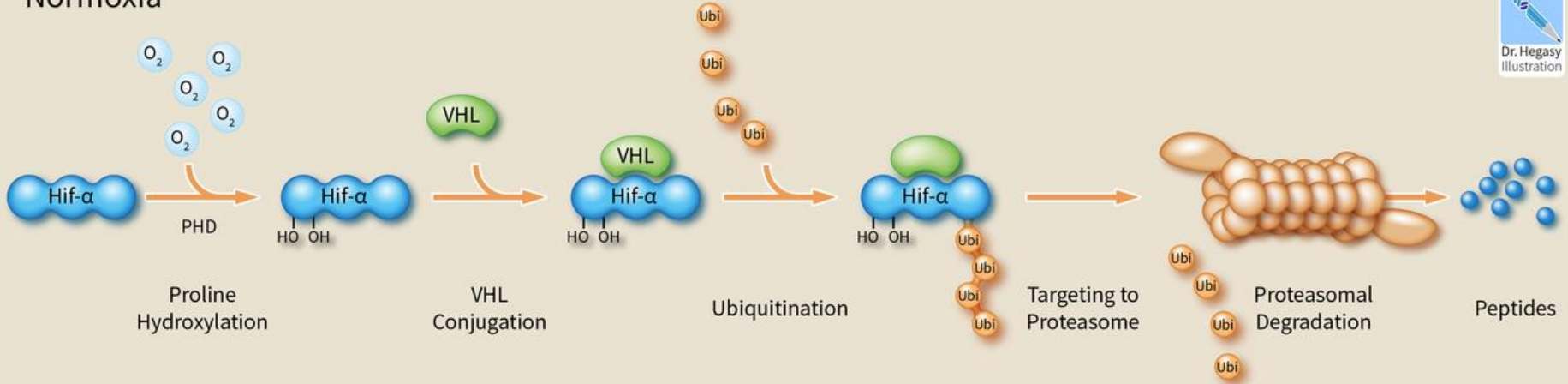
How cells detect low O₂?



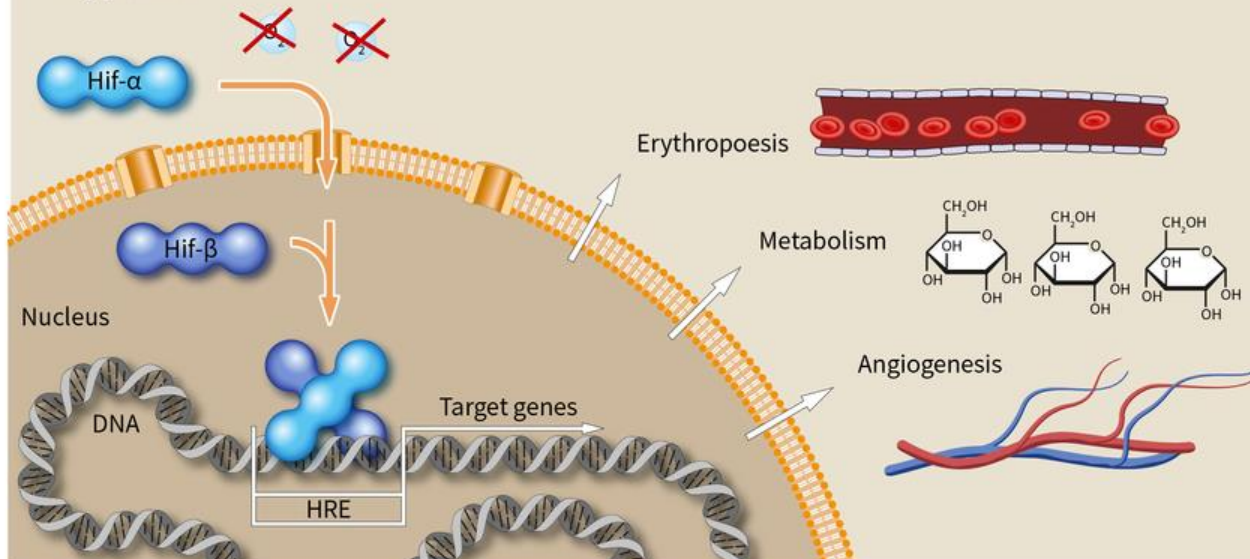
Nobel Prize in Physiology or Medicine 2019: How Cells Sense and Adapt to Oxygen Availability

