HYDROGEN FLUORIDE: HOW TOXIC IS TOXIC? (A HAZARD AND RISK ANALYSIS)

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The purpose ofthis presentation is to review the toxicity of hydrogen fluoride (HF) especially as it relates to health risks from accidental exposures, and review certain exposure limits that have been established for accidental releases. HF is widely used in the oil industry as a catalyst and in the chemical industry in the synthesis of a variety of fluoropolymers and fluorochemicals. HF vapor can be produced in fires as a breakdown product of fluorocarbon fire-extinguishing agents and in the combustion of fluoropolymers.

Anhydrous HF, a strong and powerful dehydrating agent, is highly soluble in water where it forms hydrofluoric acid. a weak acid that may not be fully ionized in water solutions. It is the nonionic HF, and not the fluoride in, which is more readily transported across cell membranes. In extracellular fluid at pH 7.4. HF is essentially completely ionized. Thus, it is this dissociation to the fluoride ion that may he the causative agent resulting in potential systemic toxicity.

The significant toxicological effects of HF exposure are manifest at the site of contact. Thus, by the inhalation route, significant deposition is predicted to occur in the most anterior region of the nasal cavity and to extend posteriorly to the lower respiratory tract if sufficient exposure concentrations are achieved. Histologically, the lesions induced at the sites of contact with HF are characterized by necrosis with an associated intlammatory response. One day after a single. I hr exposure of rats to HF concentrations of 950 to *1600* ppm. pathologic injury was limited exclusively to the anterior section of the nose [1]. The nasal lesions were characterized by extensive necrosis and squamous metaplasia of respiratory epithelium with inflammation and vascular thrombosis in adjacent submucosal tissues. No compound-related effects were seen in the trachea or lungs.

In **a** separate study, Dalby *[2]* exposed two breathing models *of* rats—a nose- and mouth-breathing model. In the latter model, rats were exposed to various concentrations of HF through **a** tracheal cannula thereby bypassing the upper respiratory tract. This exposure method is considered to be **a** conservative approach for estimating **a** "worst case" exposure in which **a** person would not breathe through the nose but inhale through the mouth thereby maximizing the deposition of HF into the lower respiratory tract.

In the nose-breathing model, 2 or 10 min exposures *of* rats to 6392 or 1669 ppm, produced similar effects, i.e., no mortality but signifcant pathological lesions in the nasal epithelium. In contrast. marked differences in toxicity were evident in the mouth-breathing model. Indeed, mortality was evident following **a** 10 min exposure to a concentration of 1764 ppm and a *2* min exposure to 8621 ppm. Signficant inflammation of the lower respiratory tract was also evident. Similarly, **a** 2 min exposure **to** 4887 ppm produced mortality and signficant nasal damage. However, at a lower concentrations (950 ppm) following **a** 10 min exposure or 1589 ppm following **a** 2 min exposure, no mortality and only minimal irritation were observed.

Lesions of the nasal mucosal membranes of rabbits and guinea pigs exposed for 31 days to HF vapor were reported with a no-effect concentration being established at 3.0 ppm [3]. Monkeys appeared to be less sensitive to HF compared to rabbits and guinea pigs when exposed to 18.6 ppm, 6-8 hrs/day, 6 days/week [4]. Other inhalation toxicity studies have been done with HF in experimental animals. However, the results of these studies continue to show similar outcomes, i.e., upper and lower respiratory tract inflammation.

In any consideration for exposure limits, human data will usually by necessity take precedence over animal toxicity data. For HF, there are controlled human exposure studies at high concentrations, albeit some data are from the 1930s. Humans are reported to have tolerated, with mild nasal irritation (subjective response), 32 ppm for several minutes [5]. Exposure of human to about *3* ppm for an hour produced slight eye and upper respiratory tract irritation. Even with an increase in exposure concentration (up to 122 ppm) and a decrease in exposure duration to about 1 min, skin, eye and respiratory tract irritation occurs [4]. Repeated exposures of humans at concentrations up to 4.7 pprn, **6** hrs/day for IO-SO days. were tolerated without severe effects [6,7]. It appears that an irritation threshold exists at about **3** pprn where mild irritation of the upper airways and eyes occur. In prolonged exposure at about 5 ppm, redness of the skin has also resulted.

It is important for a risk analysis to distinguish between normally healthy individuals (e.g., fire-fighters) and those with compromised health. Exposure to higher concentrations of HF would be expected to be tolerated more in healthy individuals, whereas, at equal concentrations, escape-impairing effects may occur in those with compromised health. Therefore. an assumption in the following discussion is that the effects described at the various concentrations and durations are for the healthy individual.

HF does not clearly exhibit a concentration-times-time (C*t) relationship, but appears to exhibit a C^2*t relationship, particularly as it applies to experimental animal mortality. With regard to inflammation, HF does exhibit a dose-response relationship although a concentration and time relationship does not seem to exist.

