## III. BIOLOGIC EFFECTS OF EXPOSURE

### Extent of Exposure

Anhydrous hydrogen fluoride is a colorless liquid or gas which fumes in moist air and has a pungent irritating odor. Its aqueous solutions are also colorless, and fume above a concentration of 40-48%. [1,2] It is manufactured by allowing sulfuric acid to react with acid-grade fluorspar (97% calcium fluoride) in heated rotary or stationary kilns. Hydrogen fluoride is evolved as a gas, purified, and then condensed as liquid anhydrous hydrogen fluoride. [3] Apposite properties are presented in Table XII-1. [2,4,5]

A comparison of the properties of hydrogen fluoride with those of other hydrogen halides indicates deviations from expected values because of polymerization of the hydrogen fluoride molecule. [6-8] The degree of polymerization varies depending on the partial pressure of the hydrogen fluoride and the temperature. At workplace airborne concentrations of HF at or near the recommended limits, the partial pressure will be low enough that negligible polymerization of HF will occur. [9] In this situation, it is probable that the molecular weight of hydrogen fluoride is 20. To account for any uncertainty in this figure, the environmental limits are expressed in mg/cu m instead of in ppm. [10,9] When airborne HF concentrations are converted from ppm to mg/cu m in this document, it is assumed that airborne HF exists as a monomer.

Hydrogen fluoride was first prepared by Margraff in 1768 and was characterized by Scheele in 1771. [11] Between 1876 and 1931, considerable quantities of aqueous hydrofluoric acid were produced and used for cleaning

sand from castings and for etching glass. [12] In 1931, anhydrous hydrogen fluoride was first produced commercially. [12] The use of anhydrous hydrogen fluoride as a catalyst in alkylation processes for making high-octane fuel blends began in 1942. [3]

Prior to 1954, the steel industry was the largest consumer of fluorspar from which hydrogen fluoride is generated. Since then, the quantity of fluorspar used for the manufacture of hydrogen fluoride has surpassed that used in the steel industry. [3] In 1958 and 1971, approximately 52% of all fluorspar consumed in the US was used for making hydrogen fluoride. [3,13] Some production figures for hydrogen fluoride are given in Table III-1.

In 1974 production reached 375,000 tons; however, there were no major plans for expansion of hydrogen fluoride production capacity. [16] Currently the major uses of hydrogen fluoride are in the production of cryolite for the aluminum industry, [17] in the manufacture of fluorocarbon compounds, as a

TABLE III-1

HYDROGEN FLUORIDE PRODUCTION

| Year | Total production of anhydrous hydrogen fluoride in short tons. Includes that used to make aqueous hydrofluoric acid |
|---|---|
| 1967 | 161,260 |
| 1968 | 192,265 |
| 1969 | 221,536 |
| 1970 | 224,405 |
| 1971 | 219,481 |
| 1972 | 241,119 |

Adapted from references 14 and 15

TABLE III-2

1974 HYDROFLUORIC ACID CONSUMPTION

| Use | Thousands of Tons |
|---|---|
| Fluorocarbons manufacture | 180 |
| Aluminum (cryolite and aluminum fluoride) | 140 |
| Petroleum (alkylate catalysis) | 15 |
| Stainless steel | 10 |
| Uranium processing | 10 |
| Fluoride salts manufacture | 15 |
| Miscellaneous (glass etching, electronics, etc) | 30 |

From reference 16

catalyst in alkylation processes, in steel pickling, uranium processing, enamel stripping, glass and quartz etching and polishing, and in various electroplating operations. [18] Consumption of hydrogen fluoride is listed in Table III-2. Hydrogen fluoride is often produced by other industrial processes using fluorides, eg, welding and aluminum production.

Table XII-2 lists some occupations with potential exposure to hydrogen fluoride. NIOSH estimates that 22,000 workers are potentially exposed to hydrogen fluoride in the US.

## Effects on Humans

(a) Odor Threshold

Sadilova [19] in 1968 reported the results of odor threshold determinations for hydrogen fluoride using 17 subjects with normal odor perception. The method used was described only as that commonly employed in the Soviet Union. A total of 672 tests were made with concentrations

ranging from 0.02 to 0.22 mg HF/cu m. The concentration of HF which was the minimum perceptible for 10 of the 17 subjects was 0.03 mg HF/cu m. For all subjects, the odor threshold ranged from 0.03 to 0.11 mg/cu m.

Lindberg [20] in 1972, using 17 subjects, estimated the threshold of odor for hydrogen fluoride for the "most sensitive persons" (6 people) at a level of 0.04 mg HF/cu m, with the "maximum imperceptible concentration" being 0.02 mg/cu m.

(b) Effects on Skin

Hydrofluoric acid is one of the most corrosive of the inorganic acids. [21] Fluoride ion readily penetrates the skin and travels to deep tissue layers causing liquefaction necrosis of the soft tissues [22-25] and decalcification and corrosion of bone [21,23]. The tissue destruction is accompanied by severe pain, [22-25] which has been attributed by Klauder et al [24] to the calcium precipitating property of the ion which produces immobilization of tissue calcium and a resulting relative excess of potassium in the tissues so that potassium nerve stimulation ensues.

Jones [22] in 1939 described 12 cases of HF acid burns of the skin. One worker received several HF acid burns on the right forearm from 100% hydrofluoric acid. The forearm was immediately soaked in sodium bicarbonate solution, but pain became increasingly severe and the affected area took on a grayish appearance. Pain was almost immediately relieved after calcium gluconate solution was injected into and under all affected areas. Two days later, the burn areas became coagulated and gradually sloughed off during the next 13 days. Complete healing with scar formation occurred in about 1 month.

Another worker [22] splashed 80% HF acid inside his rubber gloves and on his right forearm resulting in whitish discoloration of the skin. Injection of the affected areas with calcium gluconate and application of magnesium oxide paste immediately relieved the pain. Three days after the accident only slight inflammation was evident; this quickly subsided.

Four workers [22] received HF acid burns from a 60% solution in separate accidents. Three were splashed with the acid and one sustained a burn because of a pinhole in the rubber glove worn during the immersion of his hands in the acid solution. The effects of the acid on the skin ranged from mild erythema to tissue destruction. No explanation was offered for the difference in effects. Pain was described as ranging from slight to excruciating. Complete healing of the burns took from 2 to 6 weeks.

In still another case, [22] a laborer with unprotected hands picked up a piece of carbon impregnated with 50% HF acid. Two hours later, his fingertips became extremely painful and the affected skin took on a whitish appearance and became leathery. He was treated by prolonged soaking of the hands in a hot solution of sodium bicarbonate followed by an application of magnesium oxide paste which was reapplied every 4 hours. The persistence of pain for several days indicated that the treatment was unsatisfactory. The skin became necrotic, and dead tissue sloughed off. Over the next 3 months, gradual healing with scar formation occurred. Three other workmen received minor burns from a mixture of hydrofluoric and sulfuric acids of unknown concentrations. These three men experienced mild pain and healing was uneventful. Exposure of two workers to HF acid vapor of unknown concentration resulted in erythema of the face and neck and slight blistering of the lips. The skin inflammation cleared up within 1 day. No respiratory tract irritation was reported in these two cases.

Dale [23] in 1951 described an HF acid burn in a woman employed in the manufacture of glass measuring tubes. Using a 60% aqueous solution of HF, she etched graduations on the measuring tubes. Her right rubber glove became perforated without her knowledge and acid entered the glove. It was about 4 minutes before she experienced pain. The glove was immediately removed and the hand washed in a warm saturated solution of sodium bicarbonate. Magnesium oxide paste was applied and she was taken to the hospital for injection of calcium gluconate into and under the burn. The following day she was in great pain, the hand and fingers were grossly swollen, and the burned skin was white and insensitive. A grey blister which formed on the palm was opened and was found to contain seropurulent fluid. The three medial fingers became necrotic, in some areas down to the bone. A split-skin graft was applied to the palm and the necrotic portions of the fingers were removed. Healing was almost complete 60 days after the accident.

Klauder et al [24] in 1955 described a skin injury in a worker whose fingers came in contact with a 10% HF acid solution. About 1 hour after contact the distal phalanges of both index fingers and thumbs became painful and appeared inflamed and edematous. Later, the affected skin became marble-white. The pain became increasingly severe. Ten cubic centimeters of a 10% solution of calcium gluconate was administered intravenously on two occasions and 1 teaspoon was taken orally three times daily for 4 days. A paste containing calcium gluconate was applied to the injured area. Several days later, part of the epidermis detached, exposing a granulating surface. Complete healing with slight scar formation took place about 1 month after the burn. The authors suggested that the severe

pain which characterized the HF acid burn was related to immobilization of calcium resulting in potassium nerve stimulation.

Dibbell et al [25] in 1970 reported three cases of HF acid burns of the skin. A glass-blower sustained a burn of the right index and middle fingers. Approximately 12 hours after the accident, the workman complained of a severe burning sensation. Twenty-four hours later, the skin was blistered, white, and edematous. The white areas were surrounded with an erythematous flair. The burned areas were excruciatingly painful. Necrotic tissue was debrided and the nail of the index finger removed. The edema and erythema subsided rapidly and the burned areas healed satisfactorily during the next 14 days.

Another worker [25] suffered a skin burn when, through a hole in her protective glove, HF acid gained access to the skin of her right thumb. There was a gradual increase of pain and 5 hours after the accident the distal segment of the thumb was tender, white, and edematous. Sixteen days later, she was admitted to a hospital with painful necrosis of the affected area. Healing occurred in 6 weeks. Follow-up examination 2 years later revealed about a 20% loss of the distal thumb pulp.

In 1974, Browne [21] reported that 38 cases of HF splashes and 10 cases of HF vapor burns were treated successfully using calcium gluconate gel. The most extensive skin burn treated with the gel occurred when an employee was splashed with anhydrous HF on the outer side of his right leg affecting an area of about 88 sq in. (570 sq cm). He flushed the area almost immediately with copious amounts of water for 3-4 minutes during which time most of his trousers disintegrated but some fabric remained stuck to the skin. He then applied, within seconds, large quantities of

calcium gluconate gel (2.5% calcium gluconate and an antiseptic agent) and kept rubbing it in until additional first aid was received some 10 minutes later. Gel was applied and massaged in until the pain subsided about 1.5 hours later. Healing was virtually complete in 31 days. It was noted that the deep burns were located in those areas where the fabric stuck, creating a barrier through which neither the initial washing nor the gel completely penetrated.

