THE HEALTH EFFECTS OF CHLORAMINES IN POTABLE WATER SUPPLIES: A LITERATURE REVIEW

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INTRODUCTION

The cholorination of surface water supplies high in organic content (i.e. principally humic acids) has been shown to produce elevated levels of trihalomethanes (THM's) (Bellar et al., 1974: Rook, 1974; Symons et al., 1975) and certain of the THM's such as chloroform have been shown to increase the occurrence of cancers in various animal models (Anon, 1977; Eschenbrenner, 1945; Hill et al, 1975; Kimura et al., 1971). Additionally, epidemiological studies report an increased risk of cancer mortality associated with the practice of chlorinating water (Kuzma et al., 1977; Page et al., 1976; Symons, 1977). Since most major surface supplies in the country are chlorinated and many of them are likely to have elevated THM levels, there is throught to be a potential risk to human health (Anon, 1977; Eschenbrenner, 1945; Kuzma et al., 1977; Symons, 1977). Therefore, the Environmental Protection Agency (EPA) has proposed an interim standard of 100 μg-L for THM's until more evidence can be accumulated on their health effects (EPA, 1978).

According to the EPA this is likely to "cause many water suppliers to turn to alternative disinfectants" (EPA, 1978). In order to restrict the use of alternatives that might be less effective or have undesirable side effects, EPA is proposing restriction on their use including a proposal to prohibit the use of monochloramine as a primary disinfectant (EPA, 1978) since it is reported to be a poor biocide, and in order to obtain a 100 percent kill with the same contact period, it would require nearly 25 times as much chloramine as free chlorine (EPA, 1977-'78); Symons, 1977; Butterfield, 1946). However, chloramine formation may be used to provide a residual in distribution systems once the water is chlorinated (EPA, 1978), and a number of reasons suggest its use may increase:

a. Murphy et al. (1975), reported that the presence of ammonia or amino groups results in chloramine formation and retards reaction of chlorine with soluble organics and other compounds. Chloramine generation also retards trihalomethane formation (EPA, 1978; Murphy et al., 1975).

b. Although chloramines were reported to be a less effective disinfectant than free available chlorine (EPA, 1977-'78). Brodtman and Russo 1979, reported that chloramination when used as a primary disinfectant is an effec-

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tive biocide since when properly applied at effective dosages (1.5 - 1.8 mg-L) chloramine produces 100 percent kills of pathogenic bacteria species and also effectively reduces total bacterial populatons to an acceptable range.

c. An inventory of municipal water supplies conducted in the early 1960's showed 308 of 11,590 water supplies surveyed (including 30 of the 100 largest cities in the U.S.) were using an ammonia chlorine process. Chloramine disinfection has been practiced because the persistence of monochloramine provides a residual in the distribution systems whereas a free residual of chlorine could not be maintained (Durfor and Becker, 1962). This practice also reduces unpleasant odors and tastes apparent with chlorine disinfection (Symons, 1977; Brodtmann and Russo, 1979).

For these reasons, it is not unlikely that chloramine disinfection may be on the increase, as has been suggested (Kjellstrand et al., 1974). The primary unresolved question is, what are the health effects of chloramines? This concern was recently reiterated in the Federal Register (EPA, 1978). Certainly more should be known concerning the potential toxicity of chloramines and by-products before chloramine generation becomes adopted as a standard procedure for a majority of community water supplies where THM formation and/or maintenance of chlorine residuals is a problem. This paper presents a review of the literature concerning the health effects of chloramines to serve as a starting point from which further studies may be made.

THE HEALTH EFFECTS OF CHLORAMINES

A. Mutagenicity

It has only been within the previous four years that chlorination of public water supplies was linked to an increased risk of cancer. There are no studies on the carcinogenicity of chloramines and only a single study on its mutagenicity. Shih and Lederberg (1976), using a reversion of trpC to trp^+ in *Bacillus subtilis* showed chloramine to be a weak mutagen. Furthermore, they suggested the involvement of DNA targets since some DNA-repair mutants were more sensitive to chloramine.