Awarded to William G. Kaelin, Sir Peter J. Ratcliffe, and Gregg L. Semenza

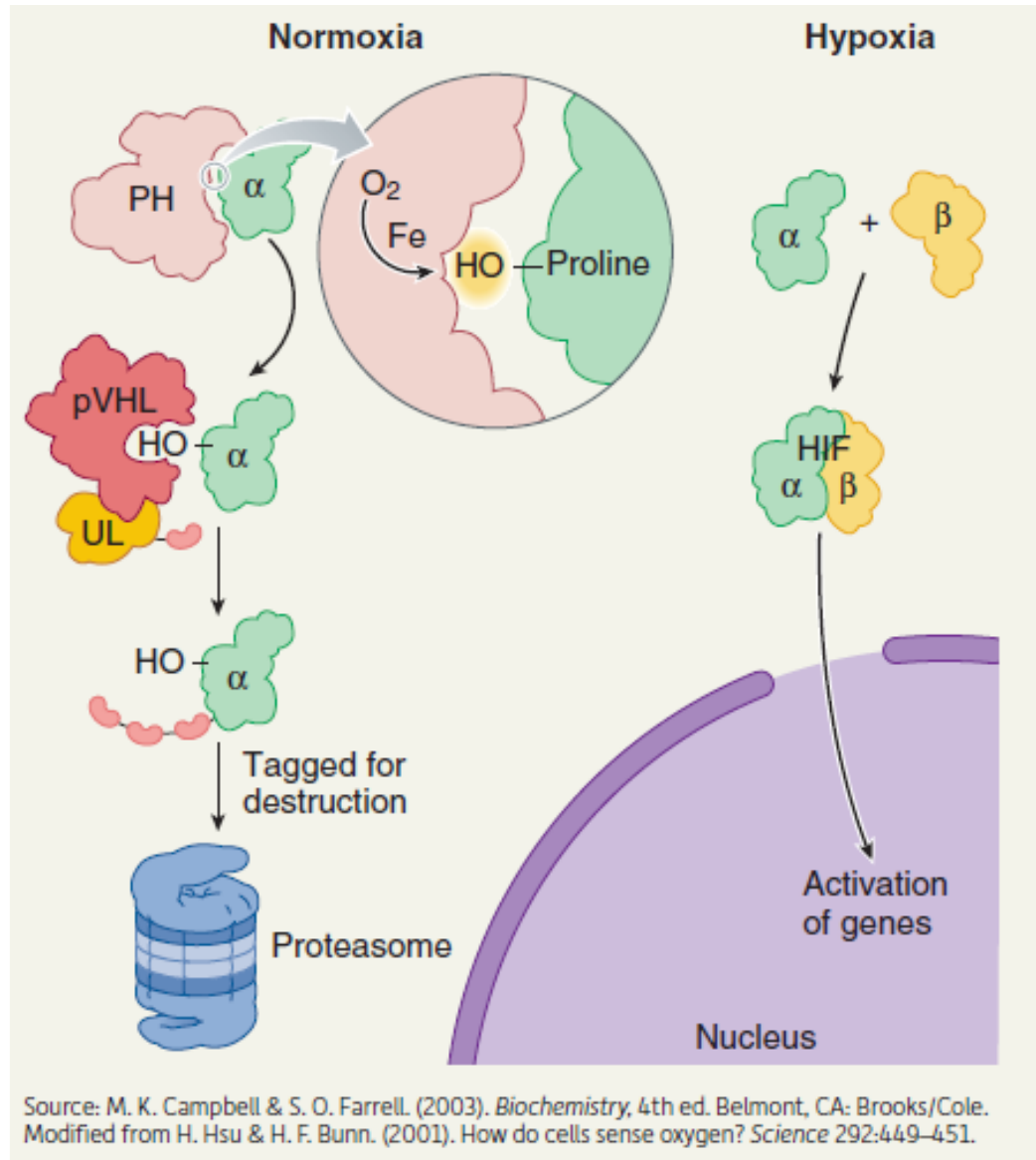
Normoxia

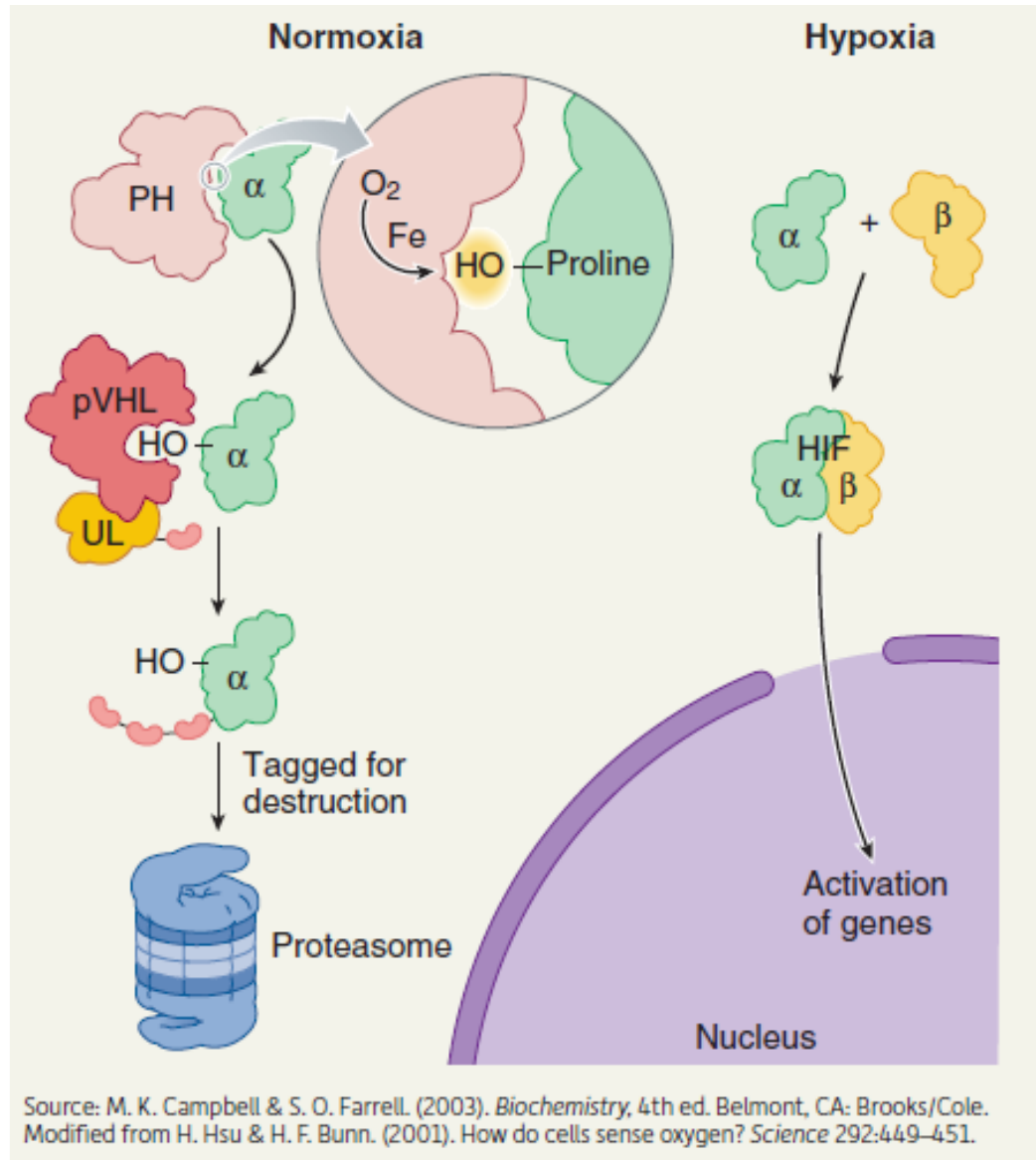


Hypoxia



- Hypoxia-inducible factor alpha subunit
 - Hypoxia-inducible factor beta subunit = Aryl Hydrocarbon Receptor Nuclear Translocator, ARNT
 - PHD Prolyl Hydroxylase Domain protein
 - VHL von Hippel-Lindau protein
 - Ubi Ubiquitin
 - HRE Hypoxia response element
- Illustration: www.hegasy.de





Native Tibetan humans living permanently at high altitudes in the Himalayas have Hb and red-cell concentrations similar to humans at sea level!



Genomic analysis indicates that genes in their HIF system have mutated to become less sensitive to hypoxia, thus blunting the EPO response.

