

**GAS EXCHANGE (Oxygen and Carbon Dioxide exchange with the environment)****I. LIMITS TO AEROBIC METABOLISM (Factorial Scope  $\cong$  10 X)**

- Possible Causes?
  - 1) *Ventilation* – limit to how fast ambient air/water can be supplied
  - 2) *Diffusion* – from respiratory surface  $\rightarrow$  blood, blood  $\rightarrow$  tissues
  - 3) *Oxygen Transport* – blood oxygen affinity and carrying capacity, blood flow rates
  - 4) *Oxidative Metabolism* – limit to how fast aerobic ATP production can operate
- Which system is THE limiting step is not known with great certainty (although it doesn't seem to be lung diffusing capacity for mammals). It is likely that rates at any one step in the pathway do not markedly exceed others. This concept is known as *Symmorphosis*.

**II. DIFFUSION**

- Rate of diffusion is determined by Fick's Law:

$$M_x = [D_x * A * (C_{ext} - C_{int})]/L$$

$M_x$  = mass of gas x transferred per unit time (= rate of diffusion)

$D_x$  = diffusion coefficient (measure of ease of diffusion, dependent on size of molecule and solubility coefficient; constant for a given gas and respiratory medium)

A = surface area for diffusion

$C_{ext} - C_{int}$  = concentration gradient across diffusion barrier

L = thickness of diffusion barrier

- From Fick's Law, we see that gas ( $O_2$  or  $CO_2$ ) diffusion is dependent on:
  - 1) Total surface area of respiratory structures (increased S.A.  $\rightarrow$  increased diffusion)
  - 2) Permeability of the surface ( $D_x$  [a constant], thickness)
  - 3) Gradient of  $O_2$  or  $CO_2$

**III. RESPIRATION IN WATER AND AIR**

- A) Water and air present two very different sets of problems and limitations.

- Life originated in the water.
- Large-scale (high % of organisms within a particular taxon) adaptations for air breathing have occurred only in Arthropods (includes insects) and Vertebrates. This is due to the difficulty of dealing with the problem of dehydration.

**B) Comparison of Water and Air Breathing**

1. *Partial Pressure* = pressure exerted by an individual gas in a gas mixture. PP of gas in water = PP of gas in air with which water is in equilibrium.
2. Amount of gas dissolved in water depends on:
  - a) Solubility
  - b) PP in gas phase
  - c) Temperature (increased temperature decreases solubility)
  - d) Presence of other solutes (SW < FW)
3. Oxygen Absorbency Coefficient (OAC) = measure of  $O_2$  concentration in water, expressed as volume % (ml  $O_2$ /100 ml water) after equilibration with a gas sample where  $pO_2 = 760$  mm Hg.

<u>Temperature</u>	<u>Volume % (OAC)</u>
5°C	4.28
15°C	3.50
40°C	2.30

- How much O<sub>2</sub> available to a water-breather at 15°C?  
3.5 X 21% (O<sub>2</sub> in air) = 0.7 volume %
  - How much O<sub>2</sub> available to an air-breather at 15°C?  
21% of ambient air is O<sub>2</sub>, so 21 volume %
  - So, about 30-times more oxygen is present in water than in air (at 15°C)
  - If calculate with O<sub>2</sub> at lung surface (about 13 volume %), air has about 19-times more O<sub>2</sub> available than water.
  - Bottom Line = Oxygen availability is much greater for air-breathers than for water-breathers.
4. Viscosity and Density – water is much denser and more resistant to flow than air, so much more energy is necessary to mover water over the respiratory surfaces.
- This is why lungs don't work well in water → we can't move water over the respiratory surfaces fast enough.
  - Coupling the decreased availability of O<sub>2</sub> in water with its increased viscosity and density, we see that much more energy is required for water breathing than for air breathing.
  - Water-breathers use about 20% of RMR for ventilation
  - Air-breathers use about 1-2% of RMR for ventilation
5. Diffusion is much faster in air than in water (by about 8000-times), so diffusion requires much less time for equilibration in air than in water.
- This means that air-breathers experience few problems with depleting the O<sub>2</sub> supply, but this can be a problem for water-breathers (that is why they have mechanisms to achieve water flow over the gills).

#### IV. VENTILATION

- 4 Mechanisms:
  - 1) Skin = most primitive; simple diffusion from environment (no circulatory system) suffices for small invertebrates.
  - 2) Gills = larger aquatic invertebrates and aquatic vertebrates (fish and aquatic amphibians).
  - 3) Lungs = used by vertebrates (including some fish) and some terrestrial invertebrates
  - 4) Tracheae = found in insects.
    - Consist of small openings on the body that lead to a system of tubes that branch and lead to all parts of the body. (**Overhead – Willmer et al., p. 148**)
    - Allow direct delivery of O<sub>2</sub> to the tissues, which is very efficient and allows the extremely high factorial scopes (100-200 X) found in some insects.
- *Measurement of Ventilation:*
  - Minute Volume = breaths/min X volume medium/breath = volume medium/min
  - Breathes/min is the *respiratory frequency* or *breathing rate*
  - Volume/breath is the *tidal volume*
  - For Humans: Minute Volume at rest  $\cong$  6 liters/min, during activity  $\cong$  100 liters/min
  - Variation exists among animals in how minute volume increases during activity. Breathing Rate and/or Tidal Volume may increase. Birds and mammals increase both, reptiles tend to increase only tidal volume.
  - Usually, there is a conservative relationship such that Minute Volume is tightly correlated with metabolic rate in Tetrapods. This is not so for fish (MR doesn't increase 1:1 with Minute Volume), probably due to the resistance to flow of water.