At concentrations of <SO ppm for several minutes, imtation of upper respiratory tract and the eyes would be expected to occur. At these low concentrations, escape-impairing effects would not be expected in the healthy individual. As HF concentrations increase to SO-IO0 ppm, an increase in imtation is expected. For short duration periods (10-30 min), irritation of the skin, eyes, and respiratory tract would occur. At 100 ppm for 30-60 min, escape impairing effects would begin to occur, and continued exposure at 100 ppm and greater for an hour could be lethal in the absence of medical intervention. As the concentration of HF increases to 100 to 200 ppm, the severity of irritation increases, and the potential for delayed systemic effects also increases, e.g., severe, escape-impairing irritation of the eyes and respiratory tract. At these concentrations, humans would also be expected to shift their breathing pattern to mouth breathing. Therefore, deeper lung irritation is expected. At greater concentrations (>200 pprn), respiratory discomfort, pulmonary (deep lung) imtation, and systemic effects are possible. Continued exposure at these concentrations may be lethal in the absence of medical treatment.

Generation of HF from fluorocarbon fire extinguishing agents does represent a potential hazard. In the foregoing discussion, the duration of exposure was indicated for 10 to 60 min. Under those conditions at which HF would be generated, the actual exposure duration would be expected to be less than 10 min and would more likely be about a 5 min exposure. As Dalby [2] showed, exposing mouth-breathing rats to HF concentrations of about 600 ppm for 2 min was without effect. Similarly, exposing mouth-hreathing rats to a HF concentration of about 300 ppm for 10 min did not result in any toxicity. Therefore, one could surmise that humans exposed to similar concentrations for less than 10 min would be able to tolerate such concentrations. However. some caution needs to be employed in over-interpreting these data. Although the toxicity data would suggest that humans could tolerate these large concentrations for less than 10 min, those individuals with compromised lung function or those with cardiopulmonary disease may he more susceptible to the effects of HF. Furthermore. even in the healthy individual. irritation of the upper respiratory tract and eyes would be expected, and escape could be impaired.

Occupational exposure limits have been established for HF. The limit set by the American Conference of Governmental Industrial Hygienists (ACGIH); Threshold Limit Value (TLV") represents exposure of normally healthy workers for an 8 hr workday or 40 hr workweek. For HF, the limit established is 3 ppm, and represents a ceiling limit, i.e., the airborne concentration that should not be exceeded at any time during the workday. This limit is based principally on tlie potential for HF to induce irritation and prevent possible systemic effects with repeated, long-term exposure, e.g., fluorosis. These limits are not considered relevant for fire extinguishing use of fluorocarbons during emergency situations.

In contrast to the ACGIH TLV"'. the American Industrial Hygiene Association (AIHA) Emergency Response Planning Guideline (ERPG) represents limits established for emergency release of chemicals. These limits are established to also account for sensitive populations, e.g., those with compromised health. However, in the case offirc extinguishing use and generation of HF, these limits may he more relevant than limits such as the TLV*. The ERPG limits 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 et al. [5] and Largent [6]. ERPG-3 (SO ppm) is based on animal data and is tlie maximum nonlethal level for nearly all individuals. This means that this level could be lethal to some susceptible people.

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 six-fold as high). because of the uncertainty associated with extrapolation to shorter times. These 10 min values could bc used in emergency planning in fires where HF vapor is generated: ERPG-3 = I70 ppm; ERPG-2 = SO ppm; ERPG-1 = 2 ppm.

REFERENCES

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6. Largent, E. J. (1960). The Metabolism of Fluorides in Man. *Arch Ind. Health* 21:328-323.
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Hydrogen Fluoride: Physical and Chemical Properties

Description	-Gas at atmospheric conditions -Liquid in cylinders under pressure -Solutions in water
Chemistry	Strong Acid; pka = 3.45
Boiling Point	19.4°C
Odor	Pungent odor Odor threshold 0.04 to 0.13 ppm
Density	1.015 g/ml @ 0°C
Conversion Factor	1 mg/m^3 + 1.2 ppm
Environmental Effects	Causes foliar damage to plants at <1 ppm in atmosphere

Emergency Response Planning Guidelines (ERPG)

ERPG-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
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 health effects or symptoms that could impair an individual's ability to take protective action.

ERPG-1
The maximum airborne concentration below which it is believed 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 odor.

