A REVIEW OF THE INHALATION TOXICITY OF HYDROGEN FLUORIDE

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The purpose of this talk is to review the toxicity of hydrogen fluoride especially as it pertains to health risks from accidental exposures. I presently am chairman of the AIHA's Emergency Response Planning Committee. We are in the process of updating the ERPG document on hydrogen fluoride, so much of the data I am presenting are from the AIHA ERPG documentation.

HF is widely used in the oil industry as a catalyst and in the chemical industry in the synthesis of a variety of fluoropolymers. HF vapor can be produced in fires as a breakdown product of fluorocarbon fire extinguishing agents and in the combustion of fluoropolymers.

Hydrogen fluoride is a strong acid that can etch glass. It is a gas at room temperature and is supplied as a liquefied gas in cylinders, and is also widely used in water solutions. It has a pungent odor and can be detected by smell at concentrations lower than irritating levels. It can cause plant damage at less than 1 ppm, and I believe there have been cases where accidental release clouds could retrospectively be tracked by the damage to surrounding vegetation.

Generally the toxicity of HF is due to its acidic nature and also as a result of toxicity of the fluoride ion. Acidity is of most concern at concentrations above the irritation threshold of about 3 ppm, whereas fluoride ion toxicity is most important at low concentrations and will add to the fluoride body burden incurred from fluoridated water, food, toothpaste etc. Ingested soluble fluoride is quite toxic with the lethal concentration in man reported to be 30 to 60 mg/kg [1].

Liquid solutions of HF can cause severe bums, and lower concentrations can cause deep bums that are not immediately apparent hut penetrate the skin causing to cause hums deep in the tissues.

Based on inhalation lethality data, the guinea pig appears to be the most sensitive species followed by the mouse, rabbit, rat, and monkey. The mode of death in animals appears to be direct toxicity to the lung as evidenced by the presence of pulmonary edema. W. Dalbey [2] conducted simulated emergency 10-min inhalation exposures in rats some of which were cannulated to bypass the nose to simulate mouth breathing. Higher toxicity was produced in the mouth breathing rats presumably because HF was able to penetrate to the deeper areas of the respiratory tract. A comparison of Dalbey's concentrations with previous data shows that the 10-min data followed Haber's rule (C **X** T = K) in that the 10-min lethal concentrations were roughly **6 X** the lethal level seen in 1-hr rat exposures.

The RD50 or median respiratory rate depression in mice is generally a good qualitative indicator of effects of irritants in man. The RD50 for HF has been reported to be 151 pprn [3]. Based on comparisons with other irritants like acrolein and hydrogen chloride, the RD50 may be an intolerable exposure concentration in humans.

There are controlled human HF exposure studies in man, at high concentrations, albeit some of the data are from the 1930s [4]. These human data are the basis for the present ERPG-2 values and necessarily take precedence over even new animal data. It appears that an irritation threshold exists at about 3 ppm where mild irritation of the upper airways and eyes occurs. In prolonged exposure at about 5 ppm, redness of the skin has also resulted. The highest reported concentrations tolerated in controlled exposures were 122 ppm for 1 min.

Moving on to chronic exposure, there has been no evidence of resultant carcinogenicity in populations where water is fluoridated (IARC). The ACGM TLV for HF is 3 ppm, and this value was set to protect against irritation and fluorosis.

The AMA ERPGs consist of three levels for use in emergency planning, and they are 1-hr values. ERPG-I (2 ppm) is based on odor perception and is below the concentration at which mild sensory irritation has been reported (3 ppm).

ERPG-2 (20 ppm) is the most important guideline value set and is the concentration at which mitigating steps should be taken (such as evacuation, sheltering, donning masks). This level should not impede escape or cause irreversible health effects and is based mainly on the human irritation data obtained by Machle [4] and Largent [1]; in addition, it is well below the mouse RD50 of **151** ppm.

ERPG-3 (50 ppm) is based on animal data and is the maximum nonlethal level for nearly all individuals. This means that this level could be lethal to some susceptible people. This value is meant to be used only for emergency planning, action steps in a real emergency should be taken at ERPG-2.

A comparison of the ERPG values for hydrogen chloride, hydrogen fluoride, and sulfur dioxide shows that the values are quite similar for HCl and HF, but that the values for sulfur dioxide are quite a bit lower. Exercising asthmatics are very susceptible to the effects of sulfur dioxide, and these values take this population into consideration. If there were ERPG values for carbonyl fluoride, these would be lower still.