- V. GILLS = involved in aquatic respiration
- Must provide a flow of water over the gill surface, otherwise water at the gill surface would be rapidly depleted of O<sub>2</sub> because diffusion in water is relatively slow.
  - This can be accomplished in two ways:
    - 1) Moving the gill through the water – used by small aquatic invertebrates (e.g., aquatic insect larvae) and amphibians with external gills (when in still water). Limiting factor = resistance to movement of gill through water.
    - 2) Moving water over the gills – much more common method of ventilating gills. This can be accomplished by living in moving water (e.g., streams) or by one of three methods in still water.
      - a) *Ciliary Flow* = cilia create water currents. Used in mollusc gills.
      - b) *Pump-like Action* = pump water over gills. Used by fish and crabs.
      - c) *Ram Ventilation* = swimming thorough water with mouth open. Used by tunas, mackerels, sharks, and paddlefish.
  - Gill Surface Area is associated with the animal's way of life. For example, active fishes maintain a higher gill surface area than sluggish fishes. (**Overhead – Willmer et al., p. 411**)
  - For adequate gas exchange in water (recall low O<sub>2</sub> availability relative to air) a *high rate of water flow* and *close contact* between water and gill surface are necessary.

#### Gill Structure in Fishes

- 1) Gills lie under a bony plate (operculum), which opens to the outside. This provides protection and allows sufficient flow of water over the gills.
- 2) *Countercurrent Exchange* = water and blood flow in opposite directions, which allows very efficient O<sub>2</sub> extraction at the gill lamellae (**Overhead – Willmer et al., p. 410**).

#### Hypoxic Conditions

- Tropical still waters often provide hypoxic conditions (= low O<sub>2</sub> availability; recall that warm water holds less O<sub>2</sub> than cold water).
- How do fish in these waters obtain sufficient oxygen?
  - 1) Expensive to maintain high surface area of gills (osmotic considerations, etc.), so they don't have markedly increased gill surface area.
  - 2) Many fish will gulp air and use a vascularized mouth or esophagus for gas exchange; some fishes actually possess lungs. Supplementary air breathing allows them to survive periods of hypoxia, although they usually aren't capable of normal levels of activity during these periods.
- Lungfish are the most adept at supplementary air breathing (some are obligate air-breathers), but they still can't support high levels of activity this way because of a low surface area of the lungs.
- During extreme drought periods, when the ponds they are living in dry up, lungfish will aestivate (dormant state) within a mucous case. They may survive in this state for five years or more, until the ponds fill up again.

#### VI. LUNGS

- 1) Fishes = lungs are simple sacs with only minor subdivision at best. Thus, they have a low surface area and this doesn't support high levels of aerobic activity.
- 2) Amphibians/Reptiles = amphibians with only minor subdivision, reptiles with modest subdivision – still not highly aerobic organisms.
  - Amphibians use a buccal force pump (like fish) to ventilate the lungs
  - Reptiles use a suction pump system (similar to mammals, but less efficient since no diaphragm is present)

- 3) Mammals = highly branched subdivision within the lung. Ventilate respiratory surface using a *negative pressure system* with a diaphragm. Bi-directional air flow over the respiratory surface.
- This lung is capable of supporting higher levels of aerobic metabolism
- 4) Birds = complicated air sac respiratory system allows *unidirectional airflow* over finely subdivided lungs.
- Gas exchange occurs in air capillaries, which open to a parabronchus, through which air passes in only one direction. **(Overhead – Willmer et al., p. 152)**
  - Blood flow in the avian lung is via a *crosscurrent mechanism* relative to airflow. This functions similar to a countercurrent system and is highly efficient for O<sub>2</sub> extraction. **(Overhead – Willmer et al., p. 152)**
  - This system is capable of supporting the very high levels of aerobic metabolism associated with flight in birds.
  - Also, it allows normal activity at high altitudes (e.g., some geese migrate over the Himalayas)
    - Tucker (1968) exposed mice and house sparrows to an atmospheric pressure of 350 mm Hg (corresponds to 20,000 ft. in altitude).
    - Mice were barely able to crawl, but sparrows were able to fly about normally
    - Mice and sparrows had similar mass, MR, and blood oxygen affinity, so differences were likely explained by the increased oxygen extraction efficiency of the bird lung resulting from the specialized respiratory system.

**CUTANEOUS RESPIRATION** = gas exchange across the body surfaces. This works in both air and water, but requires a thin, moist, highly vascularized skin to be effective.