Largent [26] in 1961 reported inhalation studies of HF involving five human subjects, all five being exposed in six separate experiments for 6 hours/day, 5 days/week for 10-50 days at concentrations averaging 1.42-4.74 ppm (1.16-3.89 mg/cu m) and ranging from 0.9 to 8.1 ppm. Exposure at an average concentration of 1.42 ppm (1.16 mg/cu m) ranging from 0.9 to 2.0 ppm (0.7-1.64 mg/cu m) was reported to have no noticeable effect. At concentrations averaging 2.59, 2.72, 3.39, 4.22, and 4.74 ppm (2.12, 2.23, 2.78, 3.46, and 3.89 mg/cu m), the exposed subjects experienced very slight irritation of the face and eyes, and frequent cutaneous erythema was noticed. Flaking of the epithelium, resembling mild sunburn, was reported by one subject after 10 days of exposure. The concentration of HF to which he was exposed averaged 3.39 ppm (2.78 mg/cu m). Application of a face cream to the skin relieved the burning sensation. Irritation and erythema of the face subsided quickly after exposure was terminated.

In summary, the reports presented, [21-26] typical of many cases reported in the world literature, demonstrate that HF and HF acid burns differ from other acid burns in several ways. They cause intense pain which may persist for several days. [22-25] The onset of pain from up to 60% aqueous HF acid solutions may be delayed for several hours. [22,24,25]

The absence of any warning of injury after contact with weaker solutions may result in neglect on the part of the worker to seek prompt first aid. [22,24,25] Hydrofluoric acid solutions stronger than 50-60% and anhydrous HF cause almost immediate pain. [22,23,25] The skin, after contact with HF acid, takes on a blanched appearance, becomes edematous, and may suffer deep extensive destruction of tissue with a tendency to heal slowly. [22-25] Since the degree of tissue destruction not only depends on the concentration of the acid, but also on the duration of contact, immediate irrigation of the affected skin with water is of utmost importance.

Prolonged exposure at airborne HF concentrations averaging as low as 2.59 ppm (2.12 mg/cu m) and ranging from 1.8 to 8.1 ppm (1.5-6.6 mg/cu m) resulted in very mild skin irritation in five out of five human subjects during an experimental study. [26]

(c) Effects on Eyes

Based on the destructive action from skin contamination, one would expect that eye contact with HF acid solutions and anhydrous HF would cause severe and probably permanent damage to the eye, but specific accounts of such injuries were not found in the literature.

McLaughlin [27] in 1946, in reviewing chemical burns of the human cornea, listed two workers having corneal burns from HF acid with prompt healing within 48 hours, and no loss of vision. Details as to the severity of exposure were not given.

Bertuna [28] in 1969 described an eye injury in a 25-year-old man at an alkylation process site who was accidentally exposed to concentrated HF acid spray. Examination of the eyes after profuse water irrigation showed beginning necrosis of the bulbar conjunctivae and practically complete loss

of epithelium on the right cornea and partial deepithelization of the left cornea. Five hours after the accident, the patient complained of photophobia and examination revealed marked edema of the eyelids and corneas and intense chemosis. Three days later, the edema of the eyelids was reduced and reepithelization of the corneas occurred. Recovery progressed rapidly, both corneas were completely clear by the thirty-fifth day, and visual acuity returned to normal.

Largent [26] in 1961 noted mild eye irritation in five human subjects exposed to HF at concentrations which averaged 2.59-4.74 ppm (2.12-3.89 mg/cu m) HF during an experimental study. No eye irritation was noticed at concentrations averaging 1.42 ppm (1.16 mg/cu m) and ranging from 0.9 to 2.07 ppm (0.74-1.70 mg/cu m).

(d) Respiratory and Systemic Effects

Burke et al [29] in 1973 reported an unusual case of systemic fluoride poisoning from possible absorption of fluoride through the skin. A 30-year-old laboratory technician was splashed with 100% anhydrous HF on the right side of the face, the neck, and the right arm when a connecting tube ruptured. Within 3-5 minutes, he was placed under the emergency shower and washed for 15 minutes, but he suffered skin burns of the contaminated areas. During the first 24 hours after the accident, he was stuporous, unresponsive to stimuli other than pain, severely nauseated, and he vomited small amounts of brownish, bile-colored fluid. His pulse rate dropped to 48 beats/minute within 6 hours after the accident. Blood pH at this time was 7.21 (normal 7.35-7.45), carbon dioxide combining power was 21.5 mEq/liter (normal 24-30), serum potassium was 6.1 mEq/liter (normal 3.6-5.0). An ECG taken 10 hours after the accident showed slight S-T

elevation in lead AVL, V1, V2, and V3, which disappeared within 3 days. Microscopic analysis of the urine on the third day following the accident showed 25 red blood cells, 10 white blood cells, and a few granular and hyaline casts. The urine sediment became normal by the sixth day. The only respiratory symptom was a mild throat irritation during the first hour after the accident. Repeated chest X-rays were all negative. Results of liver and kidney function tests were also normal. Bone and dental X-rays 3 months later revealed no abnormal bone structure. The skin defects at the burn sites required plastic surgery.

The authors [29] estimated that approximately 5 g of HF was spilled on the skin, resulting in second- and third-degree burns over 2.5% of the body surface. The urinary fluoride level 3.5 hours after the accident was 87 mg/liter. During the following 6 hours, it dropped to 56 mg/liter and decreased gradually at a linear rate during the following 2.5 days. The total urine fluoride excretion was calculated to be about 400 mg during the first 3 days after the accident, with 75% excreted within the first 24 hours. Thereafter, F was excreted at a constant daily rate of about 20 mg. The absence of respiratory involvement in this case suggested to the authors that absorption through the skin led to severe systemic fluoride poisoning. Blood samples taken 4 and 10 hours after the accident showed fluoride levels below 0.3 mg/100 ml. The normal blood F concentration may be approximated from the work of Hall et al, [30] who found that the mean serum fluoride concentration in a series of 26 human sera obtained at routine preadmission examinations of subjects entering the hospital for various surgical procedures was 3.7 μg/100 ml. Insofar as the records indicated, none of the patients suffered from chronic renal diseases or

overt bone diseases, two types of illness that might have affected serum fluoride concentrations.

Dieffenbacher and Thompson [31] in 1962 reported overexposure to HF in two men employed in a petroleum refinery. One worker was burned on the face, both ears, and areas of the neck by 10% anhydrous HF in propane, which remained on the skin for about 30-35 seconds. He immediately put his head in a tank of "soda bicarb," and shortly thereafter showered thoroughly. Oxygen was administered because of dyspnea, but he died about 2 hours after the accident. Autopsy findings included congestion and hemorrhages in the lower respiratory tract. Both lungs were edematous. There were numerous subepithelial hemorrhages in the kidney pelvises and marked hyperemia of the brain, especially in the white matter of the cerebrum. A few grossly visible, small hemorrhages were found in the posterior portion of the interventricular septum of the heart. Since propane has a very low toxicity, the authors attributed the respiratory changes to pulmonary absorption of HF. While it was speculated that the cardiac changes might also have resulted from HF pulmonary absorption, the cause of the hemorrhages in the kidney pelvises and marked hyperemia of the brain was not discussed. The other workman was blowing out tubes which had contained an oil-HF mixture. Accidentally applied air pressure splashed the material on his chest and under his protective hood, contaminating the left side of the face and neck. Vapors under the hood were strong, and the workman had difficulty in breathing. After taking a shower, he was transferred to a hospital where he was given supportive treatment. Breathing was difficult and on examination, moist rales were heard in both lungs. During the next 12 hours, his breathing improved. Cardiac

enlargement, increased bronchiovascular markings, and fluid in the left costophrenic angle were observed by X-ray. By the seventh day, the heart had returned to normal size, but there was still fluid in the left lung base. A 3-day fluoride balance study showed no abnormally high levels of F excretion.

Mayer and Guelich [32] in 1963 reported three accidental deaths from HF exposure. Six workers in two separate accidents were splashed with 70% HF acid. In one accident, four workmen lifted a 20-gallon drum of 70% HF acid to the edge of a vat. When the bung was removed, HF acid was splashed upon all four men. Two men jumped into a nearby vat of water and were unharmed. The other two men lay on the floor and other workmen poured water over them. No safety shower was available. One of these men died 2 hours after the accident from pulmonary edema. The other suffered severe chemical burns, but survived.

In another accident, [32] a 5-pint glass bottle containing 70% HF acid exploded, splashing two workmen with the acid. They were showered and taken to a hospital where they died from pulmonary edema 2 hours after the accident. The authors concluded that the 150-mmHg vapor pressure of HF over a 70% acid solution at 80 F could produce a breathing zone concentration of 10,000-100,000 ppm (8,000-80,000 mg/cu m) in the event that a workman's clothing, particularly in the chest area, became contaminated.

Greendyke and Hodge [33] in 1964 described two accidental deaths from HF overexposure. The two workers were splashed with HF acid when a bottle containing the acid exploded. They were immediately showered and transferred to a distant hospital. On examination, one worker showed no

respiratory distress or pain. Burns of various size and degree covered 15% of the body surface. Except for a moist cough and a few wheezes in the chest, he was doing well until sudden respiratory distress occurred about 4 hours after the accident. He died soon afterward. Autopsy findings revealed dilatation of the heart and an acutely inflamed bronchial tree with partially ulcerated mucosa. The lungs showed severe hemorrhagic edema. Analysis of the blood revealed an F concentration of 0.4 mg/100 ml (normal is about 4 $\mu$g/100 ml [30]).