The ERP Committee has special 10-min ERPG HF values under consideration at the request of some HF producers. Since the exposure time is much shorter than the standard 1-hr values, the proposed values are higher (but not 6 X as high), because of the uncertainty associated with extrapolation to shorter times. These 10-min values could be used in emergency planning in fires where HF vapor is generated.

The above ERPG values can be used in conjunction with atmospheric modeling to predict effects of an HF release in a plant or community. A critical point to remember is that actions need to be taken at ERPG-2 because above this value injuries will likely occur in the exposed population.

REFERENCES

1. Largent, E.J., *Fluorosis - **The Health Aspects of Fluorine Compounds,*** Columbus, OH. Ohio State University Press, 1961.
2. Dalbey, W.E., (personal communication to the AMA ERP Committee), August 1996, Mobile Corporation.

3. Hext, P.M., ***Hydrogen Fluoride: Assessment of Sensory Irritation Potential in*** *Mice*, November 11, 1996 (personal communication to the AMA ERP Committee) ICI Central Toxicology Laboratory, Alderley Park, Cheshire, United Kingdom.
4. Machle, W., Thamann, F., Kitzmiller, K., and Cholak, J., "The Effects of the Inhalation of Hydrogen Fluoride," ***J. Ind. Hyg. Toxicol.*** 16(2):129-145 (1934).
5. Hodge, H.C., and Smith F.A., "Occupational Fluoride Exposure," ***J. Occ. Med.*** 19(1):12-39 (1977).

CHEMICAL STRUCTURE	H - F
DESCRIPTION	- Gas at atmospheric conditions - Liquid in cylinders under pressure - Solutions in water
CHEMISTRY	Strong Acid, Etches Glass
MOLECULAR WEIGHT	20
BOILING POINT	19.4°C
ODOR	Pungent Odor Odor Threshold 0.04 to 0.13 ppm
DENSITY	1.015 g/ml @ 0 °C
SOLUBILITY	Soluble in Water
ENVIRONMENTAL EFFECTS	Causes Foliar Damage to Plants at < 1 PPM in Atmosphere

HF EXPOSURE

Industrial Workers
- Aluminum Smelting
- Accidental HF Releases
- Pyrolysis of Fluoropolymers and Fluorochemicals
  Hot Wire Cutting

Firefighters
- Pyrolysis of Fluoropolymers
- Breakdown of Extinguishants

Military
- Breakdown of Extinguishants in 'Combatand Accidents

GENERAL TOXICITY

Two Toxicity Factors
- Strong Acidity
- Fluoride

Oral: Toxicity of Fluoride
Lethal Dose in Animals (based on sodium fluoride) = 20 to 100 mg/kg

Dermal and Eye:
Liquid solutions cause severe burns
Penetrates skin causing deep burns
Treatment: Inject Calcium Gluconate

HYDROGEN FLUORIDE: ACUTE TOXICITY

MONKEY	- I-HR LC50	1774 PPM
RAT	- 1-HR LC50	- 1000 - 2300 **PPM**
RABBIT	- 90-MW LC 100	666 PPM
MOUSE	- 1-HR LC50	342 - 501 PPM
GUINEA PIG	- 1-HR LC100	250 PPM

Simulated Emergency **Exposure**

10-Min HF Exposures in Rats (W. Dalbey [2])

Nose Bypassed:	1770 ppm, 1 of 20 rats died
Nose Breathing:	7010 ppm, no rats died
Conclusions:	Mouth breathing more toxic, produces deep lung injury. Nose breathing scrubs out water soluble HF produces upper respiratory effects.

Haber's Rule

(Usually holds for lethality)

Concentration X Time = Constant

$$C \times T = K$$

$$C^n T = K$$

HF Sensory Irritation

Respiratory Rate Depression in Mice

RD50 = 151 ppm

HYDROGEN FLUORIDE: EFFECTS IN HUMANS

Concentration	Time	Effects
122 ppm	1 min.	Highest concentration that two men tolerated for more than one minute. Conjunctival and respiratory imtation was marked but bearable. Smarting of exposed skin in < 1 min (Machle et al. [4])
61 ppm	1 min.	Conjunctival imtation; marked nasal irritation; discomfort in larger air passages; definite sense of "taste"
32 ppm	3 min.	Discomfort; smarting of nose and eyes was mild; "sour taste"
4.1	6 hr./day	Very slight irritation of the face and eyes; 10-50 days frequent cutaneous erythema (Largent [1])
~3 ppm	1 hr.	Slight imtation of upper airways and eyes.

