37.1

INTRACELLULAR AND EXTRACELLULAR ACID-BASE REGULATION IN ANIMALS: AN OVERVIEW. James N. Cameron. Univ. of Texas, Marine Science Institute, Port Aransas, TX 78373

An argument can be made for pH as a master control in biological systems. A majority of metabolic reactions both influence and are affected by pH, setting the stage for a complex feedback regulation system whose objective is maintaining constant protein charge ("Z-stat model"). The principal determinants of extracellular pH are H^+ influx from metabolism and H^+ efflux either directly via ionic exchange or indirectly via changes in CO_2 excretion. This general relation is true for all animals, though the organs and pathways for both ion movement and gas exchange differ. In aquatic animals CO_2 is excreted to water via gills or skin, but since the dominant problem in water is obtaining oxygen, CO_2 excretion is not closely regulated. Ion exchanges dominate extracellular pH regulation, with gills playing a primary role and kidneys a minor one. In terrestrial vertebrates, both lungs and kidneys have major roles in extracellular pH regulation, with a complex partitioning of responses either temporally or according to the type of acid-base challenge. The primary determinants of intracellular pH are metabolic H^+ generation and the counterbalancing ion exchanges carried out by membrane proteins. Several models are currently advanced, including a Na^+/H^+ antiporter, Na-dependent Cl^-/HCO_3^- exchange, $Na+/-HCO_3^-$ cotransport, and Na^+/monocarboxylate exchange. The similarities between animals as diverse as squid and man suggest that pHi regulating mechanisms are old and strongly conserved.

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37.2

ACID-BASE REGULATION IN TERRESTRIAL MOLLUSCS. M. Christopher Barnhart. University of San Diego, San Diego, CA 92111

The control of pH via ventilatory control of PCO_2 evolved convergently in at least 3 groups of land animals: vertebrates, decapod crustaceans, and pulmonate snails. In active snails, Otala lactea, diffusion in the gas phase presents only about 25% of total resistance to O_2 uptake but accounts for nearly 97% of resistance to CO_2 release via the lung. Thus, CO_2 release is much more ventilation-sensitive than is O_2 uptake. Changes in lung and hemolymph gas tensions demonstrate control of pH via PCO_2 during temperature change and in compensation for metabolic acidosis. In contrast to active periods, periods of dormancy are accompanied by hypoventilation, acidosis and fluctuations of pH due to accumulation and episodic release of respiratory CO_2. During dormancy, lung ventilation becomes limiting for O_2 uptake and sensitive primarily to PO_2. The precise ventilatory control of PCO_2 and pH is abandoned. Measurements using DMO indicate that CO_2 affects intracellular and extracellular pH similarly in most tissues. Effects of CO_2 on oxygen consumption of intact snails are consistent with a role in metabolic regulation during dormancy. However, the mechanism of influence on cellular metabolism is unknown and may be indirect. Unlike the respiration of whole animals, that of isolated cells and tissues of Otala incubated in physiological saline is relatively insensitive to PCO_2.

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2.

3.

37.3

EXTRACELLULAR AND INTRACELLULAR ACID-BASE REGULATION IN CRUSTACEANS. Michele G. Wheatly. Univ. of Florida, Gainesville, FL 32611

The crustacean subphylum encompasses water and air-breathing species; differences in acid-base status and regulation are related to gas properties of the media. Body fluid compartments include intracellular (IC), extracellular (EC, possibly subcompartmented) and external (for aquatic and semi-terrestrial species). pH is determined by total buffer, PCO_2 and strong ion difference (SID). IC pH, (pHi, typically 0.5 pH units below EC), plays a pivotal role in regulating cell metabolism. Regulation of pHi (via buffering, metabolism or passive inorganic electroneutral ion exchange, 1) will be illustrated during exercise, temperature change, hyperoxia and aerial exposure (aquatic species) and hypercapnia (terrestrial). The ECF is the intermediary between cells and external exchangers. pHe homeostasis also preserves the function of EC respiratory proteins. Regulation of EC acid-base disturbances (2) generated endogenously (exercise, molting) and exogenously (changes in external gas tensions, ionic composition, temperature, pH or combinations thereof) will be discussed in terms of (a)buffering by ECF and mineralized tissues (b) regulation of SID at gills and antennal gland (predominantly water breathers) and (c) ventilatory control of PCO_2 (air breathers). Evidence will be presented for bidirectional exchange of ions with the external medium at the gill and unidirectional efflux via the kidney. Finally an integrated approach to whole animal acid-base balance (3) will be illustrated in aquatic crustaceans under the following experimental conditions: hyperoxia, external dilution, exercise and aerial exposure. (Supported by NSF 89-16412).