The second worker [33] had all degrees of burns over 10% of his body surface and a small corneal ulcer in the right eye. He was acutely ill at the time of admission. He complained of nausea, numbness and tingling of hands and arms, and shortness of breath. He showed signs of bronchospasm and was cyanotic. High fever appeared within 2 hours. Urinalysis revealed 2+ albumin and numerous erythrocytes. He died 10 hours after the accident from cardiac arrest. Autopsy showed dilatation and local inflammatory changes of the heart, inflammation and partial ulceration of the larynx, trachea, and bronchial tree; extensive acute pneumonitis and pulmonary edema, and acute hyperemia in all other organs. The F content of the blood was 0.3 mg/100 ml.

Kleinfeld [34] in 1965 observed a case of acute pulmonary edema in a 29-year-old chemist who was exposed accidentally to HF when a vat containing HF acid broke. The acid spilled on the face and upper extremities, producing first- and second-degree burns. The workman developed pulmonary edema 3 hours after exposure and died 10 hours after admission to the hospital. At autopsy, severe tracheobronchitis and hemorrhagic pulmonary edema were found.

Machle et al [35] in 1934 reported the effects of airborne HF on two human subjects. The highest concentration that they were able to tolerate for more than one minute was 100 mg/cu m. At this level, there was smarting of the exposed skin in less than one minute, and conjunctival and respiratory irritation was marked. At 50 mg/cu m, the same effects were noticed with the exception of the skin irritation, but tickling and discomfort in the larger air passages were noticeable with each inspiration. At 26 mg/cu m, eye and nose irritation was mild and could be tolerated for several minutes. There was no cough or sneezing. The taste of HF was reported at all three concentrations.

Largent [26] in 1961 presented the results of experimental inhalation studies on five human subjects. They were exposed 6 hours/day, 5 days/week, for 10-50 days, at average concentrations of 1.42-4.74 ppm (1.16-3.89 mg/cu m) HF. Slight irritation of the nose was noticed in all subjects at concentrations averaging 2.59-4.74 ppm (2.12-3.89 mg/cu m) ranging from 1.8-7.9 ppm (1.5-6.5 mg/cu m). No signs or symptoms of lower respiratory tract irritation were reported at these average concentrations.

Elkins [36] reported complaints of nosebleeds in workers engaged in the HF etching process and in one plant where welders were exposed at 0.4-0.7 mg of "fluorine"/cu m. No other environmental data were provided.

(e) Effects in Bone

Wilkie [37] in 1940 described osteosclerotic bone changes in a 64-year-old worker who had been engaged in the preparation of HF for 16 years. It was noted that in addition to HF, he probably was exposed to fluorspar ($CaF_2$) dust. Radiologic examination of the spine and pelvis showed very dense sclerosis and the forearms and lower legs revealed extensive

ligamentous ossification. A 24-hour urine specimen showed a urinary F excretion of 15.22 mg/liter. The patient was completely free from any symptoms.

Largent et al [38] in 1951 found slight skeletal sclerosis in three workers exposed to HF. The ages of the workers were 46, 54, and 55 years, and lengths of service were 17, 14, and 10 years, respectively. The roentgenologic findings in one worker were described as a slight increase in the density of the lower thoracic spine, with calcification extending into the attachments of the lateral ligaments, together with some increased density in both ilia and in the sacrum. None of the workmen were disabled. Average urinary F concentrations for the three workers over a 3-year period were 12.29, 10.62, and 10.09 mg/liter, respectively. The urine samples were collected in 1-gallon jugs while the men were away from work. The period of collection covered several days, giving a reasonable representation of the average urinary F excretion for each period of collection. Additional cases of osteosclerosis in HF workers are presented in the epidemiologic studies. [39-41, HR Henderson, written communication, September 1974]

(f) Absorption and Excretion of F

In 1947, Largent [42] reported on the urinary F excretion of men employed in alkylation plants using the HF process. Urine was collected in 1-gallon glass containers during the hours when the men were not at work until 2-3 liters had been accumulated. Analysis of 502 samples received in the course of almost 3 years showed that only 1 sample had an F concentration greater than 4 mg/liter. The frequency distribution of F concentrations in the urine samples was as follows: 78% (393) were in the

range of 0.1-0.9 mg F/liter; 18% (92) in the range of 1.0-1.9; 2% (11) in the range of 2.0-2.9; 1% (5) in the range 3.0-3.9; and 0.2% (1) in the range of 4.0 mg F/liter and above. It is probable that slightly higher urinary F concentrations would have been obtained if nonreactive (eg, wax-coated) containers had been used.

Collings et al [43] conducted a study to determine the absorption of inhaled HF. Two human subjects were exposed for an 8-hour period in an industrial environment to fluorides consisting primarily of HF and silicon tetrafluoride at an average airborne concentration of 3.8 mg F/cu m. Urine specimens were collected at 2-hour intervals during exposure and for approximately 2 days afterwards. There was a rapid rise in urinary F excretion during exposure, and a peak output was reached in 2-4 hours after cessation of exposure. Within 24 hours, the urinary F levels returned practically to base levels, although a slight elevation persisted into the following day. The total amounts of F excreted daily by the two subjects were as follows: day of exposure, 9.64 and 8.56 mg F; first day after exposure, 1.67 and 2.49; second day, 0.99 and 1.31; and third day, 0.89 and 1.34. The baseline daily urinary F excretions before exposure were 0.9 and 1.2 mg F, respectively.

For comparison, [43] the two subjects were then exposed to F at an average concentration of 5.0 mg F/cu m (in rock phosphate dust) "many weeks later," after the urinary F levels had been normal for "a long time." As with HF, there was a rapid rise in urinary F output during exposure, reaching a peak 2-4 hours after exposure and decreasing to base levels within 12-16 hours after exposure. The daily urinary F outputs of the two subjects were as follows: day of exposure, 10.0 and 9.95 mg F; first day

after exposure, 1.96 and 2.99 mg F; second day, 1.28 and 1.10 mg F; and third day, 0.73 and 0.98 mg F. In proportion to the respective airborne F concentrations, the rapidity of absorption and the total amount of F excreted would indicate that HF and inorganic fluoride dust are equally well absorbed and excreted.

In a follow-up study, Collings et al [44] compared urinalyses of two subjects exposed for 6 hours to airborne fluorides (the relative proportions of gaseous and particulate F were not given) averaging 4.8 mg F/cu m in an industrial environment. One subject was considered to have had no previous F storage; the other subject had worked approximately 8 years in a plant having exposure to fluorides. An excretion curve plotted for the two subjects was remarkably similar for the first day following exposure; thereafter, for an additional and concluding period of slightly less than 3 days, the previously exposed worker maintained a consistently higher base F level than the subject with no previous F exposure. The authors suggested that the persistent high base level may have been due to a cumulative effect from repeated exposures. Urinary excretion values ranged from about 0.1 to 1.3 mg F/2 hours and were determined on the entire urine output during the study. An additional seven industrial workers exposed to airborne F concentrations from 2.5 mg F/cu m to over 10 mg F/cu m were found to excrete urinary F concentrations ranging from 5.3 to 23 mg F/liter (postshift). The values 48 hours later (preshift) were from 1.2 to 5.6 mg F/liter. Among eight other workers with exposures ranging from 0 to over 10 mg F/cu m, preshift urinary F concentrations ranged from 0.8 to 4.0 mg F/liter. The corresponding postshift samples ranged from 3.2 to 17.0 mg F/liter. [44]

Rye [45] in 1961 reported on urinary F excretion studies in two workers with no previous F exposure. They were exposed on five different occasions for an 8-hour shift to HF and silicon tetrafluoride gases at an average concentration of 2.4 ppm (1.9 mg/cu m) as F. The urinary F levels increased during the first 2 hours of exposure from a baseline value of 0.5 mg/liter, to 4.0 mg/liter, reached a peak of 7-8 mg/liter in the ensuing 10 hours, and returned to within the range of 0.5-1 mg/liter by the evening of the same day, or early morning of the next day. During the following 24-72 hours, without any additional exposure, the urinary F excretion rose at the same time of day as during exposure to a peak of 4-5 mg/liter, and only on the third day after exposure did it remain consistently at the preexposure level. The total urinary F excretion after the 8-hour exposure to gaseous F at 2.4 ppm was 4.5 mg on the day of exposure, and 3.8, 3.6, and 1.2 mg on the following days, respectively. These levels were similar to preexposure excretion of 1-1.4 mg/day.

In 1961, Largent [26] studied HF inhalation and F excretion in 5 human subjects exposed for 6 hours/day, 5 days/week, for up to 50 days at HF concentrations averaging 1.42-4.74 ppm (1.16-3.89 mg/cu m). For the purpose of studying the absorption and excretion of fluoride, the dietary intake of F by all five subjects was measured throughout the entire period of observation. No unexpectedly large variation in the uptake of dietary F was detected. There was a marked increase in fecal elimination of F from preinhalation levels of 0.062-0.195 mg F/day to 0.262-0.7 mg F/day during HF inhalation. Since there was no significant change of dietary F intake during exposure, compared with preexposure levels, the increase in fecal F excretion was reported to have been attributable only to the HF exposure.

The average daily amounts of F excreted and the average concentrations of F in urine samples collected during the experimental inhalation of HF are given in Table III-3.

Daily variations in the amount (mg F/sample) and in the concentrations (mg F/liter) in the urine of two subjects showed a rapid rise in urinary F excretion during exposure with a return to near preexposure levels on days when no HF was inhaled. Urinalysis before and after completion of the experiment did not reveal abnormal findings (EJ Largent, written communication, January 1975).