FLUORIDE EXCRETION/DISPOSITION

- ~20% F- REMOVED IN URINE WITHIN 3 HRS
- ULTIMATELY ~50% F- EXCRETED IN URINE, ~10% IN FECES, REMAINDER ACCUMULATES IN BONE, HIGHEST LEVELS FOUND IN THE AGED
- CHILDREN ACCUMULATE MORE F- IN BONE, EXCRETE LESS IN URINE DEPENDING ON AGE

FLUOROSIS

A condition caused by excessive intake of fluorides:

(>2 ppm in the drinking water)

Causes mottling and discoloration of the tooth enamel

Skeletal bones also affected

FLUORIDE

EFFECTS IN HUMAN:

- ESTIMATED LETHAL DOSE - 50 MG/KG (HODGE AND SMITH [5])
- 1 MG/L IN WATER DECREASES DENTAL CARES
- FLUOROSIS AFTER INTAKE OF 40 - 80 MG DAY > 4 YRS IN MANUFACTURING
- DECREASED URINARY F OUTPUT AND INCREASED PLASMA F CONCENTRATION IN KIDNEY DISEASE
- > 3.4 MG/M^3 (4.3 ppm)- CHRONIC INHALATION EXPOSURE, THRESHOLD FOR MINIMAL INCREASE IN WORKER BONE DENSITY

CARCINOGENICITY:

- NO EVIDENCE OF CARCINOGENICITY IN POPULATIONS WHERE WATER IS FLUORIDATED (IARC)
- NO CARCINOGENICITY IN GUINEA PIGS EXPOSED FOR 18 MOs TO 0.2 PPM OF HF

EXPOSURE GUIDELINES

ACGM TLV: 3 PPM CEILING (2.5 MG/M^3)

NAS - SUBMARINES (1 HR): 10 PPM

DUPONT CEG: 0.1 PPM

FLUORIDE DOSE/DAY

— TLV @3 PPM (2.5 MG/M^3)(CEILING) RESULTS IN A POSSIBLE EXPOSURE OF ABOUT ***1.5*** PPM (1.25 MG/M^3) *X* 10 M^3 = 12.5 MG/DAY

— IF 2 MG/L IN WATER X 2 L/DAY = 4 MG/ DAY

— CONTRIBUTION FROM FOOD, AND FOODS COOKED IN WATER, VITAMINS, TOOTHPASTE, MOUTHWASH = ––4 MG DAY

- TOTAL EXPOSURE = - 20 MG/DAY

— HISTORICAL DATA (1932) REPORTED FLUOROSIS IN WORKERS EXPOSED TO 20 TO 80 MG DAY > 4 *YRS*, HOWEVER, ESTIMATED AIR CONCENTRATIONS WERE **15** TO 20 MG/M^3.

— WHEN AIR CONCENTRATIONS WERE MAINTAWED AT OR LESS THAN 2.5 MG/M^3, YRS OF EXPOSURE HAVE PRODUCED NO OSTEOSCLEROSIS (HODGE AND SMITH [5])

HF ERPGs and DEFINITIONS

ERPG-3: 50 ppm (41 mg/m^3)

The maximum airborne concentration below which, it is believed, nearly all individuals could be exposed for up to one hour without experiencing or developing life-threatening health effects.

ERPG-2: 20 ppm (16.4 mg/m^3)

The maximum airborne concentration below which, it is believed, nearly all individuals could be exposed for up to one hour without experiencing or developing irreversible **or** other serious adverse health effects or symptoms which could impair an individual's ability to take protective action.

ERPG-1: 2 ppm (1.6 mg/m^3)

The maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to one hour without experiencing other than mild, transient, adverse health effects or without perceiving a clearly defined objectionable odor.

ERPG COMPARISON
(values in ppm)

	HCL	HF	SO_2
ERPG-1	3	2	0.3
ERPG-2	20	20	3
ERPG-3	150	50	**15**

Proposed Special IO-Min ERPGs

ERPG-3 = 170 ppm
ERPG-2 = 50 ppm
ERPG-1 = 2 ppm