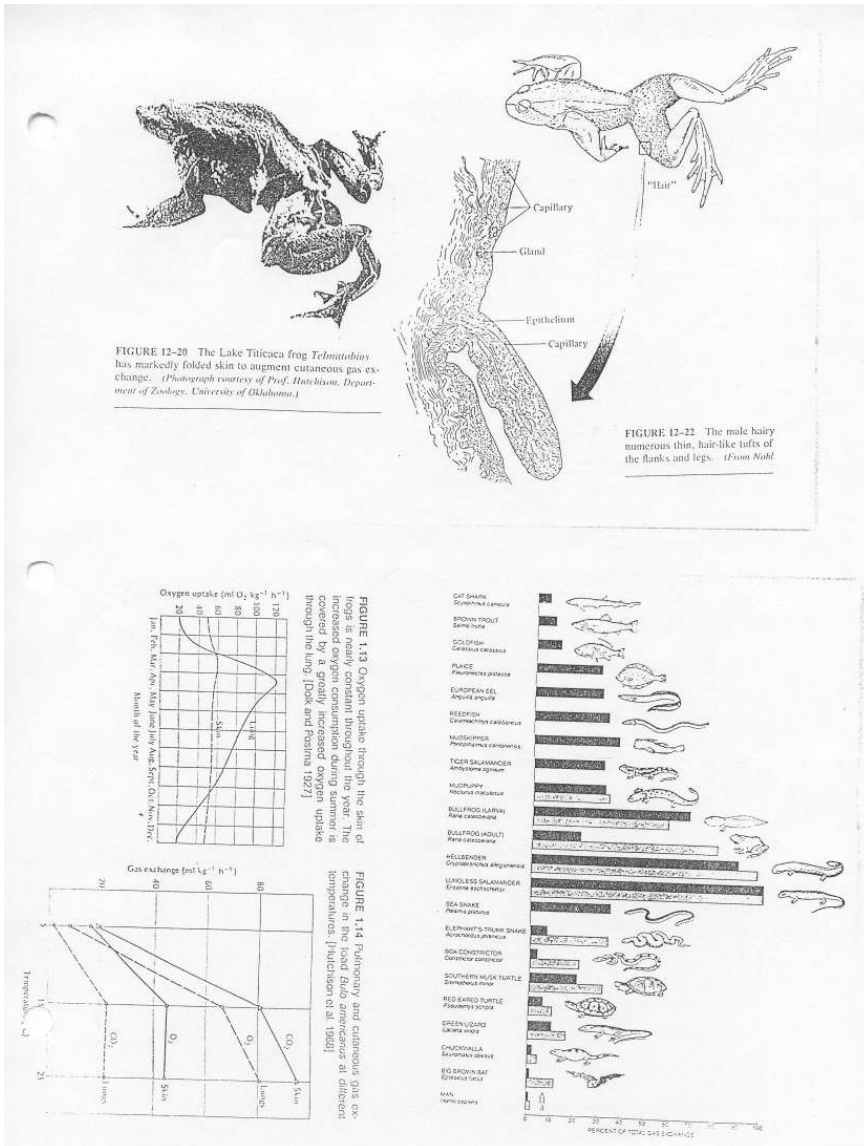
- I. Primitive Invertebrates (small) – simple diffusion of O<sub>2</sub> through surface directly to tissues suffices, so no circulatory system is needed.
- Diffusion is limited by the thickness of the diffusion barrier (recall Fick's Law). Maximum thickness for sufficient O<sub>2</sub> diffusion is about 1 mm, so cells must be within about 1 mm of the body surface for this to work.
  - The diffusion barrier consists of both the thickness of the *respiratory surface* plus the thickness of the *unstirred boundary layer* of the respiratory medium (O<sub>2</sub> depleted) immediately adjacent to the respiratory surface.
    - a) Boundary Layers may account for 80-90% of the total resistance to diffusion in aquatic situations, so they may limit gas exchange in water. The Boundary Layer is not important in air due to the much faster rates of diffusion compared to water.
    - b) The thickness of the Boundary Layer is dependent on:
      - 1) the velocity of the respiratory medium (faster velocity = smaller boundary layer)
      - 2) the diffusion coefficient of the gas (boundary layer not a problem for CO<sub>2</sub>, even in water due to the higher solubility of CO<sub>2</sub> than O<sub>2</sub> in water)
      - 3) the linear dimensions of the animal (the larger the animal, the higher the velocity required to dissipate the boundary layer)
- II. Primitive Invertebrates (large) – Includes sponges, nematodes, coelenterates, etc.
- These organisms may also depend on simple diffusion across the integument, in association with internal channels through which water may pass so that diffusion distances are greatly reduced.
- III. Complex Invertebrates – Some lack specialized respiratory structures. In these organisms, cutaneous respiration is accompanied by the appearance of a *circulatory system* that

functions to transport gas from the skin to the tissues. Blood vessels close to the skin surface pick up the O<sub>2</sub> and carry it to the tissues.

- Thus, body size no longer limits O<sub>2</sub> diffusion to the tissues.
- In invertebrate organisms, cutaneous gas exchange (CGE) remains important, even in those groups with specialized respiratory structures. CGE may account for 20-50% of total gas exchange in these organisms.

IV. Vertebrates – many fish and amphibians and a few reptiles rely to a variable extent on CGE, although a small degree of CGE is present in essentially all vertebrates (**See Handout**)

- CGE is trivial in most birds and mammals, accounting for less than 1-2% of total gas exchange, except in bats, which may lose up to 12% of their CO<sub>2</sub> through their wing membranes under certain conditions.
- CGE may account for 50% of O<sub>2</sub> uptake in some fish
- Virtually all amphibians rely on CGE to some extent. Some salamanders (Plethodontidae) lack lungs entirely and depend to a great degree on CGE (supplemented with vascularized mouth regions).
- Some amphibians show specializations that increase the S.A. of the skin for gas exchange (**See Handout**).
  - a) extra skin folds (e.g., Lake Titicaca frog)
  - b) vascularized skin papillae (African hairy frog)
- Relative importance of skin and lungs for respiration changes with temperature. Skin is more important at low temperatures, lungs at high temperatures → results in seasonal differences in the relative importance of respiratory structures. (**See Handout**).



**OXYGEN TRANSPORT**

- Circulatory System functions to deliver oxygen from respiratory surface to tissues. Efficiency of circulatory system determined by:
  - a) Blood volume flowing by tissues (heart rate, stroke volume, capillarity, diameter and elasticity of vessels)
  - b) Oxygen concentration in blood
  - c) Ability of tissues to obtain oxygen (tissues from blood, blood from air in lung)

**How is oxygen carried in the blood?**

In many inverts. Carried as dissolved oxygen in plasma.

In more active inverts. and in vertebrates dissolved oxygen insufficient, so blood contains *respiratory pigments*.

**Oxygen Carrying Capacity**

- Mammals 14-30 vol%

- Birds 10-20 vol%
- Herps. 6-12 vol%
- Fish 0.8-20 vol%

\*The lowest value for fish is from the Antarctic Icefish which has no respiratory pigments and no red blood cells. The loss of resp. pigment is an adaptation in this fish that lives in cold, well-oxygenated waters. This fish also has a *low metabolic rate* (and activity levels, MR = ¼ to ½ of allometric predictions) and *enormous gill surface area*, so oxygen dissolved in plasma is sufficient to meet its metabolic demands.

### ***Types of Respiratory Pigments***

- 1) Hemoglobin (Hb) = iron porphyrin (“heme”) + globin (protein). Vertebrate hemoglobins have 4 subunits (each with heme + globin) except for cyclostomes which have only 1 subunit. Invertebrate hemoglobins with 1 to >250 subunits.
  - Occurs in at least 10 animal phyla (see Table).
- 2) Chlorocruorins = greenish Hb, minor differences in porphyrin, otherwise identical to Hb; occurs in polychaete worms
- 3) Hemerythrins = another iron-containing protein, nonporphyrin structure; occurs in Sipunculid worms, Priapulids, some polychaetes, at least one brachiopod (clam-like bivalves).
- 4) Hemocyanins = copper-containing protein; occurs widely in inverts. including molluscs and crustaceans.