TABLE III-3

FLUORIDE ELIMINATION IN URINE IN RELATION TO THE INHALATION OF HF BY FIVE HUMAN SUBJECTS

| Subjects | Number of Days | Average Concentration of Inhaled HF | | Average Urinary F Values | |
|---|---|---|---|---|---|
| | | ppm | mg/cu m | mg/liter | mg/day |
| E.L. | 15 | 1.42 | 1.16 | 4.49 | 3.46 |
| G.G. | 25 | 2.59 | 2.12 | 9.47 | 9.33 |
| K.W. | 30 | 2.72 | 2.23 | 7.75 | 8.83 |
| G.G.* | 15 | 2.84 | 2.33 | 10.58 | 11.47 |
| K.W.* | 15 | 2.98 | 2.44 | 7.77 | 9.40 |
| E.L. | 10 | 3.39 | 2.78 | 7.30 | 6.69 |
| G.B. | 50 | 4.22 | 3.46 | 9.62 | 15.51 |
| E.L. Jr.* | 15 | 4.59 | 3.76 | 17.86 | 12.20 |
| G.B.* | 20 | 4.73 | 3.88 | 12.10 | 19.60 |
| E.L. Jr. | 25 | 4.74 | 3.89 | 15.86 | 10.77 |

*These values relate only to the final weeks of the inhalation periods of these four subjects.

From reference 26

## Epidemiologic Studies

Machle and Evans [46] in 1940 published clinical findings from a group of workmen exposed principally to HF and, to a lesser degree, to calcium fluoride dust in a HF-acid manufacturing plant. At the beginning of the plant operation 9 years prior to the publication of this study, [46] mechanical difficulties caused frequent "severe" exposures. After installation of ventilation and controls, the air was ordinarily free from HF and fluoride dust. F was not detected in air samples taken in the center of the plant under normal operating conditions. Air samples taken in the neighborhood of equipment, or while repairs were being made, revealed 11-21 mg F/cu m. Periodic physical examinations including chest X-ray, hemoglobin, and red and white cell counts over a 5-year period did not show any significant findings. The mean urinary F excretion of exposed workers was 3.65 mg/liter. Of the 46 urine samples obtained over the 5 years (time of collection during day not given), 38 contained less than 4 mg F/liter; 4 contained 4-10 mg F/liter; and 4 had 16-24 mg F/liter. Roentgenologic examinations of the pelvis and spine of 10 men working with the greatest potential exposure did not show skeletal fluorosis after 5 years of intermittent exposure.

A study of a group of 74 men who had been exposed to HF for an average of 2.7 years was reported by Evans [47] in 1940. There had been many operating difficulties and the "fumes" had been so severe at times that windows and eyeglasses would etch in a short time. On a few occasions, there had been cases of upper respiratory tract irritation. Repeated chest X-rays over a 5-year period did not reveal any visible evidence of lung changes and did not differ from those of unexposed

workers. Periodic clinical examinations and data procured for health insurance purposes did not show a higher incidence of pulmonary infection in the exposed workers. Their death rate from pneumonia and other pulmonary infections was the same as that of unexposed plant employees.

Peperkorn and Kahling [39] in 1944 studied clinical and radiologic findings in 47 employees who were exposed to HF-acid vapor and cryolite. Because of the working arrangement of the plant, a distinction between these two groups of workers could not be carried out. No environmental data were given, but on visual inspection extremely fine "fluoride" dust was found all over the plant. Nearly all of the workers complained of mild-to-moderate back pain and stiffness which in some cases included the cervical spine. Some complained of pain in the thighs. Knee complaints were often mentioned. The majority of the men reported shortness of breath on exertion. There was little evidence of cough, expectoration, or asthmatic conditions. With the exception of HF burn scars on various parts of the body and rigidity of the chest in many workers, physical findings were essentially normal. Red and white blood counts, hemoglobin, sedimentation rate, and urinalysis were all within normal values. Only one worker, age 44, who had worked for 15 years with sodium fluoride had evidence of mottled teeth. Relatively few carious teeth were observed.

On radiologic examination of the osseous system 34, or 72%, of the 47 workers showed osteosclerotic changes. [39] Of these, 14 had first-degree osteosclerosis; 11, second-degree; and 7, third-degree. Characteristics of first-degree osteosclerosis included increased bone density and thickened and misshapen structure of the trabeculae with the marginal contours of the bones exhibiting slight blurring. In second-degree osteosclerosis, these

findings were more pronounced. The outer boundaries of the bones had become more irregular, insertions of the tendons had started to calcify, and the cortical substance of the long bones was widened, restricting the medullary canal. In third-degree osteosclerosis, the bone had become radiographically opaque and the insertions of tendons and ligaments and interosseous membranes were calcified.

In the previously described osteosclerotic changes, the first evidence of change was found in the pelvis and lumbar spine. As the process advanced, the changes spread to the rest of the spinal column and the ribs, with extremities affected last.

The degree of radiologic changes increased with the duration of employment. [39] Of the 47 workers examined, 40 were exposed during the whole work shift; of these, 8 with an average employment of 9 years ranging from 2 to 20 years had no osteosclerotic changes. Fourteen workers with first-degree changes had an average employment of 12 years, ranging from 3 to 17 years. Eleven workers with second-degree changes had an average of 18 years of employment, ranging from 7 to 27 years, and 7 workers with third-degree changes had an average employment of 22 years ranging from 15 to 32 years. Of the seven workers exposed only occasionally, five having an average of 21 years' exposure time ranging from 8 to 35 years had no osteosclerotic changes, while the remaining two workers had first-degree changes after 23 and 28 years of exposure, respectively. First-degree radiologic changes were observed no sooner than after 3 years of employment; second-degree changes, no sooner than after 7 years; and third-degree changes, no sooner than 15 years. Of the seven workers with third-degree changes, six were exclusively employed in the production of HF acid,

whereas only one case originated in the cryolite shop. Although a higher prevalence of third-degree osteosclerosis was observed in HF-acid workers, first- and second-degree cases were apparently distributed at random among the different occupations. For most cases, the subjective complaints ran parallel to the severity of radiologic changes.

The case history of a 40-year-old worker who was employed for 15 years in the HF plant was presented by Peperkorn and Kahling [39] in 1944. After 7 years of employment, he began to have "rheumatic pains" which, over the years, increased until he became totally disabled. He complained of stiffness in all joints, except hands and feet. He had difficulty in breathing when walking or climbing. On physical examination, he was prematurely aged, emaciated, and pale. He had a stiff posture and walked with small steps. Chest expansion was limited, as were movements of the spine, hips, and shoulders. Red and white blood counts, sedimentation rate, blood calcium, and urinalysis were all reported normal. No urinary F levels were obtained. X-rays of the skeletal system showed third-degree osteosclerosis.

Dale and McCauley [40] in 1948 provided data on medical and dental conditions of 40 workers engaged in the production of HF acid for 2-33 years. Eleven unexposed office and warehouse workers served as controls. No workplace airborne HF levels were given, but it was reported that window glass in buildings housing the HF acid retorts corroded in a few months' time and had to be replaced periodically. Some of the workers in close proximity to the retorts experienced transitory hyperemia of the exposed skin. This was encountered more frequently during warm weather and in those workers who perspired excessively. The skin of the faces and hands

appeared dehydrated, roughened, and irritated in the majority of the workers. Ulcers, chiefly on the hands and forearms, were observed in workers who had been splashed accidentally by HF acid. Dental examination showed fewer caries and fillings in the exposed group. Dental roentgenologic examinations revealed definite changes in the trabecular pattern of the osseous structure of the upper and lower jaws in 24 of the 40 workers and questionable changes in 8. The bone changes were characterized by an increase in the number and thickness of trabeculae and a corresponding decrease in the intratrabecular or canalicular spaces. Of the 32 with dental changes, marked bone changes were seen in 4 workers, moderate changes in 15, minimal changes in 5, and questionable changes in 8, with average years of exposure of 16.3, 14.7, 5.6, and 3.8 years, respectively.

The urinary fluoride excretion of 34 exposed workers which was determined by spot samples taken just before or just after working hours varied considerably, ranging from 0.89 to 49.3 mg/liter, with a mean of 10.8 mg/liter. [40] The distribution of urinary F was as follows: 4, 6, 10, and 14 workers had urinary F levels of 0.0-2.9, 3.0-5.9, 6.0-8.9, and over 9 mg/liter, respectively. On the basis of these single urine samples, there was no apparent correlation between urinary F excretion and the degree of bone changes found by dental roentgenologic examinations.

One of these workers, [40] aged 58, with an exposure history to HF and inorganic fluoride dust of 30 years, had been examined at the Cleveland Clinic. The results were reported in 1947 by McGarvey and Ernstene. [41] The workman felt well until 3 months before his visit to the clinic when he noted fatigue and dyspnea on exertion. The physical examination produced

essentially negative results, except that the anterior-posterior diameter of the thorax was increased and the expansion of the chest was greatly limited. Urinalysis, red blood count, hemoglobin, white cell count and differential count, platelet count, bone marrow, blood serum calcium and phosphorus, and alkaline and acid phosphatases were all within normal limits. The roentgenogram of the skeletal system revealed marked radiopacity of the vertebrae, ribs, and pelvic bones with the bone structure almost completely obscured. The changes in the lower extremities were less advanced, and the bones of the upper extremities showed even less alteration. Relatively slight changes were present in the bones of the skull. A spot urine specimen taken 3 years earlier showed that this workman had been excreting F at a level of 23.1 mg/liter. [40] Alveolar bone changes noted in the mandible and maxilla at that time were described as moderate.

In 1961, Rye [45] reported the results of clinical observations, taken over a 3-year period, of workers engaged in the production of phosphoric acid. In this process, HF and silicon tetrafluoride were released, but engineering controls maintained the workplace airborne F concentrations below 3 ppm. Continuous air samples collected for one regular 8-hour shift showed an average exposure to be 2.4 ppm as "gaseous fluoride." Periodic medical and radiologic examinations of the chest revealed no abnormal findings. The author reported that no significant complaints of gastrointestinal or respiratory ailments were found in comparison with a control group consisting of an unspecified number of operational employees and clerical workers not exposed to HF. Urinary spot samples at the end of the shift were taken for each worker at least once

every 3 weeks. Background urinary F levels were established by 5-10 determinations on each worker prior to his initial exposure. The author stated that no consistent urinary F excretion above 5 mg/liter was observed, but he gave no details.