Vertebrates that live at high altitudes have evolved various adaptations to help them cope with the lower oxygen levels and harsh environmental conditions found in these regions. Here are some examples:

Titicaca water frog or *Telmatobius culeus*, is a large, fully aquatic frog species found in Lake Titicaca and other high-altitude lakes in the Andes Mountains of South America. It is one of the largest fully aquatic frogs in the world, with adults reaching up to 50 centimeters in length and weighing up to 1 kilogram.

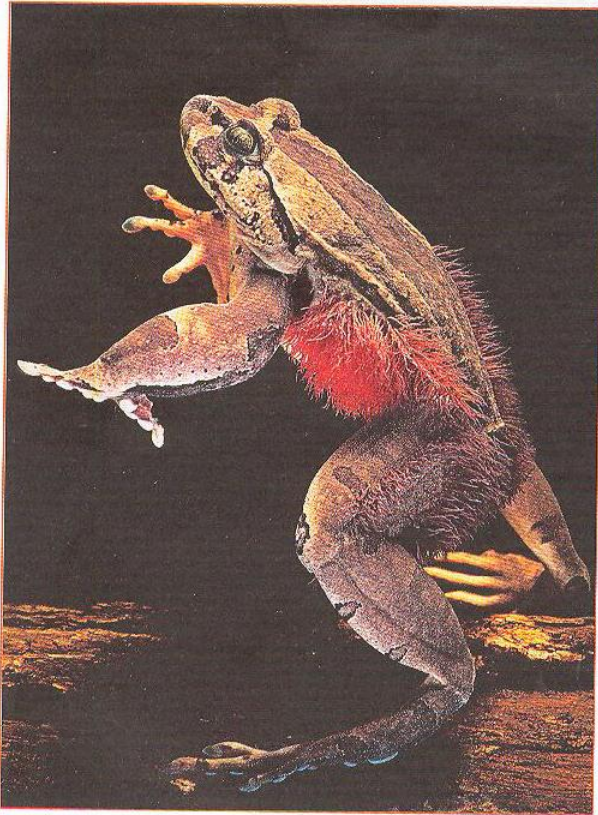
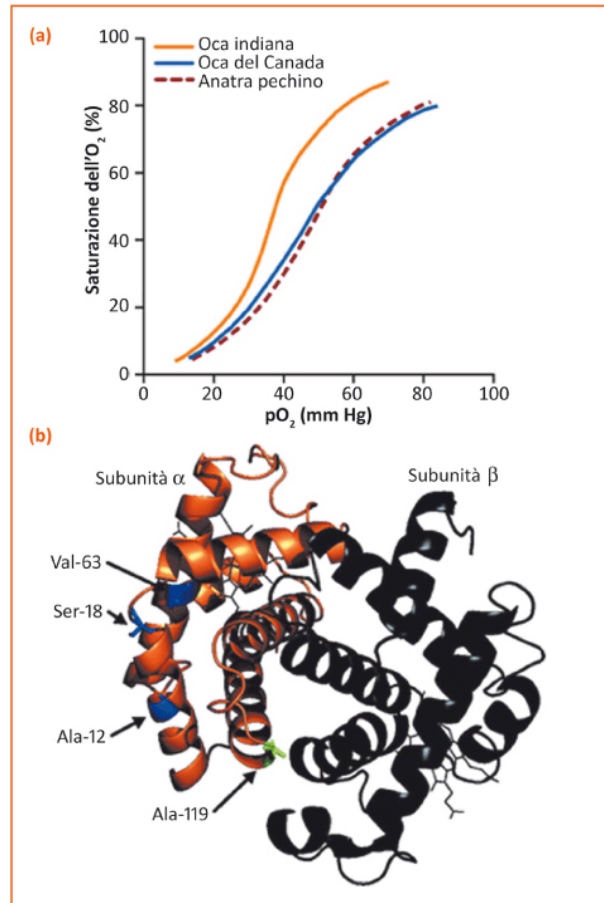


FIGURA 9.25 Durante il periodo riproduttivo, la rana *Astylosternus robustus* presenta sull'epitelio delle zampe posteriori e dei fianchi delle estroflessioni filiformi vascolarizzate che aumentano notevolmente la respirazione cutanea.