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37.4

RELATIONSHIPS BETWEEN ION AND ACID-BASE REGULATION IN FISH.

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Na^+/"acid" and Cl^-/"base" exchanges on the gills of freshwater fish are dynamically manipulated so as to correct internal acid-base disturbances, in accord with electroneutrality and SID relationships. In trout, both influx and efflux components of strong ion movements are adjusted. Kinetic analyses demonstrate that the affinities (Km) of the Na^+ and Cl^- influx mechanisms are normally maximal, and can only be decreased, but maximum capacities (Jmax) can be either increased or decreased for the purposes of acid-base correction. Changes in Jmax can be explained partially by changes in the internal availability of "acid" and "base" counterions, and partially by morphological adjustments of the gill epithelium. The branchial "chloride cell" appears to be an important site of Cl^-/"base" exchange. In catfish, reduced Cl^-/"base" exchange during compensation of hypercapnic acidosis is paralleled by a reduction in the surface area of filamental chloride cells. This phenomenon is apparently caused by a covering by adjacent "pavement cells". In addition, the pavement cells exhibit an increase of apical microvilli density and proliferation of mitochondria. We suggest the pavement cell response may contribute to elevated Na^+/"acid" exchange at this time. (Supported by NSERC grants to CMW and SFP).

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37.6

INTRACELLULAR pH REGULATION BY HEPATIC TISSUES.

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Because of its structural complexity and metabolic diversity, liver was not the tissue of choice in initial experiments on the ionic mechanisms of pHi regulation. However, as our basic understanding of pHi regulation for ostensibly simpler tissues grew, much more research focused on acid-base regulation in hepatic tissue from mammals, fish and crustaceans. This review examines three aspects of acid-base regulation in hepatic tissues from a comparative viewpoint: (1) ionic transport mechanisms (e.g., Na^+/H^+ exchange, lactate transport, bile acid transport, etc.); (2) the role of physicochemical buffering; and (3) the complex interplay between metabolism and acid-base regulation. We pay particular attention to recent studies which demonstrate marked transport and metabolic heterogeneity within and between hepatocytes, and to the potential of hepatocytes in long-term culture to serve as models for adaptations to chronic acid-base disturbances.

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37.7

REGULATION OF ACID-BASE STATUS IN HUMANS DURING EXERCISE.

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During and shortly after heavy exercise intramuscular $[H^+]$ may exceed 300 nEq/l (pH less than 6.5). The response to this acid challenge involves the movement of water, strong ions and CO_2 between a number of body fluid compartments and tissues. The main contributors to the increase in $[H^+]$ in the active muscle are reductions in [SID] of up to 35 mEq/l (net effect of a >45 mEq/l increase in $[La^-]$, >20 mEq/l reduction in $[K^+]$ and 30 mEq/l reduction in $[CrP^{--}]$), and increased PCO_2 to >100 mmHg, together with a 7% increase in muscle water. In venous blood draining the active muscle, large increases in $[La^-]$ and $[K^+]$ are found in plasma and RBC, PCO_2 increases and plasma water falls by 15%, tending to increase [Atot]. CO_2 is rapidly excreted in the lungs; thus in arterial plasma, reductions of 10 mEq/l in [SID], secondary to increases in $[La^-]$, are counteracted by reductions in PCO_2. Erythrocytes in venous and arterial blood take up La^-, but $[La^-]$ increases to only half the plasma $[La^-]$; K^+ is also taken up in RBC. Inactive tissues take up K^+ and also take up and metabolize La^-, at the expense of an increase in CO_2 production. Studies in isolated muscle and intact animals during exercise indicate important roles for osmolar factors together with active and passive membrane ion transport, in addition to local fuel utilisation, circulation and ventilation, in the overall response of the organism to an acute acid-base challenge.

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