ERPG Limits for HF

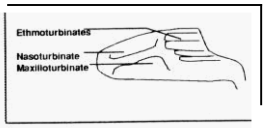
	1-hr	10 min
ERPG-1	2 ppm	2 ppm
ERPG-2	20 ppm	50 ppm
ERPG-3	50 ppm	170 ppm

Acute Toxicity Data for HF: Animal Data

Monkey	1-hr LC_{50}	1774 ppm
Rat	1-hr LC_{50}	~1000-2300 ppm
Rabbit	90-min LC_{100}	666 ppm
Mouse	1-hr LC_{50}	342-501 ppm
Guinea Pig	1-hr LC_{100}	250 ppm

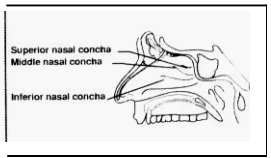
Anatomy of the Upper Respiratory Tract

RAT



- Obligate nose breathers
- Turbulent inspiratory flow over lateral meatus
- Complex turbinate structure
- Highly developed olfactory system (50% of surface area)
- Relatively high surface area/body weight
- Cell types are regular and discrete

HUMAN



- Oro-nasal breathers
- Less turbulent inspiratory flow over middle meatus
- Simple turbinate structure
- Poorly developed olfactory system (10% of surface area)
- Relatively low surface area/body weight
- Cell types are histologically irregular, OLF is mixed

Minute ventilation/Surface area
Rat = 0.02 L/min/cm²
Human = 0.05 L/min/cm²

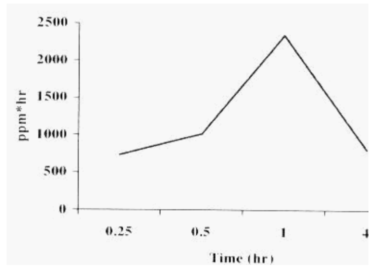
Effects of 2- and IO-Minute Exposure to HF in the Mouth-Breathing Rot Model

Endpoint	2-Minute Exposure	10-Minute Exposure
mortality	not tested	**7014 ppm** 80% mortality
mortality	not tested	**3847 ppm** 50% mortality
mortality histology	**8621 ppm** 5% tracheal inflammation, exudate & necrosis-, bronchial exudate & necrosis; alveolitis	**1764 ppm** 5% tracheal inflammation, exudate & necrosis-, bronchial necrosis
mortality histology	**4887 ppm** 10% tracheal inflammation, exudate & necrosis-, bronchial exudate & necrosis; alveolitis	**950 ppm** none tracheal inflammation, exudate & necrosis
mortality histology	**1589 ppm** none tracheal inflammation, exudate &	**271 ppm** none tracheal inflammation

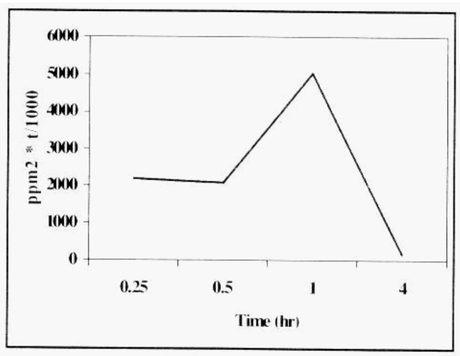
Effects of 2- and 10-Minute Exposure to HF in Normal Nose-Breathing Rats

Endpoint	2-Minute Exposure	10-Minute Exposure
mortality	not tested	**7014 ppm** none
mortality	not tested	**3847 ppm** none
mortality clinical signs histology	not tested	**1669 ppm** none rales & nasal discharge necrosis & hemorrhage in nose
mortality clinical signs histology	**6,392 ppm** none necrosis & hemorrhage in nose	

C t Correlation?



*C^2*t Correlation?*



HF: Effects in Humans - Controlled Studies

Exposure Concentration (ppm)	Time	Effect
122	1 min	Eye. URT. shin irritation
61	1 min	Eye, URT irritation. discomfort in larger ai: passages, "taste"
32	3 min	Discomfort. smarting of eyes nose. "sou: taste"
- 3	60 min	Slight irritation, URT, eyes

Possible Effects of HF Exposure

- *At <50 ppm*
  - 10 min: minimal irritation
  - 30 min: increasing upper respiratory tract irritation
  - 60 min: moderate to severe irritation
- *At 50-100 ppm*
  - 10 min: mild irritation
  - 30 min: increasing irritation, respiratory difficulty
  - 60 min: severe irritation, possible systemic effects
- *At 100-500 ppm*
  - 10 min: moderate irritation - escape impairing
  - 30 min: severe irritation, respiratory difficulty
  - 60 min: severe irritation, systemic effects
- *At 500-1000 ppm*
  - 10 min: escape impaired, lethal with increasing time

Possible Effects of HF Exposure: Short Durations

5 Minute Maximum Exposure

- <50 ppm - Minimal eye irritation
- 50-100 ppm - Increasing eye irritation including nasal irritation
- 100-200 - Moderate irritation of skin, eyes and respiratory tract
- >200 ppm - Definite irritation of tissue surfaces; could become escape impairing

Conclusion

- HF is extremely irritating to skin and mucous membranes
- The effect.?of HF are manifested at the site of contact
- A C^2t is more probable of a predictor of the effect of HF
- At short durations (<5 min.), escape-impairing effects are probable at ~200 ppm.