Migratory birds



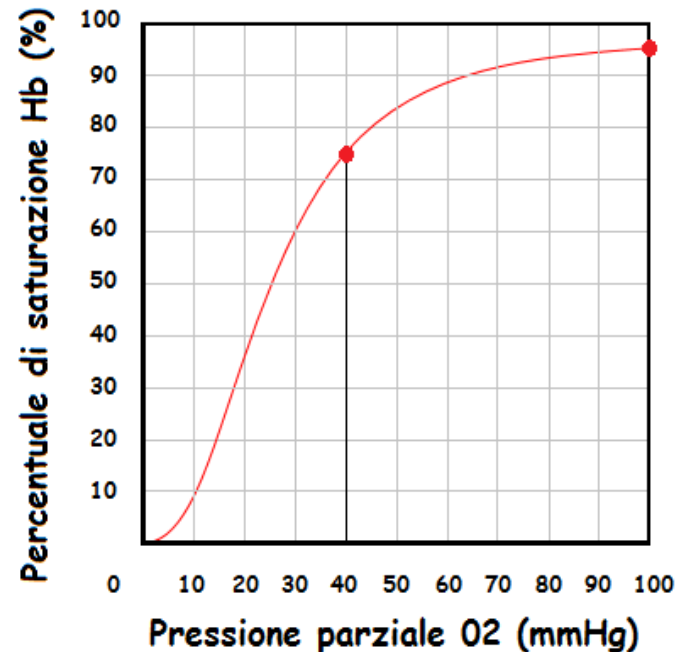
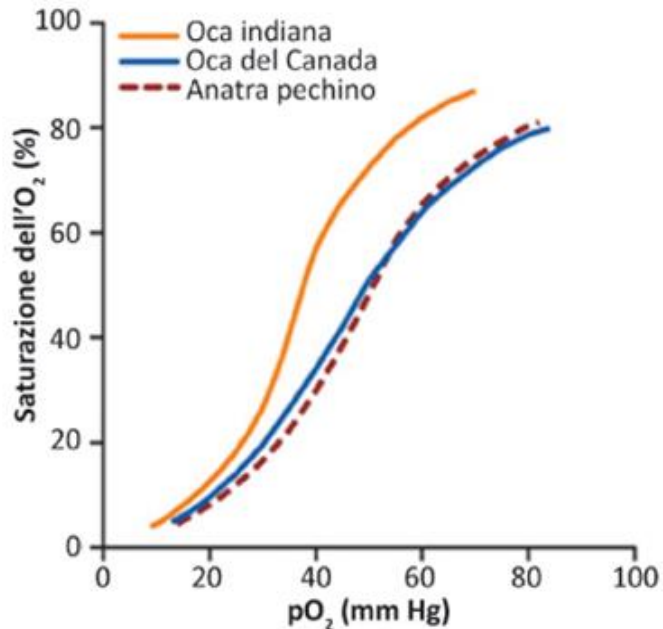
■ **FIGURA 9.56** L'oca indiana (*Anser indicus*) sorvola la catena dell'Himalaya al di sopra dei 9.000 m, dove la pressione parziale di ossigeno è di circa 50 mmHg.



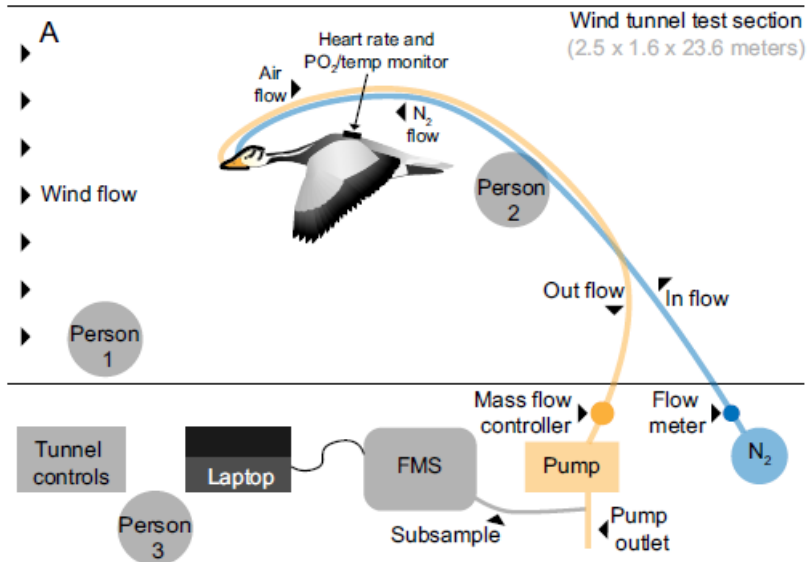
■ **FIGURA 9.57** Adattamenti dell'emoglobina nell'oca indiana (*Anser indicus*) alle quote elevate. (a) L'affinità dell'O₂ per l'emoglobina nell'oca indiana è superiore a quella di anseriformi di pianura, come mostrato dallo spostamento della curva di saturazione dell'O₂ verso sinistra. (b) La subunità α dell'emoglobina dell'oca indiana contiene 4 sostituzioni di aminoacidi. In particolare, la sostituzione della Pro¹¹⁹ con Ala (caratteristica unica in tutte le emoglobine degli uccelli) ha una grande influenza sul legame dell'O₂ perché modifica le interazioni tra le subunità α e β.