### **OXYGEN DISSOCIATION CURVES (Hb)**

- A) Number of oxygen binding sites is determined by number of subunits in resp. pigment molecule. Each subunit with 1 binding site. Hemoglobin with 4 subunits, myoglobin = a form of Hb found in muscle cells containing only one subunit.
- B) Mb (and cyclostome Hb) are monomers and show *hyperbolic* dissociation curves (a.k.a. oxygen equilibrium curves); In Hb polymer, the binding of oxygen at one site facilitates the binding of oxygen at other sites (= *cooperativity*); results in a *sigmoid* curve (see Handout). The sigmoid response results from cooperativity and allows Hb to efficiently load or unload oxygen as conditions dictate (see Handout).
- C) Oxygen Affinity = degree to which Hb and oxygen are attracted. A high affinity Hb has a dissociation curve further to the left than a low affinity Hb. Species differences in Hb-oxygen affinity result from differences in amino acid sequence of globin molecules. A convenient measure of oxygen affinity is  $P_{50}$  = partial pressure of oxygen at which one-half of the heme groups have bound oxygen (see Handout).
- D) Effectors of Oxygen Affinity
  - 1) *Temperature* – binding of oxygen to Hb (by weak reversible chemical bonds) is an exothermic reaction; thus an increase in temperature weakens these bonds and favors dissociation of oxygen; an increase in temp. shifts the curve to the right.
  - 2) *pH* – decreased pH shifts curve to the right
  - 3) *CO<sub>2</sub>* – increased CO<sub>2</sub> shifts curve to the right; effects oxygen affinity directly by binding to Hb and altering conformation and indirectly by decreasing pH ( $\text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}^+ + \text{HCO}_3^-$ ). (See Handout).  
*Bohr Effect* = rightward shift resulting from decreased pH (or increased carbon dioxide);  
 Bohr Coefficient ( $\theta$ ) =  $\Delta \log P_{50} / \Delta \text{pH}$ ; Magnitude of Bohr Effect increases with

increasing Hb concentration, increasing temperature, and/or increasing ionic strength of plasma.

*Root Effect* = extreme rightward shift resulting from increased carbon dioxide or decreased pH; results in incomplete saturation at high pO<sub>2</sub>. Appears to be an exaggerated Bohr effect; occurs in teleosts and some herps. Plays an important role in secretion of oxygen into swim bladder in teleosts.

- 4) Organic Phosphates and Other Modulators – Organophosphate compounds and inorganic ions inside RBC bind to Hb to modify conformation of oxygen affinity. Generally increased conc. of modulator causes a rightward shift.
- Modulators vary among vertebrates: (see Handout)
    - Fish = ATP, GTP, inositol pentaphosphate (IPP)
    - Amphibs. = ATP, 2,3-diphosphoglycerate (DPG – from glycolysis), small amounts of GTP
    - Reptiles = ATP, small amts. of GTP; *Crocodyles* – only HCO<sub>3</sub><sup>-</sup>
    - Birds = DPG (embryo), IPP (adults)
    - Mammals = DPG
  - For evolutionary scenario of organic phosphate modulation see Handout.

## ADAPTATION OF OXYGEN TRANSPORT

Altitude – Increased elevation results in decreased partial pressure of oxygen.

- 1) *Long-term Adaptation*
  - a) High altitude species often have higher oxygen affinity (decreased P<sub>50</sub>) relative to low altitude species. Increased oxygen loading at lungs, but decreased unloading at tissues. Results in a net increase in oxygen delivery.
    - (i) Deer Mouse – decreased P<sub>50</sub> at high altitude due to decreased DPG in RBC. (See Handout)
    - (ii) Bar-headed Goose – lower P<sub>50</sub> than close relatives from moderate altitudes
    - (iii) Lake Titicaca Frog – low P<sub>50</sub> and high hematocrit relative to other anurans
  - b) High altitude species often show increased hematocrit and hemoglobin conc. which increases oxygen carrying capacity (O<sub>2</sub>Cap).
    - (i) Humans – native to altitude show 5-15% increase in hematocrit, 10-20% increase in hemoglobin conc.
    - (ii) Some lizards also show increased hematocrit and hemoglobin conc. at moderately high altitudes.
- 2) *Short-term Adaptation*
  - a) increased blood oxygen carrying capacity (increased erythropoiesis) – takes weeks for full expression
  - b) Change in blood oxygen affinity – immediately see slight increase in affinity due to respiratory alkalosis, followed within hours by increased DPG which gives net rise in P<sub>50</sub>.

## B. Body Size

- 1) Oxygen affinity of whole blood is positively correlated with body mass (P<sub>50</sub> negatively correlated) in mammals and birds, at least on an interspecific basis.
- 2) Lower affinity Hb in small mammals and birds facilitates oxygen unloading at tissues and helps meet high metabolic demands of small endotherms.
- 3) Many deviations to this general trend exist.
  - a) High altitude animals tend to have relatively high oxygen affinity

- b) Burrowing animals also tend to have relatively high oxygen affinity as an adaptation to potential low oxygen levels in burrows.
- 4) Reptiles generally show similar scaling relationships to endotherms; intraspecific comparisons in many vertebrates show varying results – positive and/or negative relationships have been documented.
- 5) Interspecific scaling effects apparently are due to variations in intraerythrocytic organic phosphate concentrations, as stripped Hb solutions do not show a similar correlation.

### C. Diving

1. No adjustment of oxygen affinity
2. No clear relationship between diving and  $P_{50}$  or diving and magnitude of Bohr effect.
3. Metabolic support of diving:
  - a) Short Dives - primarily aerobically supported
  - b) Long Dives - primarily anaerobically supported and often accompanied by a reduction in total metabolism (**See Overhead**).
4. Primary Oxygen Stores during Dive:
  - a) In lungs - high affinity Hb advantageous, enhanced Bohr effect disadvantageous
    - (i) If carry large amount of air in lungs, then diving to depths (increased pressure) increases dissolved gases (principally  $N_2$ ) in blood, which upon resurfacing will come out of solution causing bubbles in the blood = bends.
    - (ii) Diving mammals and birds carry little air in lungs and may even exhale prior to diving. Reliance on oxygen in lungs during diving *is* practiced by some herps., but these don't dive to great depths.
  - b) In blood and tissues - high affinity Hb disadvantageous, enhanced Bohr effect advantageous.
    - (i) Most work has been done on whales and seals.
    - (ii) Generally higher oxygen carrying capacity in divers than in terrestrial species, but there is a limit to increasing Hct and [Hb] as blood becomes too viscous. So, also get an increase in blood volume in divers.
    - (iii) Divers also have higher myoglobin levels in muscles than non-divers so oxygen stored in tissues is higher.
    - (iv) End Result = higher total blood and tissue oxygen stores in divers than in non-divers (e.g., seal with about double the  $O_2$  stores of a human of equal mass).