The data obtained from studies of human exposures to HF alone are limited and insufficient to derive a standard which will prevent osteosclerosis. It therefore becomes necessary to make use of relevant studies which include reports on particulate or mixed particulate and gaseous inorganic fluoride exposures. The comparative absorption and excretion study of inhaled inorganic particulate fluorides and HF or silicon tetrafluoride by Collings et al [43] clearly indicates that the metabolism of F in humans is the same, independent of whether the F ion is inhaled as gaseous or as particulate inorganic fluorides. The absorption and excretion studies after inhalation of HF by Largent [26] and Rye [45] support the findings of Collings et al. [43] Based on the results of these investigations, relevant data obtained from any inorganic fluoride study can therefore be applied in establishing a standard for the prevention of osteosclerosis from HF exposure. The following inorganic fluoride studies are most relevant.

Derryberry et al [48] in 1963 reported the prevalence of osteosclerosis in 74 workers in a fertilizer-manufacturing plant in relation to fluoride exposure. Fluorides in the form of dust and gases in varying combinations and concentrations were produced throughout the process. Data were collected from clinical examinations, the working environment, and urinary F excretion throughout the 25 years of operation. Yearly, since 1952, a urine specimen was collected at the end of the shift on 5

consecutive days. An average daily (8-hour) exposure for each job was established by determining the time-weighted concentration of airborne F in the job environment. From these data, a weighted airborne exposure was calculated for the period of employment of each worker. Radiologic examination revealed a minimal, or questionable, increase in bone density in 17 (23%) of the 74 workers examined. The increased bone density was not associated with any musculoskeletal disability.

The range of individual TWA exposures to F was 0.50-8.32 mg/cu m, with 1.78-7.73 mg/cu m being associated with increased bone density or with a questionable increase in such density. [48] The difference in averages between the increased bone density group (average exposure: 3.38 mg F/cu m) and the remainder of the exposed group (average exposure: 2.62 mg F/cu m) was evaluated by NIOSH and found to be significant by both t test (one-tailed on logarithms of data, $t = 2.75$, $p = 0.0045$) and rank test ($Z = -2.2$, $p = 0.014$). Table III-4 shows the incidence of increased bone density as it relates to the level of time-weighted exposure during employment. It demonstrates that exposure to higher workplace airborne concentrations of F resulted in a relatively greater incidence of increased bone density.

Workers with a "high exposure," defined by Derryberry et al [48] as those with 50% or more of their postshift urine samples equaling or exceeding 4.0 mg F/liter, were likely to have increased bone density. Within the group of workers with increased bone density, 60.9% of the urine samples were 4.0 mg F/liter or greater in contrast with 47.5 % of the samples submitted by the group of workers without increased bone density. This difference is significant by both t test and rank test as performed by NIOSH (one-tailed analysis with $t = 2.44$, $p = 0.0095$ and $Z = -2.0$, $p =$

TABLE III-4

RELATIONSHIP OF WEIGHTED EXPOSURE DURING EMPLOYMENT TO INCIDENCE OF INCREASED BONE DENSITY IN 74 INORGANIC FLUORIDE WORKERS

| Weighted exposure mg F/cu m | 0-1.50 | 1.51-2.50 | 2.51-3.50 | 3.51-4.50 | 4.51-5.50 | 5.51-6.50 | 6.51-7.50 | 7.51-8.50 |
|---|---|---|---|---|---|---|---|---|
| Number of workers | 13 | 26 | 17 | 11 | 1 | 2 | 0 | 4 |
| Number with increased bone density | 0 | 5 | 6 | 4 | 0 | 1 | 0 | 1 |
| Percent | 0 | 19 | 35 | 36 | 0 | 50 | 0 | 25 |

From reference 48

0.036). The average excretion concentrations for the increased bone density group and the group without increase were 5.13 and 4.53 mg F/liter, respectively. Although the difference in average excretion concentrations is small, it is based on the averages of 38 urine specimens/man permitting a statistical evaluation suggesting that the difference is real ($t = 1.41$, $p = 0.085$ and rank test, $Z = -1.8$, $p = 0.023$). Table III-5 demonstrates that as the average urinary fluoride concentration increased there was a corresponding increase in the percentage of suspected osteosclerosis cases. Studies by the US Public Health Service [49] in 1967 evaluated the effects of chemical irritants on exposed workers in a chemical plant where HF was one of the primary chemicals produced. The two major sources of HF exposure were the firing kilns and process equipment leaks. Twenty-eight samples of airborne HF were taken with sampling periods ranging from 10 to 30 minutes. Results ranged from 0.07 to 10.0 ppm (0.06-8.2 mg/cu m), with a mean of 1.03 ppm (0.85 mg/cu m). Thirty-three samples for particulate F

TABLE III-5

RELATIONSHIP OF AVERAGE POSTSHIFT URINARY F CONCENTRATION TO INCIDENCE OF INCREASED BONE DENSITY IN 74 INORGANIC FLUORIDE WORKERS

| Average urinary F excretion mg/liter | 2-2.9 | 3-3.9 | 4-4.9 | 5-5.9 | 6-6.9 | 7-7.9 | 8-8.9 | 9-9.9 | 10+ |
|---|---|---|---|---|---|---|---|---|---|
| Number of workers | 10 | 23 | 20 | 9 | 3 | 1 | 5 | 2 | 1 |
| Number with increased bone density | 1 | 4 | 5 | 3 | 1 | 0 | 3 | 0 | 0 |
| Percentage with increased bone density | 10 | 17 | 25 | 33 | 33 | 0 | 60 | 0 | 0 |

From reference 48

were all under 0.5 mg/cu m, with a range of 0.1-0.49 mg/cu m. Pulmonary function tests were performed on 305 chemical workers including 11 workers exposed to HF, and a control group of 88 workers in a box plant. The mean of the chemical plant workers' ages was 44 years and these workers were, on the average, 14 years older than the box-plant workers. The observed values for Forced Vital Capacity (FVC), 1-second Forced Expiratory Volume (FEV 1), and FEV 1/FVC for the total group were within about 3% of the predicted normal with no significant difference between the chemical workers and the control group.

The residual volume (RV) expressed as percentage of total lung volume (TLVol) was 30.8% in the chemical workers, as contrasted with 26.8% for the box plant workers, with both values within normal limits (35% being the upper limit of normal). [49] As pointed out by the authors, the difference can be explained by the higher average age of the chemical workers, since

RV/TLVol usually increases with advancing years.

From the analysis of the pulmonary function data, the authors [49] concluded that ventilatory function in the chemical and box plant workers was, in most of the workers, within the acceptable age-adjusted normal limit. The decrease in function found in a small percentage of the workers appeared to be caused by smoking and not to be work-related.

Before-shift and after-shift urinary excretions were analyzed for F in 25 workers exposed to HF or particulate fluorides and in 10 nonexposed office employees. [49] Before-shift specimens were collected after the workmen had been away from the plant on their days off, and after-shift samples were collected after each consecutive workday for 5 days, and pooled for each man. The before-shift urinary F concentrations ranged from 0.33 to 4.48 mg/liter, compared to 0.95-26.6 mg/liter for the after-shift samples. Corresponding levels for the control group were 0.50-1.88 mg F/liter before the shift, and 0.50-2.38 mg F/liter for after-shift specimens. Of the 11 HF workers, 4 exceeded 5 mg F/liter (6.85, 8.80, 17.5, 26.6). The two workers with the highest urinary F levels had accidental exposures ("gas out" and reboiler leak) during the week of urine collection. Roentgenologic examinations of the lumbar spine of four HF workers with after-shift urinary F concentrations of 4.31, 6.85, 17.5, and 26.6 mg/liter did not show any skeletal fluorosis.

Additional follow-up data on environmental and urinary F levels on the same plant population have been provided by HR Henderson (written communication, September 1974). Data obtained between March 1968 and April 1973 using an automatic HF analyzer showed the following results: 2.1% of the total of 23,280 samples were 5 ppm (4.1 mg/cu m) and over; 1.3%,

between 4 and 5 ppm (3.3-4.1 mg/cu m); 1.5%, between 3 and 4 ppm (2.5-3.3 mg/cu m); 3.2% between 2 and 3 ppm (1.6-2.5 mg/cu m); 11.4%, between 1 and 2 ppm (0.8-1.6 mg/cu m); and 80.3%, between 0 and 1 ppm (0-0.8 mg/cu m). Periodic urinary F samples taken for 6-10 years on 13 HF workers revealed that the average before-shift levels for the workmen ranged from 2.0 to 5.7 mg/liter, while average after-shift samples ranged from 4.2 to 24.7 mg/liter.

One of the four workers who earlier [49] had no X-ray evidence of osteosclerosis showed borderline or "first-degree" osteosclerosis on follow-up examinations 2 years later (HR Henderson, written communication, September 1974). There was no disability associated with the increased bone density. His average before-shift urinary F level was 5.3 mg/liter, ranging from 2.6 to 16.3 mg/liter, and average after-shift urinary F level was 11.5 mg/liter, ranging from 2.0 to 30.0 mg/liter. This worker had been employed for 11 years as a helper and kiln operator with HF exposure in the higher range of air concentrations sampled around the furnace.

In 1972, Kaltreider et al [50] reported the results of roentgenographic examinations and urinary F studies of potroom workers in two aluminum plants. In one plant, X-ray examinations of 79 potroom workers revealed increased bone density in 76. Forty-six workers (58.3%) were classified as having slight fluorosis, showing only accentuation of trabeculation and slight blurring of the bone structure; 4 (5.1%) had "moderate, diffuse structureless" bone appearance; and 26 (33%) were classified as having marked fluorosis. Limited motion of the dorsolumbar spine was found in 22 (20.6%) of the entire group of 107 potroom workers, compared to none in a control group (108 workers with no history of F

exposure). The 8-hour time-weighted average F exposures of the potroom workers ranged from 2.4 to 6.0 mg F/cu m. The average urinary F concentration in spot samples taken during the day was 8.7 mg/liter for pot tenders, 9.8 mg/liter for tapper-carbon changers, and 9.6 mg/liter for cranemen. The average urinary F excretion for the controls was 0.7 mg F/liter. With the exception of a higher incidence (no data given) of aching joints, particularly those of the upper extremities in the exposed group, the medical history was not different in the two groups. Limited motion of the dorsolumbar spine was found in 22 (20.6%) of the potroom workers compared to none in the control group.