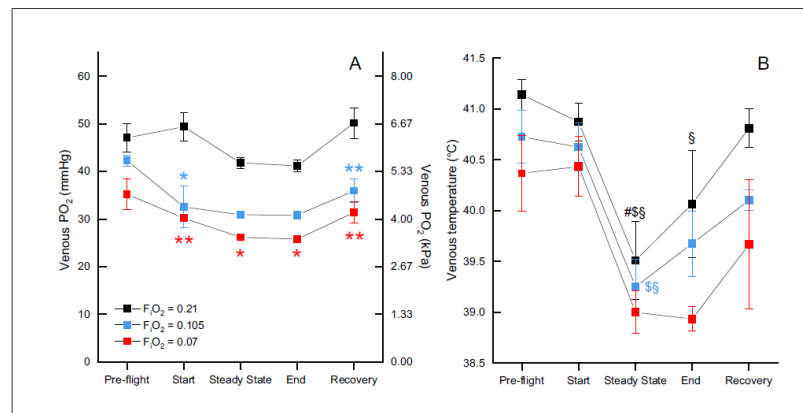
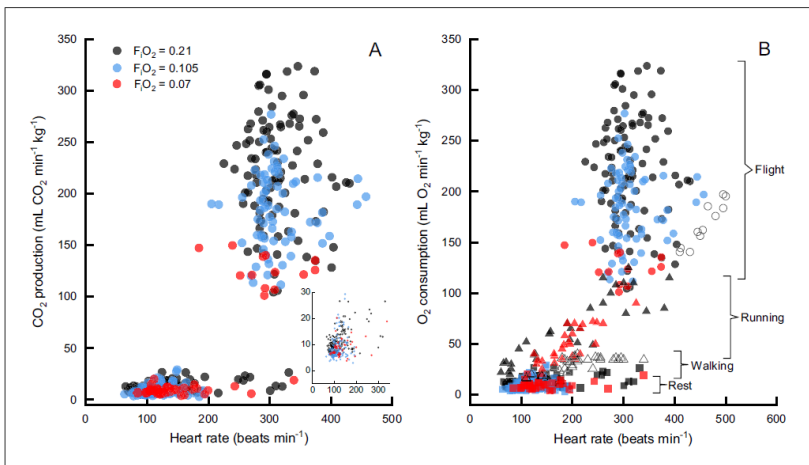
Curva di saturazione percentuale emoglobina-ossigeno

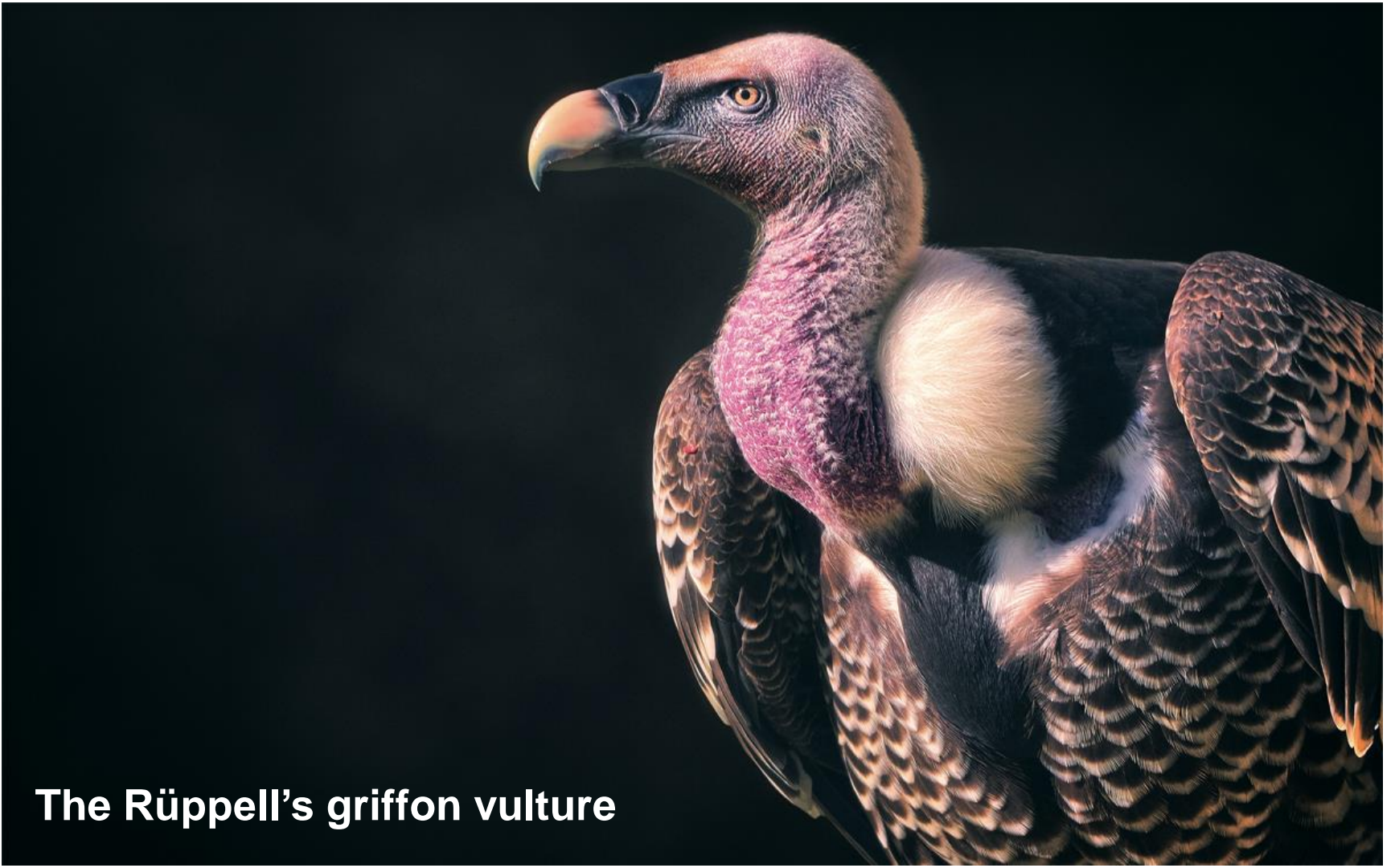
La curva di dissociazione dell'emoglobina mette in relazione la quantità percentuale di emoglobina legata all'O₂ e la pressione di O₂. La quantità di O₂ ceduta ai tessuti dipende dalla PO₂ arteriosa e venosa.