D. Development - proceeds in a specialized microenvironment that is potentially hypoxic (e.g., outer layers of egg present significant diffusion barrier, uterine environment in mammals less well oxygenated than maternal tissues).

1. Fish - Many show decrease affinity and decreased temperature sensitivity as development proceeds. **SEE OVERHEAD.**

2. Amphibians - Decreased oxygen affinity and increased sensitivity to acid on metamorphosis from tadpole to adult. Changes due to replacement of larval Hb with adult Hb having a lower oxygen affinity. High affinity and low Bohr effect are adaptive in stagnant ponds (low O<sub>2</sub> and potentially high CO<sub>2</sub>) where tadpoles live. **SEE HANDOUT.**
3. Reptiles - Decreased O<sub>2</sub> affinity throughout development, apparently involves increased organic phosphate levels within RBC.
4. Birds - Complex pattern of changing oxygen affinity throughout development. Initial increase in affinity leading to a plateau at high affinity, affinity decreases prior to hatching. **SEE HANDOUT.**
  - Changing oxygen affinity related to changing concentrations and types of organic phosphates (ATP early, DPG later in development, IPP in adult), and replacement of embryonic Hb types with adult Hb.
  - Adaptive value of this pattern difficult to determine. Increased O<sub>2</sub> affinity to a certain age may allow increased O<sub>2</sub> extraction from hypoxic env. of egg, decreased affinity just prior to hatching may be related to exposure of embryo to ambient air.
5. Mammals - High oxygen affinity fetal blood, low oxygen affinity adult blood. Allows loading of oxygen from maternal to fetal blood. **SEE HANDOUT.**
  - Differences in affinity associated with:
    - a) Different types of Hb
      - (i) Ruminants show fetal Hb with intrinsically lower P<sub>50</sub>.
      - (ii) Primates have fetal Hb that is less responsive to DPG, and therefore has a higher affinity.
    - b) No structural difference, but increased levels of DPG in adults (dog, horse, mouse, opossum, etc.).

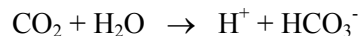
## CO<sub>2</sub> TRANSPORT IN BLOOD

I. Carried largely in chemical combination rather than as free dissolved CO<sub>2</sub> (although CO<sub>2</sub> much more soluble in aqueous solutions than oxygen).

A. Bicarbonate Ions - 80 to 90% of CO<sub>2</sub> in venous blood.



1. The vast majority of CO<sub>2</sub> from tissues diffuses through plasma into RBC.
2. Carbonic Anhydrase in RBC catalyzes conversions of:



- So that reaction proceeds rapidly to the right (rapid conversion impt. so that Bohr effect can enhance tissue unloading).
- 3. Build up of bicarbonate ions within RBC causes diffusion of bicarbonate ions into plasma; Chloride ions diffuse in from plasma to balance charges = Chloride Shift.
- 4. Most CO<sub>2</sub> in the plasma is also carried as bicarbonate ions, but conversion is much slower.

B. Combined with Hemoglobin - CO<sub>2</sub> binds to terminal amino groups on globin molecules, not to oxygen binding site. **SEE HANDOUT FOR REVIEW.**

- End Result is that the amount of CO<sub>2</sub> carried in the blood is greatly increased over the amount

- of CO<sub>2</sub> dissolved in water at normal partial pressures (40-45 torr for mammals).
- CO<sub>2</sub> Dissociation Curves = total CO<sub>2</sub> concentration in blood relative to pCO<sub>2</sub>; oxy- and deoxy hemoglobin differ slightly since oxyHb is a slightly stronger acid and therefore binds less CO<sub>2</sub> (Haldane Effect = decreased CO<sub>2</sub> affinity as oxygen saturation increases).
- Release of CO<sub>2</sub> into air or water is essentially a reversal of the process at the tissues.

**SEE HANDOUTS FOR CO<sub>2</sub> DISSOCIATION CURVES.**

II. CO<sub>2</sub> RELEASE (from blood to respiratory medium)

1. Assume RQ = 1.0 (O<sub>2</sub> taken in = CO<sub>2</sub> released).

2. Air

150 torr O <sub>2</sub> → 100 torr O <sub>2</sub>	
Inspire	Expire
0.2 torr CO <sub>2</sub> → 50.2 torr CO <sub>2</sub>	

3. Water

150 torr O <sub>2</sub> → 100 torr O <sub>2</sub>	
Inspire	Expire
0.2 torr CO <sub>2</sub> → 3 torr CO <sub>2</sub>	

- Difference in CO<sub>2</sub> concentration on expiration is due to high solubility of CO<sub>2</sub> in water.

4. Therefore, it is much easier to dump CO<sub>2</sub> to environment for water-breathers than it is for air-breathers because the gradient is much steeper. **SEE HANDOUT.**

5. Aquatic organisms also capable of actively eliminating HCO<sub>3</sub><sup>-</sup> through gill epithelium. **SEE HANDOUT.**

6. Since aquatic organisms can more easily eliminate CO<sub>2</sub>, they tend to have much lower blood pCO<sub>2</sub> than terrestrial vertebrates (therefore blood buffering capacity lower and they are more sensitive to changes in pCO<sub>2</sub>).

III. BLOOD BUFFERS

1. Protons produced during the formation of bicarbonate ions as well as lactate produced during activity must be buffered to prevent large changes in blood pH.