In the second plant, [50] roentgenographic examination of the spine showed no increased bone density in 231 potroom workers. No airborne F concentrations were given. Since the pots were hooded in this plant, the authors concluded that airborne F exposure was less than that in the other plant where electrolytic cells were not hooded.

In 1972, NIOSH conducted a study of an aluminum reduction facility for the primary purpose of collecting and analyzing airborne dust, coal tar pitch volatiles, fluorides, carbon monoxide and sulfur dioxide. [51] In addition, a limited amount of medical information was provided by the plant medical department. Of about 200 potroom workers receiving annual pulmonary function testing, 10 individuals with known or suspected respiratory problems were selected for more detailed tests consisting of chest X-rays, spirometry, and steady-state CO diffusion studies. Eight individuals (presumably all members of the selected group) were reported to have a respiratory problem prior to employment or a strong family history of asthma. Neither smoking histories nor actual results of respiratory

tests were reported, but 7 of the 10 workers were stated to have marked-to-severe obstructive airway changes as evidenced by a reduction of FEV 1 and maximum breathing capacities. Although the age distribution was not provided, the examining physician expressed concern about "the young age distribution of the workers"; one of the workers was 39, and three workers were in their early forties. In addition, the results of urinary F analyses covering a 1-year period and involving about 155 workers (including potroom and cryolite workers) were made available. The average of the preshift samples was 2.35 with a range of 2.0-2.8 mg F/liter. The average of the postshift samples was 4.8, ranging from 3.2 to 6.5 mg F/liter. Results of breathing-zone and general air samples for gaseous and particulate F in the potroom over a 5-day period were all less than 0.094 mg F/cu m. Breathing-zone and general air samples taken during the same time period in the cryolite area were all less than 0.34 mg F/cu m (gaseous and particulate F). Because there was a previous history of respiratory disorder in most of those exhibiting obstructive airway changes, and fluoride was but one of several contaminants present in the potroom area, it is not reasonable to conclude that obstructive airway changes developed as a direct result of exposure to gaseous and particulate fluorides.

## Animal Toxicity

Inhalation studies involving animals exposed to HF at concentrations ranging from 3 to 660 ppm (2.5-540 mg/cu m) were reported by Ronzani [52] in 1909. Five guinea pigs and five rabbits died in 0.5 and 1.5 hours, respectively, while being exposed to HF at an airborne concentration of 660

ppm (540 mg/cu m). When five guinea pigs and five rabbits were exposed to HF at 250 ppm (205 mg/cu m), they died in 1.0 and 3.0 hours, respectively. All animals showed severe signs of irritation from the start of the experiment, with increasingly labored breathing. Autopsy showed ulcerations of the upper respiratory tract and of the cornea of the eyes. The lungs were hyperemic and edematous. At 50 ppm (40 mg/cu m), five guinea pigs died in 2 hours, whereas the five rabbits displayed severe signs of physical distress after 3 hours. At a concentration of 30 ppm (25 mg/cu m), guinea pigs died after one day, while rabbits, exposed to HF at the same concentration, were in such poor condition after 3 days of exposure that the experiment had to be discontinued. Continuous exposure at 10 ppm (8 mg/cu m) for 5 days was not fatal to either species. In addition to labored breathing, the guinea pigs showed only slight irritation of the eyes.

Fifteen rabbits, 21 guinea pigs, and 4 pigeons were then exposed to HF at 10 ppm (8 mg/cu m) for two 3-hour periods/day for 31 days. During these periods, two rabbits, seven guinea pigs, and one pigeon died. At autopsy, opacity of the corneas with ulcerations, lesions of the nasal mucous membranes, emphysematous lungs, bronchopneumonitis, and interstitial pneumonitis were found. The autopsy of one of the rabbits surviving the exposure periods showed similar, but less severe, pathologic findings. All surviving animals had lost up to 23% of their original weight and had severe anemia. After immunization against typhus, four surviving rabbits were considerably less efficient in producing agglutinizing substances than were controls; after immunization five experimental guinea pigs showed a marked decrease in production of specific antibodies. Exposed guinea pigs

had reduced resistance to bacterial infection in the lungs. While experimental animals were less resistant than controls to the effects of inoculation with diplococcus and tuberculous bacilli, the opposite was true in the case of anthrax.

Further experiments [52] using HF concentrations of 7.5, 5, and 3 ppm (6, 4, and 2.5 mg/cu m) established 3 ppm (2.5 mg/cu m) as a no-effect concentration. A 30-day exposure of 16 rabbits, 20 guinea pigs, and 3 pigeons to HF at 3 ppm (2.5 mg/cu m) did not produce any pathologic changes.

Machle et al [35] in 1934 reported on acute effects in rabbits and guinea pigs exposed to HF at concentrations of 24-8,000 mg/cu m for periods ranging from 41 hours to 5 minutes. Three rabbits and three guinea pigs were used for each exposure. Evidence of eye and respiratory tract irritation was noticeable in all animals at all concentrations, although for those animals exposed at 50 and 24 mg/cu m for 5-15 minutes, signs were mild and not immediate. Slowing of the respiratory rate was uniform and particularly noticeable in rabbits. Paroxysmal coughing and sneezing occurred more frequently as the airborne HF concentration was increased. One rabbit exposed 6 hours/day for a total of 41 hours at 24.5 mg HF/cu m suffered considerable liver and kidney damage. Weakness and the appearance of illness were prominent in all animals exposed at more than 500 mg/cu m for 15 minutes or longer. Signs became increasingly severe as the airborne HF concentration was increased. Animals exposed at concentrations of 3,000 mg/cu m or more for 5-15 minutes exhibited edema or cloudy swelling of organs and tissues. No deaths occurred at concentrations of 1,000 mg/cu m for up to 30 minutes of exposure, at 100 mg/cu m for 5 hours, or at 24

mg/cu m for 41 hours. Rabbits which survived returned to normal appearance and activity in a few days to a few weeks, while guinea pigs showed a definite tendency to delayed response and death between the fifth and tenth week following exposure. The predominant lesions found in exposed animals were pulmonary hemorrhage, congestion, emphysema, and edema, with secondary infection in many instances; hepatic congestion with evidence of parenchymal necrosis and fatty degeneration; splenic congestion and edema; renal congestion, edema and tubular necrosis; and myocardial congestion, edema, and necrosis. Corneal erosions and ulcerations of nasal turbinates were observed in numerous animals exposed to "higher" concentrations. A number of these changes were also common to control groups, and were therefore considered as normal occurrences. The authors were unable to determine to what extent these changes were due to spontaneous disease processes, infection, nutritional causes, or to possible dietary deficiencies.

In 1935, Machle and Scott [53] studied the distribution of F in the tissues of animals exposed to airborne HF at different concentrations and exposure times (expressed in milligram-hours). Six rabbits were used as controls. The exposed animals were divided into two groups. Group 1 consisted of four rabbits with an exposure of 1 mg-hour or less; three were exposed to HF at 53 mg/cu m, and one to HF at 24 mg/cu m. Group 2 consisted of four rabbits, one guinea pig, and one monkey, with an exposure of 4.56 mg-hours; all were exposed to HF at 15.2 mg/cu m. The interval between exposure and autopsy ranged from 9 to 14 months. The results indicated that abnormal amounts of F were held in tissues, chiefly in bones, for as long as 14 months following exposure.

Machle and Kitzmiller [54] in 1935 reported the effects of airborne HF on five rabbits, three guinea pigs, and two Rhesus monkeys exposed at a concentration of 15.2 mg/cu m for 6-8 hours daily except on weekends until a total of 309 hours of exposure had accumulated. Eight rabbits, five guinea pigs, and one monkey were used as controls. Except for two guinea pigs, all animals survived 8 months after conclusion of the exposure; all except one monkey were then killed and necropsied. There was no pronounced response following introduction of the animals into the exposure chamber. Occasional coughing was noted only in one monkey during the first week of exposure. Slight lacrimation was exhibited by all the animals. Erythrocyte counts of the exposed rabbits were significantly lower than those of controls. No evidence of injury to the corneas or nasal passages was observed. Significant pathologic findings were limited to the lungs, liver, and kidneys and were marked in the two guinea pigs that died during the study. One guinea pig that died after 160 hours of exposure showed a large pulmonary hemorrhage. The bronchial epithelium was thickened and sloughed off in many areas. The liver was moderately congested and showed advanced fatty degeneration. The other guinea pig that died after 134 hours of exposure showed a low-grade inflammatory reaction in the alveolar walls with atelectasis, and marked degenerative changes and hyperplasia of the bronchial epithelium. The liver showed scattered necrosis, some changes in fatty tissue, and diffuse periportal fibrosis. The kidneys had spotty tubular necrosis. The guinea pig that survived showed pulmonary hemorrhages, alveolar exudates, and cellular infiltration of the alveolar wall with irregular thickening. The liver showed considerable lobular degeneration and necrosis. The lungs of all rabbits revealed leukocytic

infiltration of the alveolar walls with or without edema or thickening, and secondary infection was evident in two animals. Marked degeneration of fatty tissue was seen in the livers of two rabbits. Extensive renal tubular degeneration and necrosis associated with fibrous tissue replacement were found in all exposed rabbits. Glomerular changes consisted of inflammation and degeneration. Except for the kidneys, which showed long-standing degenerative and inflammatory changes, the organs of the monkeys showed scarcely any lesions attributable to exposure.