Curva di dissociazione dell'emoglobina in tre esemplari di oche (a sinistra) e, a destra, nell'uomo.







The Rüppell's griffon vulture

The Rüppell's vulture



L'avvoltoio di Rüppell presenta la massima tolleranza all'ipossia: vola fino a 11300 m (pO_2 di 36 mm Hg) ed esprime 4 emoglobine con diverse affinità per l' O_2 per la sostituzione di alcuni aa. La disponibilità di una cascata di tre ulteriori livelli di affinità costituisce un adattamento a rapidi e frequenti cambi di altitudini, quando l'avvoltoio si porta a quote basse per catturare una preda.

Vertebrates that live at high altitudes have evolved various adaptations to help them cope with the lower oxygen levels and harsh environmental conditions found in these regions. Here are some examples:

- **Increased lung capacity:** Many high-altitude vertebrates have larger lungs or more efficient respiratory systems, allowing them to extract more oxygen from the thin air
 - ✓ polmoni e gabbia toracica ampi
 - ✓ trachea corta per un basso spazio morto respiratorio
- **Larger hearts:** Some high-altitude animals have larger hearts or more efficient circulatory systems, allowing them to pump more oxygen-rich blood around their bodies.
 - ✓ cuore di grosse dimensioni
 - ✓ ventricolo destro più robusto per una perfusione polmonare più elevata e risposte vasocostrittrici più deboli a livello polmonare.

- **Higher red blood cell concentration:** High-altitude animals may have more red blood cells, which contain the oxygen-carrying protein hemoglobin. This enables them to transport more oxygen around their bodies.
 - ✓ eritrociti più piccoli ma più numerosi
 - ✓ maggior sviluppo della rete capillare
- **Improved oxygen-binding capacity:** Some high-altitude vertebrates have evolved hemoglobins with a higher affinity for oxygen, meaning they can extract more oxygen from the air they breathe.
 - ✓ una affinità dell'emoglobina per l' O₂ più elevata degli individui che abitano a livello del mare.
- **Efficient oxygen utilization:** Some animals at high altitudes have evolved more efficient systems for using oxygen, such as increased mitochondrial density in their cells.

- **Changes in metabolism:** Many high-altitude animals have adapted to the low-oxygen conditions by altering their metabolic pathways, such as switching from carbohydrate to lipid metabolism to conserve oxygen.
- **Changes in body size and shape:** Some high-altitude animals have evolved smaller body sizes, which reduces their oxygen requirements. Others have developed longer limbs or more streamlined bodies to improve their oxygen uptake and movement in thin air.

Examples of high-altitude mammals with these adaptations include the Tibetan antelope, which has a high red blood cell concentration and improved oxygen-binding capacity, and Yak



Yak (*Bos grunniens*)

Lo yak (*Bos grunniens*) è un ruminante del Tibet e delle regioni montagnose della Cina che vive abitualmente ad altezze comprese tra 4.000 e 6.000 m, dove la pressione parziale di ossigeno è compresa tra 70 e 90 mmHg.

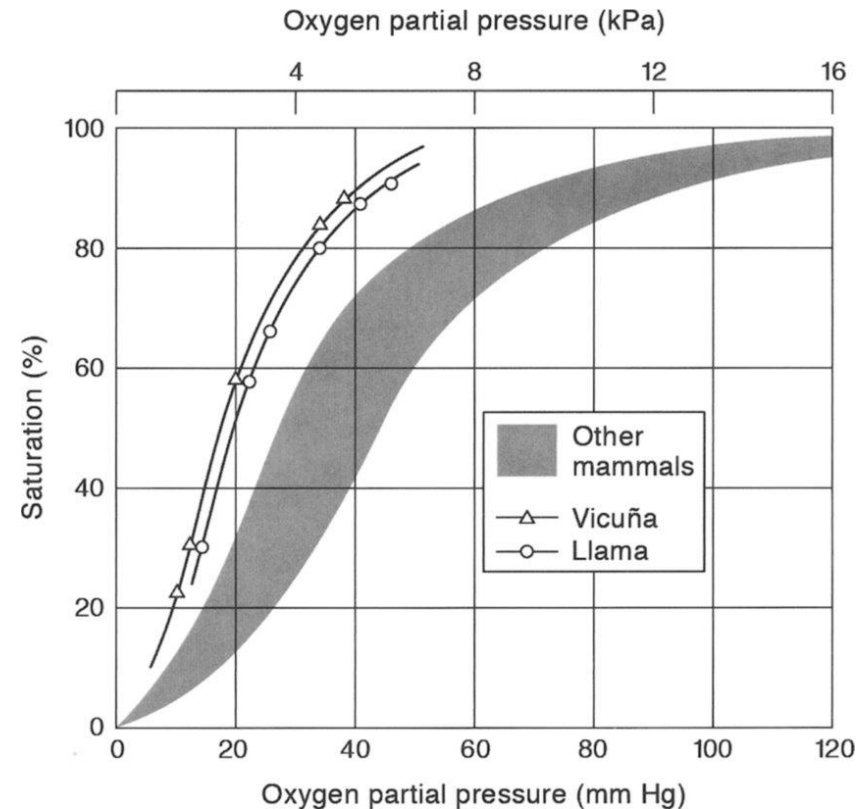
Special Morphological Structures	Function
Compact body, thick outer hair covering, and nonexistence of functional sweat glands	Minimize dissipation of body heat during winter
Thin-walled pulmonary arteries with little smooth muscles	Facilitate superefficient O ₂ flow under hypobaric hypoxia
Larger lungs and hearts	Aid oxygen uptake
Shorter tongue and greater lingual prominence	Improve forage digestibility through efficient grinding of food

Camelidi andini

Anche l'emoglobina dei camelidi andini, che vivono tra 3000 e 5000 m, ha una curva di affinità per l'O₂ diversa rispetto agli altri mammiferi che vivono a livello del mare, per due sostituzioni amminoacidiche.



