BY-PRODUCTS OF DISINFECTION OF WATER AND POTENTIAL MECHANISMS OF OCULAR AND OTHER ORGAN INJURY AND HEMOSIDEROSIS IN MARINE MAMMALS

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Abstract

Several disease processes are seen commonly in aged sea lions (*Zalophus californianus*) and harbor seals (*Phoca vitulina)*. Cataracts, corneal disease, non-infectious kidney disease with interstitial nephritis and amyloid, carcinomas of the genitourinary system and severe hemosiderosis are more common than expected in my experience. Incidence of cataracts of 80% and measured liver irons of 9700 ppm and 14,000 ppm (Normal 480-1600ppm) are examples. My hypothesis is that these processes can at least partially be explained by the effects of oxidant disinfectants and by-products of disinfection produced when they are used. I discussed the potential effects on the eye in an abstract for the 2009 IAAAM conference.

Oxidizing agents including chlorine, ozone, and bromine are commonly used as disinfectants to maintain clarity, and reduce microscopic organisms in life support systems for marine mammals. These compounds can cause injury by themselves if in too high a concentration. Interaction of these agents with compounds dissolved in the water produces by-products of disinfection. The compounds produced are not commonly measured and cannot all be measured with the same techniques so their concentration and identification are not usually known. Presence of bromine in incoming water or its use as a disinfectant can significantly change the compounds produced and increase their rate of production.[4] Chlorination or ozonation of water with even a small amount of bromine can produce bromate levels higher than the drinking water limit of 10 ppb especially in sunlit pools.

It has been considered that the risks from these compounds are low and that the advantages of eliminating pathogens far outweighs their dangers but that has not been proven.[8] Hypochlorous acid (HOCl) the active compound in chlorine disinfection is a very important physiological compound. It is produced by activated phagocytes as they react to immune system stimulation.[5] It can kill bacteria in vivo but it also produces chloramines in vivo which can diffuse from the original site and cause changes in surrounding tissues by oxidizing proteins.[10] Hypochlorous acid is produced by myeloperoxidase in vivo. Its production and effects are implicated in a number of non-infectious disease processes including heart disease, kidney disease and some cancers.[5,10]

Some of the by-products of disinfection are volatile and can be absorbed by inhalation or penetration of tissues.[2,9] Safe levels for human drinking water are based on drinking 2 liters of water daily and taking one short shower or bath.[9] Our animals are in or near the water 24 hours a day. Determination of equivalent doses for aquatic animals would require experiment and looking for products of their metabolism because there could be constant uptake by inhalation, absorption or orally while metabolic processes constantly degrade the absorbed compounds. Humans swimming in chlorinated pools have been shown to have measurable levels of

chloroform in their blood.[1] The values were higher for more athletic swimmers suggesting inhalation as a main route of entry. Marine mammals must be considered athletic swimmers. Some of these compounds including chloroform and bromoform are heavier than air and can be in higher concentrations just over the surface where marine mammals inhale.

The simplest compounds of interest include the halogenated methanes including chloroform, bromodichloromethane, dibromochloromethane, and bromoform. These compounds have been shown to be toxic to liver and kidney and the mechanism of toxicity involves initial oxidation by cytochrome p450 enzyme systems.[3,6] This produces reactive oxygen species (ROS) which can oxidize cellular components causing injury. Chloroform produces carbonyl chloride (also known as phosgene gas) and 3 HCl. These resulting compounds may cause the actual cellular injury.

The legion of compounds identified as and suspected to be by-products of disinfection include compounds with the potential to be carcinogenic.[2] Excretion in urine of the compounds or their metabolic products may be implicated in the induction of neoplasia in the genitourinary system.

Oxidative stress produced by any means has been found to stimulate the production and activity of Heme-Oxygenase.[7] It has been found to be stimulated by many different compounds and by physical factors such as heat or ultraviolet light. Its action is to break down heme molecules to biliverdin, free iron and carbon monoxide (CO). Biliverdin is reduced to bilirubin and in low levels the bilirubin may quench ROS and act as an antioxidant similarly to glutathione. Iron is sequestered in ferritin molecules which when produced in abundance may form the hemosiderin found in the livers with high iron. Studies have shown that pre-treatment with ferritin may be protective to cells in tissue culture subjected to oxidative stress. CO at physiologic levels has significant physiologic effects including modulating blood vessel dilation and studies have shown it to be of benefit in ischemia/reperfusion disease models and in ventilator induced lung injury models. Certainly the respiratory and circulatory systems in diving animals could suffer similar stresses. [7]

Heme-oxygenase breaks down heme molecules which are required for cytochrome p450 enzymes, myelopeoxidase, myoglobin and hemoglobin function. It appears that controlling the levels of heme molecules in cells helps to protect against excessive production of ROS. Heme-Oxygenase has a role in returning free iron into circulation for reuse. Over production of heme-oxygenase, differences in the enzyme in diving mammals, or interfering with the return of free iron to the normal regulatory pathways could explain the high levels of sequestered iron in these sea lions.

Measures to reduce injury from oxidant disinfectants and their by-products could include reducing or eliminating oxidant levels in circulating water, measuring bromine levels in source water, not using bromine as a disinfectant, reducing precursors such as total organic carbon and nitrogenous wastes, and improved ventilation. Reducing total organic carbon and nitrogenous wastes requires such means as foam fractionation, biological filtration, flocculation and best of all water changes.

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