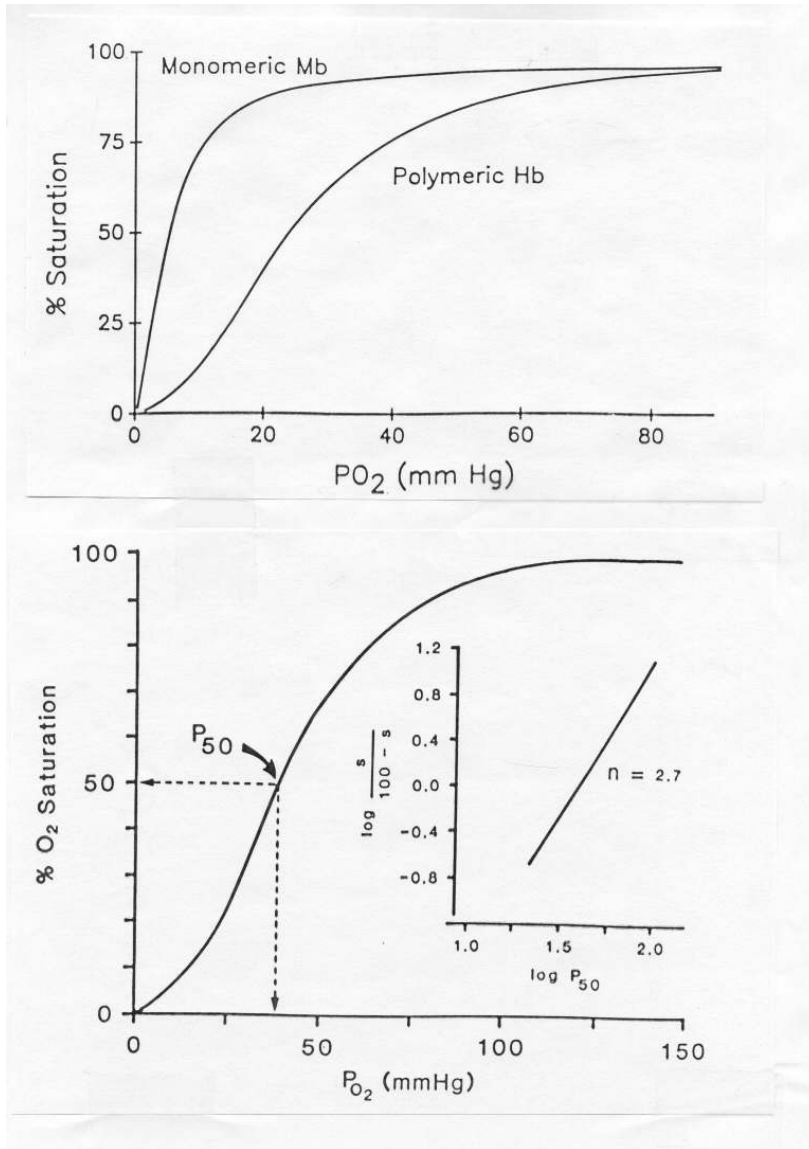
2. The major buffering substances in the blood (require negatively charged groups to accept protons) are:

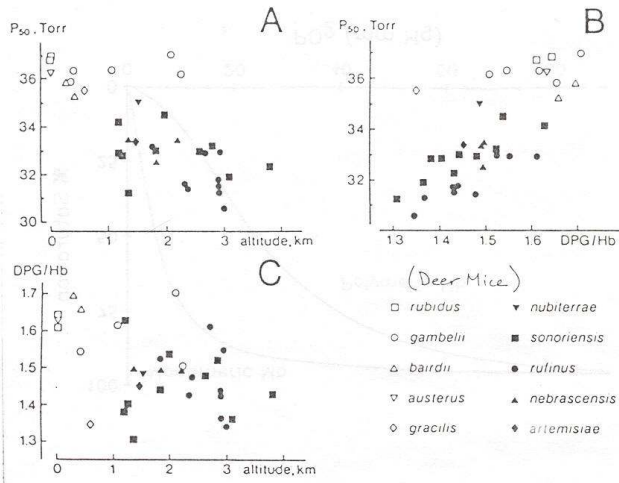
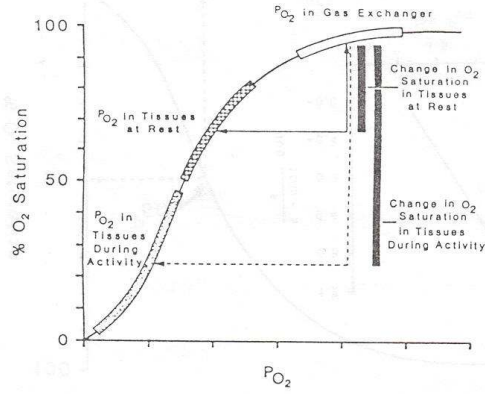
- a) Carbonic Acid - Bicarbonate System - (H<sup>+</sup> + HCO<sub>3</sub><sup>-</sup>)
- b) Blood Proteins - Hb, plasma proteins
- c) Phosphates - modifiers of oxygen affinity

3. Active animals have increased blood buffering capacities relative to sluggish animals. This relationship is true both within and among vertebrate Classes.

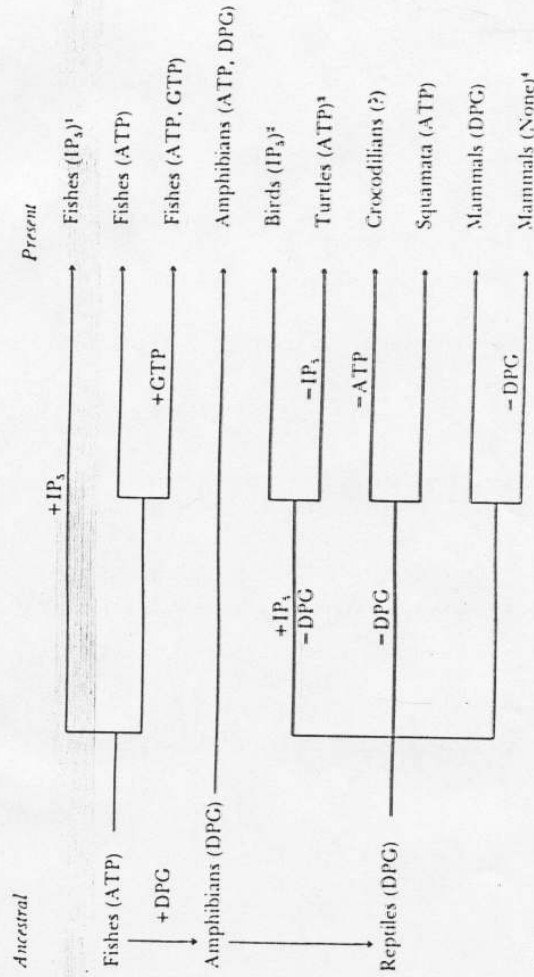
4. Fish that deal with hypoxia regularly often show increased blood buffering capacities relative to normoxic fishes.