FIGURA 9.58 I camelidi andini come la vigogna (*Vicugna vicugna*) hanno un'emoglobina con elevata affinità per l'O₂ e ciò consente a questi animali di vivere ad altitudini comprese tra 3.000 e i 5.000 m, nonostante non presentino un ematocrito elevato.



L'emoglobina in ambienti estremi: *Riftia pachyptila*

Riftia pachyptila, also known as the giant tube worm, is a species of marine invertebrate found in the deep sea hydrothermal vents of the Eastern Pacific Ocean.

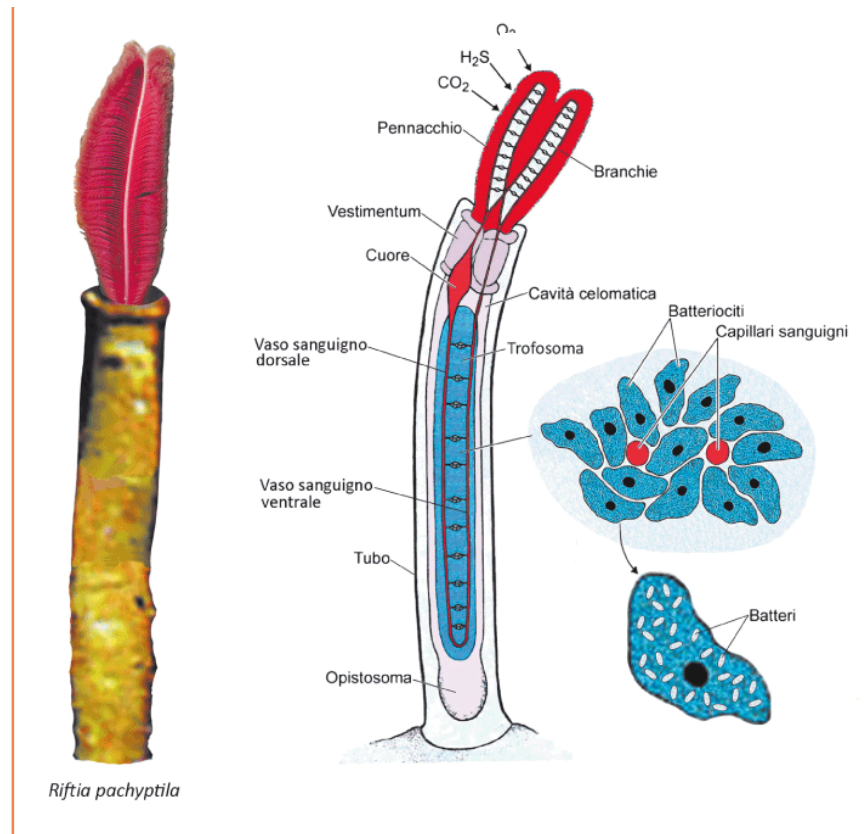
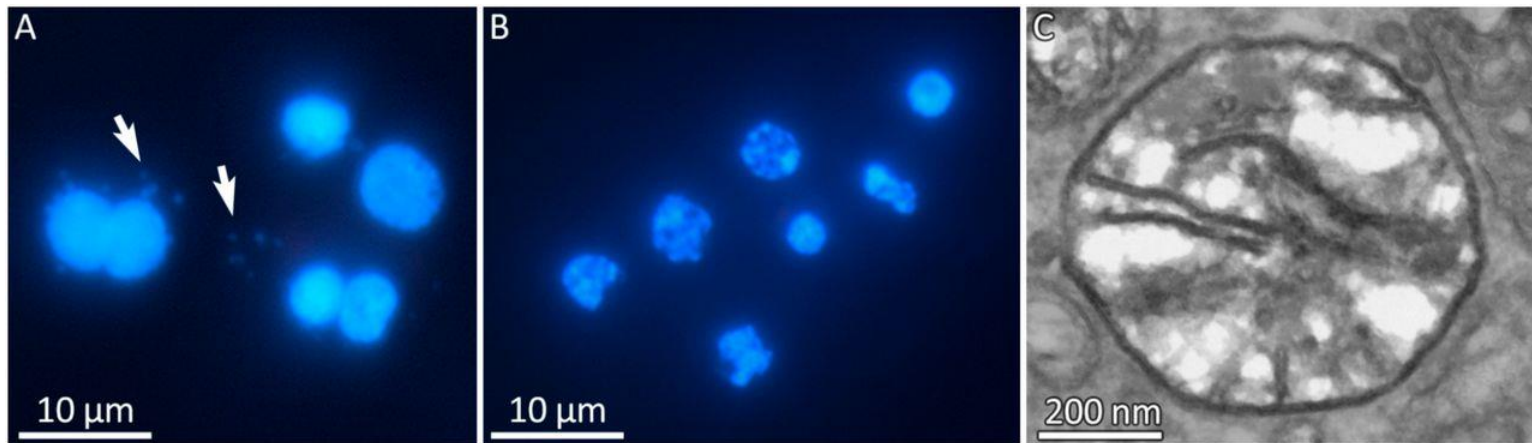