Stokinger [55] in 1949 reported the exposure of 29 rats, 20 mice, 20 guinea pigs, 18 rabbits, and 4 dogs to gaseous HF at 25 mg HF/cu m and 7 mg HF/cu m for 6 hours/day, 6 days/week for 5 weeks. A second group of 15 rats, 20 mice, 10 guinea pigs, 10 rabbits, and 5 dogs was exposed at 7 mg HF/cu m for the same period. Subcutaneous hemorrhages, particularly noticeable around the eyes and on the feet, developed in rats within a few days. Mice were similarly affected, but to a lesser degree. In dogs, an inflammation of the scrotal epithelium became apparent after the third day of exposure. These findings were confined mainly to the group exposed at the 25 mg HF/cu m level, but hemorrhagic areas, less severe in nature, did develop on the feet of rats at the 7 mg/cu m level. Death occurred only at 25 mg HF/cu m and exclusively in rats and mice which had a mortality rate of 100%. Deaths occurred in rats throughout the entire exposure period, while all mice died by the seventieth hour of exposure. At the 25 mg HF/cu m level, rats showed pronounced loss in weight; rabbits, only a slight loss; dogs, no change; and guinea pigs, after a consistent gain, a loss in weight following the third week of exposure. Approximately normal weight gains were observed in all animals at the 7 mg HF/cu m level.

Determinations of blood calcium, alkaline phosphatase, and serum protein in dogs and rabbits showed no changes of significance at either level. Overnight urinary F excretion of rabbits exposed at the 7 mg HF/cu m level increased 5-fold over control values. There was a significant increase in blood fibrinogen level in dogs and rabbits exposed to HF at 25 mg/cu m, while the prothrombin time remained normal.

At autopsy, 27 out of 44 animals examined showed hemorrhages and edema of the lungs. [55] Degenerative testicular changes and ulceration of the scrotum were found in four dogs. In rats, renal cortical degeneration and necrosis were noted in 27 of 30 animals. The above pathologic changes were found only at the 25 mg HF/cu m level. At the 7 mg HF/cu m level, localized hemorrhagic areas in the lungs were noticed only in one out of five dogs. Serial determinations of fluoride concentration in bone of animals exposed to HF from 25 to 95 hours at 25 mg/cu m showed a progressive increase of fluoride. The F content of the teeth of rats increased as much as 300%. Somewhat smaller increases were found in the femur. Increases in the F content of the maxillary and mandibular bones of dogs ranged from 200 to 300%. The F content of bones of animals exposed to HF at 7 mg/cu m for 166 hours was, on the average, somewhat lower than that found at the higher level. At almost equal Ct (concentration x time) values of 1200 and 1162 (25 mg HF/cu m for 50 hours and 7 mg HF/cu m for 166 hours, respectively), F deposition was approximately the same.

Blood F levels following exposure to HF were determined by Smith and Gardner [56] in 1949. Ten rabbits were exposed 6 hours/ day for 1-5 days to HF at a concentration of approximately 29 mg/cu m. Two rabbits served as controls. Blood specimens, obtained by heart puncture, were taken from

two animals after each exposure day. Postexposure samples were obtained at intervals up to 6 days after termination of exposure. Blood F levels determined immediately after exposure to HF ranged from 35 to 122 μg/100 ml blood, as compared to 9-15 μg/100 ml in the two control animals. The blood F level reached a plateau during the first day of exposure and did not significantly increase in spite of continued exposure. Lower, but still abnormally high, blood F levels (15-48 μg/100 ml) persisted for at least 3 days after cessation of exposure. Normal values were reached 6 days after exposure. The only outward evidence of an adverse effect was irritation of the eyes.

Stokinger et al [57] in 1950 reported the effects of airborne HF on 20 rats exposed 6 hours/day, 5 days/week at an average concentration of 8.0 mg HF/cu m for a total of 124 hours. A second group of 10 rats was exposed on alternate days to the same concentration for a total of 62 hours. One animal in the second group died, but the cause of death appeared to be infection and not the exposure. The weights of the animals never went below preexposure values; in fact, a progressive weight increase occurred during exposure. Microscopic examinations revealed no lesions attributable to the exposure to HF. The F content of teeth and bones in the first group of animals was 1.5-1.8 times the F content of similar teeth and bones in the second group.

In 1955, Klauder et al [24] described the irritant action caused by application of various concentrations of HF acid on the skin of rabbits. Hydrogen fluoride at concentrations of 1-50% was placed separately on the inferior dorsal aspect of the shaved ear, allowed to remain for 5 minutes, then rinsed in running water for 15 minutes. No reaction resulted from

applications of 1-4% HF acid. Transitory blanching occurred from applications of 6-10% HF acid. After applications of 12-22%, crust formation appeared in about 24 hours at the site of the blanching and disappeared in about one week. Applications of 25% and 30% HF acid caused blanching, followed by redness and, later, by crust formation. These effects, along with blisters and superficial ulceration, were observed at 35% and 40%. The reactions were more pronounced when the HF acid concentration was raised to 50% and were followed by deep ulcerations. In the study employing higher concentrations, acid solutions were applied to both ears of some animals, after which one ear was rinsed with water and the other was not. The reaction on the unrinsed ear was more pronounced than that of the rinsed one, substantiating the importance of immediately rinsing the site of HF acid contact.

Rosenholtz et al [58] in 1963 reported on brief single exposure effects in animals. Rats were exposed in groups of 10 to HF in various concentrations for single 5, 15, 30, and 60-minute periods. The calculated LC50 values for rats were 4,060, 2,200, 1,670, and 1,070 mg/cu m, respectively. The LC50 for 10 guinea pigs exposed for 15 minutes was 3,540 mg/cu m. All animals showed signs of respiratory distress and conjunctival and nasal irritation. Pathologic studies revealed nasal passage necroses, renal tubular damage, hepatocellular congestion and inflammation, and acute inflammation of the skin. No pathologic changes of the lower respiratory tract were reported.

The acute toxicity of short 5-minute exposures to HF was reported by Higgins et al [59] in 1972. Ten rats and 15 mice in each group were exposed to HF in a series of concentrations to determine LC50 values. The

animals were observed for 7 days following exposure in order to include any delayed deaths due to pulmonary edema. The 5-minute LC50 for rats was 18,200 ppm (14,900 mg/cu m) and for mice it was 6247 ppm (5120 mg/cu m).

The response of enzyme systems in the skin of the guinea pig to the toxic action of the fluoride ion was investigated by Carney et al [60] for the purpose of evaluating the effectiveness of various agents commonly used for first-aid treatment of HF and HF-acid burns. The experimental system used consisted of freshly excised guinea pig ear skin incubated at 37 C on a special growth medium to which various amounts of HF acid or sodium fluoride were added. First-aid treatments were simulated by adding fluoride-binding compounds to the medium or by transferring the skin to a fresh fluoride-free medium. The responses measured were: the inhibition of enolase activity, skin respiration (oxygen uptake), and tetrazolium reductase activity. The results indicated that transferring the skin to a fresh medium to simulate washing was an effective method of counteracting the toxicity of the fluoride ion. It was pointed out by the authors, however, that washing can remove fluoride from the surface of the skin, but if calcium compounds (F binding agents) are injected into the tissues to inactivate F ions, the compound calcium fluoride is formed which remains in place. Two calcium compounds, calcium chloride and calcium gluconate, were found to be nontoxic to skin in the laboratory and were both effective in counteracting the fluoride ion. Magnesium was less effective than calcium chloride and benzathonium chloride did not produce a significant effect. Lanthanum chloride effectively removed fluoride but had an adverse effect upon the respiration and viability of skin cells.

In summary, animal studies indicate the primary toxic effect of HF to be on the respiratory system [35,52,54,55] with pathologic tissue changes

also found in the kidneys [55,58] and liver. [54,58] Short exposures of up to 3 hours to HF at concentrations of 200-20,000 mg/cu m resulted in severe irritation of the respiratory tracts and eyes of rabbits, dogs, guinea pigs, rats, and mice, followed by death in the majority of the exposed animals. [35,52,58,59] The results of prolonged exposure to airborne HF at concentrations more relevant to determining a safe exposure limit were reported in three studies. [52,54,55] Rats, mice, guinea pigs, rabbits, and dogs exposed to HF at a concentration of 25 mg HF/cu m for 6 hours/day 6 days/week for 5 weeks [55] showed moderate pulmonary edema and pulmonary hemorrhage. Renal degeneration and renal necrosis were found in rats. Pulmonary, renal, and hepatic tissue damage in various degrees in rabbits, guinea pigs, and monkeys occurred at a lower concentration (15 mg HF/cu m) but in a similar exposure period. [54] Localized hemorrhagic areas in the lungs were noticed in one out of five dogs at 7 mg/cu m, [55] while inflammatory respiratory changes and a mortality of 10/40 in rabbits, guinea pigs, and doves were reported at about the same exposure level and period in another experiment. [52] When exposed to airborne HF at 2.5 mg/cu m, 6 hours/ day for 31 days, rabbits, guinea pigs, and doves experienced no adverse effects. [52] Corneal ulcerations were observed in all animals at concentrations as low as 8 mg HF/cu m. [52]

The most significant findings of the animal studies, besides the effect on the respiratory system, were renal tissue damage [55,58] and hepatic [54,58] tissue damage. These effects occurred as the result of exposures to HF at concentrations as low as 15 mg/cu m. [54]

Several animal studies [53,55,57] have shown that inhalation of HF resulted in increased deposition of F in osseous tissue. The F content of

various bone structures following exposure to HF at 25 mg/cu m increased progressively as much as 300% as exposure time was extended from 25 to 95 hours. At the 7 mg HF/cu m exposure level, the F content of these bone structures was somewhat lower. [55]

The destructive action of the F ion on enzyme systems in the skin of the guinea pig was counteracted by the use of calcium, magnesium, and lanthanum compounds. [60] Calcium proved to be more effective than either magnesium or lanthanum. In addition, the use of lanthanum had an adverse side effect.

Table XII-3 summarizes the above mentioned animal exposure-effect data.

Correlation of Exposure and Effect

(a) Acute Irritating Effects

Two workers splashed with HF and thus exposed to airborne HF at a concentration estimated by the authors to be between 10,000 and 100,000 ppm (8,200-82,000 mg/cu m) for a few minutes died from pulmonary edema 2 hours following the initial exposure. [32]

During a short exposure to airborne HF at 100 mg/cu m, smarting of the skin and marked eye and respiratory irritation were observed. [35] This was the highest concentration that could be tolerated for more than one minute. At 50 mg HF/cu m, the same effects were noticed with the exception that the skin irritation was no longer experienced. At 26 mg HF/cu m, eye and nose irritation was mild but could be tolerated for several minutes.