B. Effects on Aquatic Life

There have been a number of studies concerning chloramine effects on the health of aquatic life. This was prompted by fish kills resulting from the discharge of chlorinated effluents in streams and rivers. Although these studies cannot be used to directly predict effects on humans, they are useful in showing the toxicity of chloramines over a wide range of species, and physiologic mechanism by which chloramines affect aquatic life.

The effects of inorganic chloramines have been demonstrated on lobsters, (Capuzzo, 1977; Capuzzo et al., 1976) and a variety of fresh and salt water fish at various states of development. The effects measured included median and mean lethal concentrations, increase in dry weight and wet body weight, respiratory rate, avoidance behavior and methemoglobinemia.

In general, the most sensitive stage of fish to chloramine toxicity is the fry stage (yolk-sac within abdominal cavity) with brook trout (*Salvelinus fontinalis*) and with Coho salmon (*Oncorhynchus kisutch)* having 96H-TL50 values to monochloramine concentrations of 82 μg/L (Larson et al., 1977b) and 57 μg-L (Larson *et al.*, 1977b), respectively. Tompkins and Tsai,(1976), demonstrated that 50 percent of black-nosed dace die within three hours at 0.5 mg/L of monochloramine. When subjected to monchloramine, the 96H-TL50 for the amphipod (*Gummarus pseudolimneaus*) was 200 μg/L while all fathead minnows (*Pimephales promelas*) were killed in three days at 154 μg/L (Arthur and Eaton, 1971). Capuzzo et al. (1976), demonstrated the LC50 of larval lobsters (*Homarus americanus*) to monochloramines was 0.56 μg/L. There have been a variety of other studies concerning the effects of chloramines on aquatic life, (Capuzzo et al., 1977; Fava and Tsai, 1976; Grothe and Eaton, 1975; Health, 1977; Johnson et al., 1977; Maziarka et al., 1976) but in general the toxic effects (LD50, LC50) fall within the ranges listed above.

Capuzzo (1977), recently demonstrated that larval lobsters (*Homarus americanus*) exposed to 1.0 mg/L of chloramine exhibited greater reduction in standard respiration rates than larval lobsters exposed to an equivalent amount of free chlorine. Capuzzo postulated that the apparent effect of the chloramine and chlorine on lobster larvae was an interference with energy utilization as evidenced by lesser dry weight increases and decreased metabolic activity as compared to controls. Grothe and Eaton (1975) exposed fathead minnows to water containing 1.5 mg/L of chloramine for approximately one hour and observed methemoglobin concentration of approximately 30% as compared to less than 3% for the control fish. The higher levels produced death of the fish due to anoxia.

The results of these studies on aquatic life indicate the ability of monochloramines to interfere with energy metabolism and produce methemoglobinemia. Similar effects are seen under special conditions in humans exposed to monchloramines.

C. Chloramine Toxicity In Humans and Other Mammals

Eichelsdoerfer et al. (1975) reported that dermal exposure with chloramine (4 mg/L) was more irritating than free chlorine (20 mg/L) to the conjunctiva of rabbits. They postulated that the irritant effect of swimming pool water may be due to the presence of chloronitrogen compounds (as reaction products of CL and N Pollutants) rather than the free chlorine in the water.

The extent of published reports on the health effects of monochloramine on humans is limited to hemolytic crises in dialyzed patients. Hemolytic anemia is frequently a serious problem among patients undergoing long term hemodialysis (Eaton et al., 1973; Jacob et al. 1975; Kjellstrand, 1974; Yawata et al., 1971). Eaton et al., (1973) reported that exposure of human erythrocytes *in vitro* to monochloramines resulted in the formation of methemoglobin and depression of the hexose monophosphate pathway shunt (HMPS) with subsequent reduction in cell survival and ultimate hemolysis. This was later confirmed by Kjellstrand et al., (1974), and Jacob et al.,