CO<sub>2</sub> has less effect on elevating lethal pO<sub>2</sub> in fishes which inhabit warm, sometimes stagnant water.

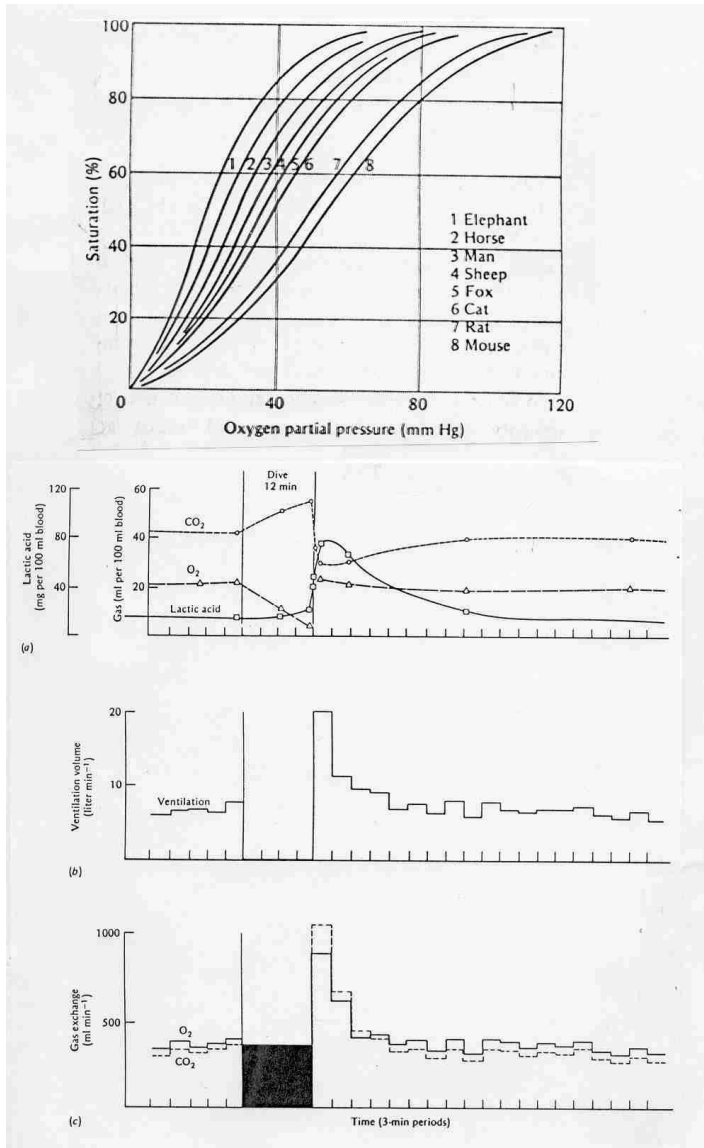


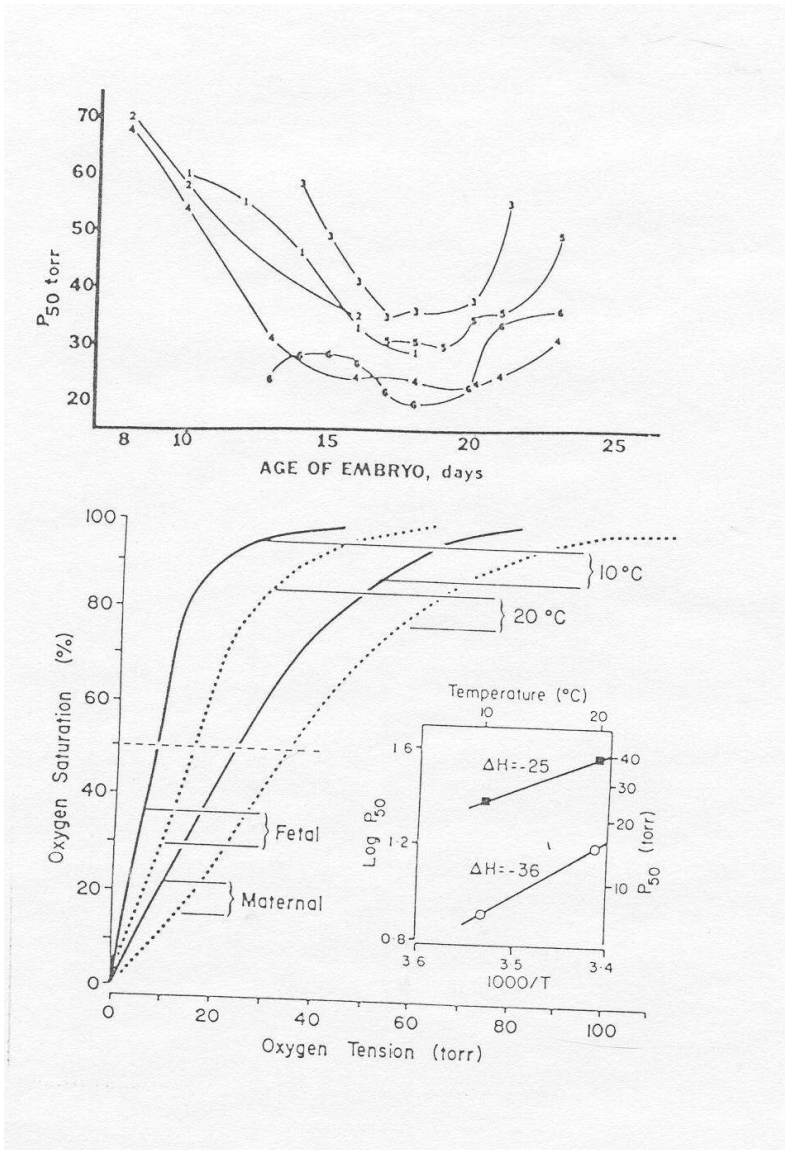


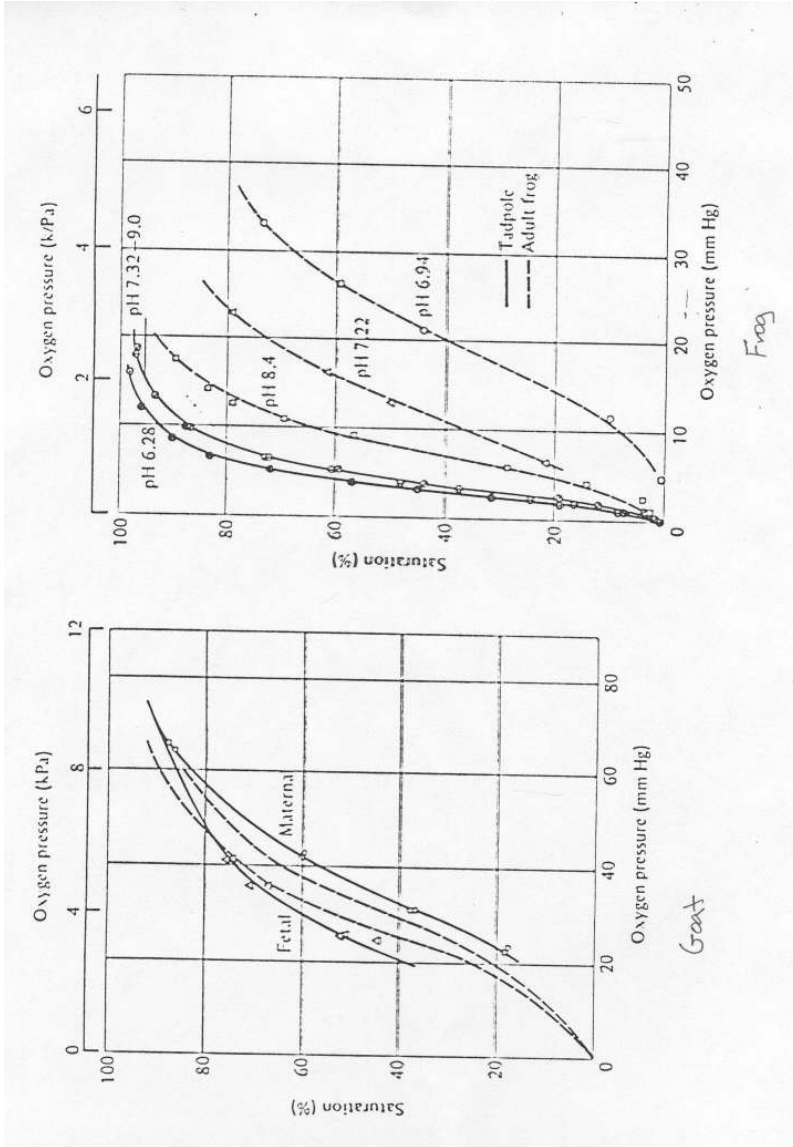
Summary; possible evolutionary lines



(P). Possible regulator: +P. First appearance of regulator: -P. Regulator disappearing: <sup>1</sup> *Araucaria rigida*; <sup>2</sup> DPG high in embryo, absent in adult; <sup>3</sup> DPG high in embryo, low to absent in adult; IP<sub>3</sub> low in adult; <sup>4</sup> Cats and ruminants, low affinity Hb.







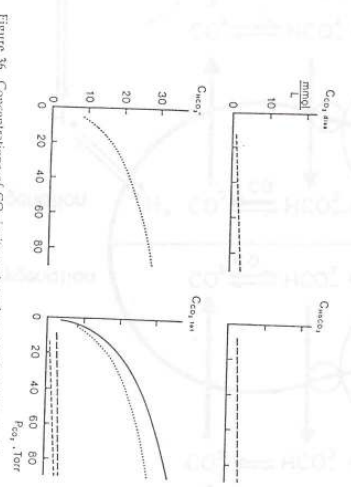
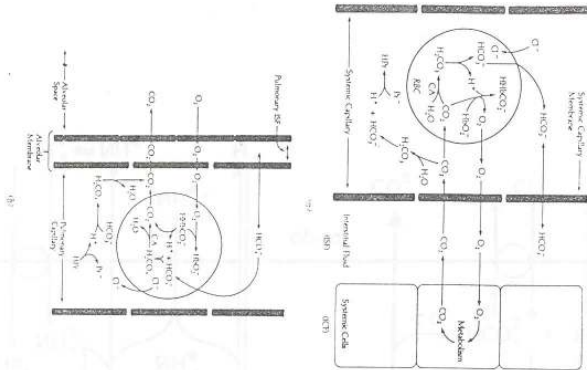


Figure 36. Concentrations of  $\text{CO}_2$  in its various forms in deoxygenated human whole blood ( $38^\circ\text{C}$ ) as function of  $P_{\text{CO}_2}$ . Upper left: dissolved  $\text{CO}_2$  (solubility coefficient =  $0.029 \text{ mmol/L} \cdot \text{mmHg}$ ). Upper right: carbamino compound. Lower left:  $\text{HCO}_3^-$  in whole blood. Lower right: total  $\text{CO}_2$  concentration of whole blood, depicted by solid line. (The line depicting  $\text{CO}_2$  dissolved in solution appears lower in apparent slope to Fig. 37. This results simply from the fact that, because the great majority of  $\text{CO}_2$  is carried in forms other than as molecular  $\text{CO}_2$ , the scale for  $\text{CO}_2$  in Fig. 37 covers a considerably greater range.) [From (48)]