Humans experimentally exposed to HF at concentrations which averaged 2.59-4.74 ppm (2.12-3.89 mg/cu m) and ranged from 1.8 to 7.9 ppm (1.5-6.5 mg/cu m) for up to 50 days developed mild irritation of the skin, eyes, and nose. [26] No signs or symptoms of lower respiratory tract irritation were reported at these airborne concentrations of HF. Exposure at an average concentration of 1.49 ppm (1.2 mg/cu m) ranging from 0.9 to 2.0 ppm (0.7-1.6 mg/cu m) did not result in any adverse effect.

(b) Effects of Chronic Exposure on the Respiratory System

Only one of the above studies [49] evaluated the respiratory effects of chronic exposure to HF. Ventilatory pulmonary function tests were performed on 305 chemical workers including 11 workers exposed to HF. Results of determinations of F in samples of air taken during the study ranged from 0.07 to 10.0 ppm HF (0.06-8.2 mg/cu m) with a mean of 1.03 ppm (0.85 mg/cu m). The observed values for FVC, FEV 1, and RV showed no significant difference between chemical workers and a control group.

Another study [45] did not reveal a higher incidence of respiratory complaints or abnormal chest X-rays in workers engaged in the production of phosphoric acid when compared to a control group. Air concentrations of HF and silicon tetrafluoride emitted during the process were kept, according to the author, below 3 ppm (2.5 mg/cu m), measured as HF. Results of air sampling were not reported except for one 8-hour exposure to gaseous fluoride which was 2.4 ppm (2.0 mg/cu m).

In a study of an aluminum reduction facility, 10 potroom workers with known or suspected respiratory problems were selected for further study out of 200 workers receiving annual pulmonary function testing. [51] Seven of the 10 were found to have marked-to-severe obstructive airway changes.

Determinations of airborne HF in the potroom made during a 5-day period were all less than 0.094 mg F/cu m. [51]

One human subject exposed to HF for 6 hours/day for 15 days at an average concentration of 1.42 ppm (1.16 mg/cu m) and exposed for 10 days at 3.39 ppm (2.78 mg/cu m) did not have abnormal pulmonary function 3 years after the experiment (EJ Largent, written communication, January 1975). One animal study [54] reported "significant pathological findings" in the lungs of five rabbits and three guinea pigs exposed to HF at 15.2 mg/cu m for 6-8 hours daily, except weekends, until 309 hours of exposure had accumulated.

(c) Effects on Kidneys

Animal studies [54,55] indicated renal tissue damage resulting from prolonged exposure to HF. The lowest airborne concentration of HF at which renal degeneration and necrosis occurred was 15.2 mg/cu m with a total exposure time of 309 hours. [54]

Serial urinalyses were performed on five human subjects (EJ Largent, written communication, January 1975) exposed in six separate experiments for 6 hours/day, 5 days/week up to 50 days to HF at six different concentrations, the averages of which ranged from 1.42 to 4.74 ppm (1.16-3.89 mg/cu m); the urinalyses did not show any abnormal findings.

(d) Effects on the Skeletal System

Several studies have reported osteosclerosis [37-39] and one study [40] has reported changes in the trabecular pattern of the osseous structure of the upper and lower jaws. However, data on airborne HF exposure were not given, making a correlation impossible. Changes in the skeletal system were found first in the pelvis and the lumbar vertebrae

[39] or were more easily discernible in those regions. [37,38] Dale and McCauley [40] recommended periodic X-ray examination of the jaws during routine examinations for fluorosis in workers exposed to chemicals. One study [46] found no evidence of skeletal fluorosis in 10 workers occasionally exposed to HF at 11-21 mg/cu m during repairs of leaking equipment. In another study, [49] four HF workers, selected for radiologic examinations of the spine because of their high postshift urinary F concentration, showed no changes in bone density at the time of the study. One of these workers showed "first-degree" osteosclerosis on a follow-up examination 2 years later (HR Henderson, written communication, September 1974). The average exposure to HF in the work area was 1.03 ppm (0.85 mg/cu m) ranging from 0.07 to 10.0 ppm (0.06-8.2 mg/cu m). The worker with osteosclerosis was a kiln operator and was exposed to HF at the higher range of concentrations found around the furnace.

The absence of environmental data in HF studies on osteofluorosis, as discussed in the section Epidemiologic Studies, makes it necessary to utilize data obtained from inorganic fluoride studies. Comparative inhalation studies of HF and inorganic fluorides [43] showed no difference in the metabolism of F.

The most comprehensive inorganic fluoride study which correlated environmental data and radiologic findings with changes in the osseous system provides sufficient data to establish a threshold for osteofluorosis. [48] From numerous determinations of F in air made over a period of many years, an 8-hour time-weighted average exposure was calculated for the period of employment of each worker. Results ranged from 0.50 to 8.32 mg F/cu m with an average of 2.81 mg F/cu m. Increased

bone density or a questionable increase in such was found in 17 of the 74 workers examined. The average exposure experienced by these 17 workers was 3.38 mg F/cu m, ranging from 1.78 to 7.73 mg F/cu m. The difference in averages between the increased bone density group (3.38 mg F/cu m) and the remainder of the exposed group (2.62 mg F/cu m) was statistically significant. Also, exposure to HF at higher airborne concentrations resulted in a relatively greater incidence of increased bone density.

In an aluminum plant study, [50] 76 osteofluorosis cases in a group of 79 potroom workers were found; 46 were classified as minimal, 4 as moderate, and 26 as marked osteofluorosis. Restrictive motion of the spine was reported in 22 workers with osteofluorosis. Moderate and marked osteofluorosis were observed only after 15 or more years of employment. Workroom levels ranged from 2.4 to 6.0 mg F/cu m.

(e) Absorption and Excretion of F

Several studies [26,43,45] have evaluated urinary F excretion during and shortly after exposure. They showed a rapid rise in urinary F excretion during the first few hours of exposure, reaching a peak 2-4 hours after exposure and returning to near normal by the next day.

In six HF workers with osteosclerosis, urinary F excretion data were reported. Three workers with markedly increased bone density had urinary F concentrations of 23.1 mg/liter (spot sample), [40] 15.22 mg/liter (24-hour sample), and 1.73 mg/liter (24-hour sample). [37] Three workers with minimal bone changes had urinary F levels of 9.3-12.3 mg/liter in samples collected after work. [38] In 25 workers exposed to HF and particulate fluorides in a chemical plant, preshift urinary F concentrations ranged from 0.33 to 4.48 mg/liter compared to 0.95-26.6 mg/liter for the postshift

samples. [49] A limited number of determinations of airborne HF (26) averaged 0.85 mg/cu m. Thirty-eight determinations of airborne particulate F were all under 0.5 mg/cu m. One worker with first-degree osteosclerosis had an average preshift urinary F level of 5.3 mg/liter, ranging from 2.6 to 16.3 mg/liter and an average postshift excretion of 11.5 mg/liter, ranging from 2.0 to 30.0 mg/liter (HR Henderson, written communication, September 1974). In the same communication, Henderson related that periodic urinary F levels over a 10-year period of 13 HF workers averaged from 2.0 to 5.7 mg F/liter (preshift) and 4.2-24.7 mg F/liter (postshift). Definite and questionable trabecular changes of the upper and lower jaws in 32 of 40 HF workers were associated with an average urinary F level (spot samples) of 10.8 mg/liter, ranging from 0.89 to 49.3 mg/liter. [40] Workers with moderate to marked changes had an average exposure of 15.1 years, while for minimal or questionable changes, the exposure period was 6.0 years.

In order to compare urinary excretion of an industrial worker presumed to have stored fluoride in the skeletal system with the excretion from a subject without stored F, two subjects were exposed to airborne fluorides averaging 4.8 mg F/cu m for 6 hours; subsequent excretion curves for the two subjects were very similar for the first day, but thereafter the previously exposed worker maintained a consistently higher base level than the subject with no previous F exposure. [44] Urinary concentrations ranged from about 0.1 to 1.3 mg F/2 hours. [44]

More comprehensive urinary F excretion data [48,50,51] have been provided in inorganic fluoride studies. In a fertilizer-manufacturing plant, [48] 17 of 74 workers with a minimal or a questionable increase in

bone density had an average postshift (average of 38 specimens/man) urinary F excretion of 5.18 mg/liter, ranging from 2.8 to 8.9 mg/liter. The other 57 workers with no bone changes excreted an average of 4.53 mg F/liter, ranging from 2.1 to 14.7 mg F/liter. As the average urinary F excretion increased, the percentage of suspected osteofluorosis increased within each excretion range.

In 1 aluminum plant, [50] 76 of 79 potroom workers developed osteofluorosis. Average urinary F concentrations as determined by spot samples taken during the work shift ranged from 8.7 mg/liter for pot tenders to 9.8 mg/liter for tapper-carbon changers. Postshift samples would probably have shown higher values since urinary F excretion reaches a maximum 2-4 hours after exposure. [26,43,45]

In a second aluminum plant, [50] the average urinary F excretion (postshift samples) of 231 potroom workers with no increased bone density ranged from 3.0 to 10.4 mg/liter over a 5-year period; improved control measures and hygienic practices probably helped prevent high urinary F levels in this group. The average preshift F excretion after 48 hours off work was reduced from 3.6 to 1.4 mg F/liter when control measures were put into effect.

Urinary F analyses covering a 1-year period and involving about 155 aluminum workers (potroom and cryolite workers) were performed on both pre- and postshift samples. The average of the determinations of F in the preshift samples was 2.35 mg/liter with a range of 2.0-2.8 mg F/liter. The average of the postshift samples was 4.8 mg F/liter, ranging from 3.2 to 6.5 mg F/liter. [51] Results of analyses of breathing-zone and general

room-air samples over a 5-day period were all less than 0.34 mg F/cu m (gaseous and particulate F). [51]

Table XII-4 summarizes the above mentioned human exposure-effect data.