(1974), who reported that chloramines shorten human erythropcyte survival *in vivo* and *in vitro* by two mechanisms. Chloramines directly oxidize hemoglobin leading to methemoglobin formation and also induce HMPS damage in red cells and so reduce the cells capacity to protect themselves against oxidant damage (i.e. hemolysis and reduced red cell survival). Methemoglobin levels of 8% were produced in human erythrocytes incubated *in vitro* with 1.0 mg/L of monochloramine[1] and this increased to 55 percent at 7.0 mg/L of monochloramine. Under similar conditions 7.0 mg/L of free chlorine failed to produce increases in methemoglobin (Kjellstrand et al., 1974; Yawata et al., 1971). Unfortunately, no data is available to predict blood levels of monochloramine resulting from the consumption of drinking water containing chloramine, but it is assumed that water would have to contain several orders of magnitude greater amounts of monochloramine to produce levels of 1.0 mg/ml in circulating blood. Until quantitative relationships have been experimentally determined, attempts at risk assessment will have inherent limitations.

Methemoglobinemia, a depressed HMPS activity, shortened erythrocyte survival, and hemolysis were also attributed to monochloramines in tap water used to hemodialyze uremic patients (Eaton et al., 1973; Jacob et al., 1975; Kjellstrand et al., 1974; Yawata et al., 1971). Monochloramines are a potentially widespread cause of erythrocyte destruction in such patients (Eaton et al., 1973; Yawata et al., 1971). Serial observations of several patients undergoing dialysis suggested that the red cell oxidant damage was cumulative over several periods of dialysis (Eaton et al., 1973). Jacob et al., (1975) demonstrated that approximately 75 percent of uremic patients have a circulating plasma factor that is responsible for the inhibition of red cell-metabolism and HMPS activity. In the majority of patients, HMPS activity was low as persons with inherited glucose-6-phosphate dehydrogenase (G-6-PD deficiency) (Jacob et al., 1975).

FUTURE RESEARCH DIRECTION

Studies on aquatic life as well as dialyzed uremic patients indicate that chloramines have the capacity to depress erythrocyte HMPS activity and oxidize hemoglobin to methemoglobin. In uremic patients, a circulating plasma factor reduced G6PD activity of the cell to a level similar to that of persons with the inherited deficiency (Jacob et al., 1975). The exposure of these sensitive cells during dialysis to water containing 3.0 ppm chloramine causes marked methemoglobinemia and hemolysis in such patients (Eaton et al., 1973). These findings suggest that further research should be directed to the question of the potential health effects of chloramines on persons with inherited G6PD deficiency and in those newborns with other deficiencies in red blood cell enzymes.

Individuals with a G6PD deficiency in their blood cells are at increased risk to a variety of oxidant compounds including certain drugs and industrial

[1]Packed cells (0.5 ml) were incubated in 50 ml of isotonic saline containing 0.0 to 7.0 mg/L of monochloramine or chlorine.

compounds because of an impaired HMPS activity (Lehman et al., 1972; Wintrobe et al., 1975). Because approximately 13 percent of the black, male populaton in the United States have a G6PD deficiency (Lehman et al., 1972; Wintrobe et al., 1975), it is important to examine the health effects of chloramine on the populaton before its widespread use is adopted.

Neonates also represent a group that should be studied for the potential health effects of chloramine. Infants and neonates consume about three times as much liquid per pound of body weight as adults (Hansen and Bennett, 1964); form metHb more readily than adults (Comly, 1945; Gruener and Shuval, 1964; Walton, 1951); and have a generally increased sensitivity to hemoglobin oxidizing agents (Emerson, 1972; Gross, 1967; Whaun and Oski, 1970).

It must be realized that exposure to chloramine via dialysis treatment results in much greater blood levels than would be expected in persons exposed to chloramines by ingestion of water. However, persons who are particularly sensitive to oxidative compounds (G6PD deficients, newborns) may experience adverse effects on blood at levels of chloramine far less than the 'normal' population.

Research should be directed to the health effects of chloramines since it is recognized that additional information is required for more quantitative risk assessment (EPA, 1978), and since there are justifiable reasons why its use may increase. Such research activity may help to set standards for allowable levels of chloramine residuals in drinking water. Studies on the health effects of chloramines should incorporate those groups that may be most sensitive to exposure. These groups could include persons with G6PD deficiency and newborns or infants.

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