Immune Response

Uses of hyperbaric oxygen therapy.

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Hyperbaric oxygen can produce a variety of effects in addition to reducing air and gas embolism. It increases the killing ability of leukocytes and is lethal to certain anaerobic bacteria. It inhibits toxin formation by certain anaerobes, increases the flexibility of red cells, reduces tissue edema, preserves intracellular adenosine triphosphate and maintains tissue oxygenation in the absence of hemoglobin. In addition, it stimulates fibroblast growth, increases collagen formation, promotes more rapid growth of capillaries, and terminates lipid peroxidation. These actions of hyperbaric oxygen are useful in treating anaerobic infections that result in gas gangrene, as well as severe aerobic infections such as necrotizing fasciitis, malignant external otitis, and chronic refractory osteomyelitis. Hyperbaric oxygen can help preserve ischemic tissues and facilitates the rapid spread and arborization of new capillaries. It promotes healing in certain problem wounds. Adjunctive hyperbaric oxygen treatment is a new approach to the management of radionecrosis. Hyperbaric oxygen treatment reduces morbidity and mortality resulting from carbon monoxide poisoning. Protocols for hyperbaric oxygen therapy are at present mostly empirical; much additional research is needed to better define therapeutic indications.

Oxygen tensions and infections: modulation of microbial growth, activity of antimicrobial agents, and immunologic responses.

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Oxygen tensions play an important role in the outcome of infections. Oxygen is cidal or static for microorganisms that lack defenses against oxidants. Hyperoxia and hyperbaric oxygen exert antimicrobial effects by increasing the intracellular flux of reactive oxygen species. In bacteria, such species cause DNA strand breaks, degradation of RNA, inhibition of amino acid biosynthesis, and inactivation of membrane transport proteins. Oxygen tensions also affect the activity of antimicrobial agents. In general, hyperoxia potentiates while anaerobiosis decreases the activity of many antimicrobial drugs. With regard to host defenses, hyperoxia elevates oxygen tensions in infected tissues to levels that facilitate oxygen-dependent killing by leukocytes. Prolonged hyperoxia inhibits DNA synthesis in lymphocytes and impairs chemotactic activity, adherence, phagocytic capacity, and generation of the oxidative burst in polymorphonuclear leukocytes and macrophages.

Immunomodulatory effect of oxygen and pressure.

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The immunomodulatory effect of hyperbaric oxygen, involving altered cytokine release by macrophages, is well described. Importantly, however, it is not known what the relative contribution is of the hyperbaric environment of the cells vs. increased oxygen tension on these hyperbaric oxygen-dependent effects. We compared, therefore, cytokine release by murine macrophages under hyperbaric oxygen, hyperpressure of normal air and normobaric conditions. We observed that hyperbaric oxygen enhanced cytokine release of both unstimulated as well as lipopolysaccharide (LPS)-challenged macrophages. Hyperpressure of normal air, however, enhanced LPS-induced cytokine production but did not elicit cytokine release in unstimulated macrophages. To further investigate the molecular details underlying the effects of hyperbaric oxygen, we investigated the effect of the p42/p44 mitogen-activated protein (MAP) kinase inhibitor PD98059 and the p38 MAP kinase inhibitor SB203580. Neither inhibitor, however, had a significant effect on the modulatory effects of hyperbaric oxygen on cytokine release. We concluded that the immunomodulatory effect of hyperbaric

oxygen contains a component for which hyperpressure is sufficient and a component that apart from hyperpressure also requires hyperoxygenation.

Iron and infection: the heart of the matter.

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Bacterial resistance to antibiotics is a major threat to clinical medicine. However, natural resistance to bacterial infection, which does not depend on antibiotics, is a powerful protective mechanism common to all mankind. The availability of iron is the heart of the matter and the successful functioning of these antibacterial systems depends entirely upon an extremely low level of free ionic iron (10(-18) M) in normal tissue fluids. This in turn depends on well-oxygenated tissues where the oxidation-reduction potential (Eh) and pH control the binding of iron by unsaturated transferrin and lactoferrin. Bacterial virulence is greatly enhanced by freely available iron, such as that in fully-saturated transferrin or free haemoglobin. Following trauma a fall in tissue Eh and pH due to ischaemia, plus the reducing powers of bacteria, can make iron in transferrin freely available and abolish the bactericidal properties of tissue fluids with disastrous results for the host. Hyperbaric oxygen is a possible therapeutic measure that could restore normal bactericidal systems in infected tissues by raising the Eh and pH.