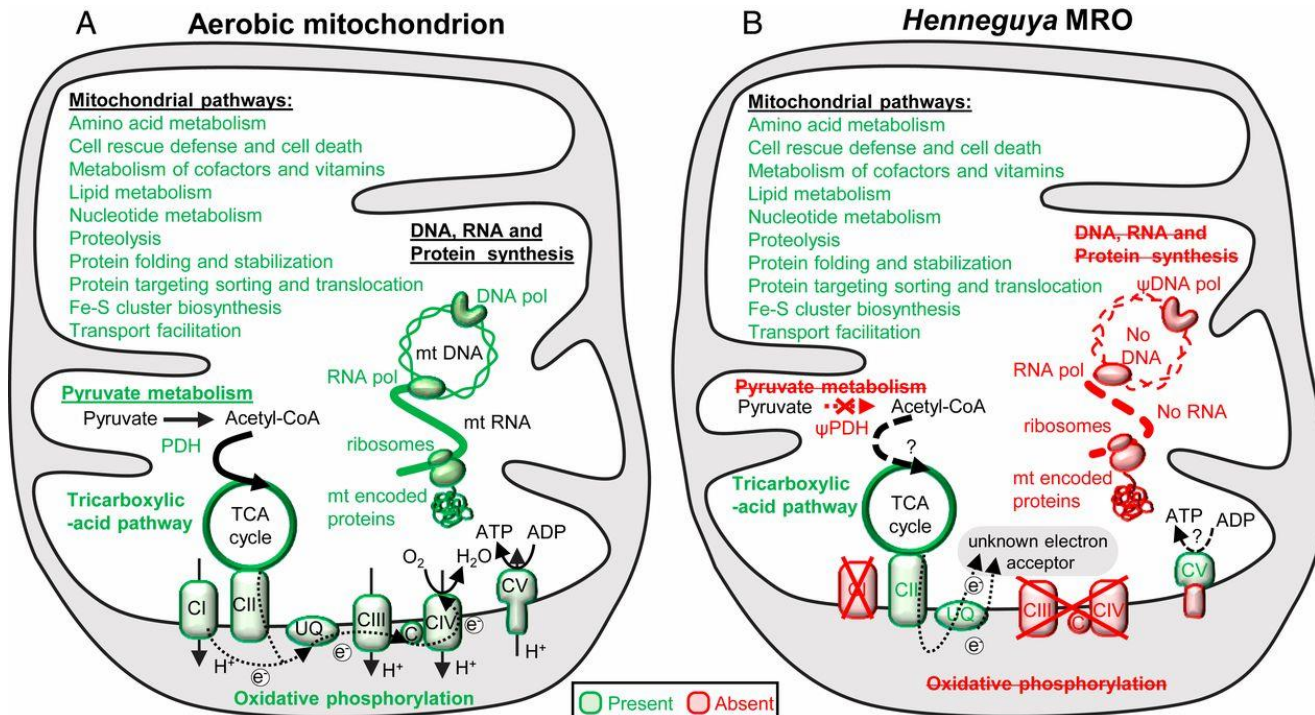
FIGURA 9.60 Il verme tubicolo *Riftia pachyptila*, che vive in corrispondenza di sorgenti idrotermali sottomarine a circa 3.000 m di profondit ,   privo di apparato digerente e possiede un'emoglobina extracellulare in grado di legare H_2S e O_2 a livello branchiale per trasferirli nel trofosoma, dove batteri simbiotici chemioautotrofi ossidano l' H_2S a solfato con produzione di ATP.

A cnidarian parasite of salmon lacks a mitochondrial genome





Microscopic evidence for the absence of mitochondria in H. salmonicola. (A and B) DAPI staining of normal 7-cell presporogonic developmental stages of two myxozoan parasites of salmonid fish. (A) M. squamalis, showing large nuclei with many smaller mitochondrial nucleosomes (arrowed). (B) H. salmonicola, showing large nuclei but surprisingly no mitochondrial nucleosomes. (C) TEM image of H. salmonicola mitochondrion-related organelle with few cristae.



C Mitochondrial / MRO pathways present in selected species

		DNA	Cristae	CI	CII	CIII	CIV	CV	TCA cycle	PDH	PFO	PNO	PFL	AOX	H ₂ synthesis	ASCT	SCS	ACS	Propionate	Glycine	
Aerobic mitochondria	<i>Hydra magnipapillata</i> (Metazoa)	+	+	+	+	+	+	+	+	+	-	-	c	-	-	+	-	-	+	+	
	<i>Kudoa iwatai</i> (Metazoa)	+	+	+	+	+	+	+	+	+	-	-	-	-	-	-	-	-	-	+	p
	<i>Thelohanellus kitauei</i> (Metazoa)	+	+	+	+	+	+	+	+	+	-	-	-	-	-	-	-	-	-	p	p
	<i>Myxobolus squamalis</i> (Metazoa)	?	+	+	+	+	?	+	+	+	-	-	-	-	-	-	-	-	-	p	p
	<i>Myxobolus cerebralis</i> (Metazoa)	?	+	+	+	+	?	+	+	+	-	-	-	-	-	-	-	-	-	p	p
Hydrogen-producing mitochondria	<i>Bastocystis</i> sp. (Stramenopiles)	+	+	+	-	-	-	p	+	+	+	+	+	+	+	+	+	-	c	+	
	<i>Acanthamoeba castellani</i> (Amoebozoa)	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+
Hydrogenosomes	<i>Trichomonas vaginalis</i> (Metamonada)	-	-	p	-	-	-	-	-	+	-	-	-	-	+	+	+	+	-	p	
	<i>Piromyces</i> sp. (Nucleotmyceta)	-	-	+	+	+	+	+	+	-	-	+	+	-	+	+	+	+	-	p	p
Mitosomes	<i>Giardia intestinalis</i> (Metamonada)	-	-	-	-	-	-	-	-	c	-	-	-	-	c	-	-	-	c	-	
	<i>Nematocida parisii</i> (Microsporidia)	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-
	<i>Cryptosporidium muris</i> (Alveolata)	-	+	-	+	-	-	+	+	-	-	-	c	-	+	-	-	-	c	-	p
	<i>Henneguya salminicola</i> (Metazoa)	-	+	-	+	-	-	p	+	+	-	-	-	-	-	-	-	+	-	-	p

Legend
 + = present
 - = absent
 p = partial
 c = in cytosol
 ? = unknown
 Myxozoa