Occupational Fluoride Exposure

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INTRODUCTION

Normal Intake

Fluoride is wellnigh ubiquitous; detectable traces occur in almost all substances. It follows that man, regardless of where he lives, takes into his body every day measurable amounts of fluoride. He inhales traces of fluoride; according to Martin and Jones (1971),[1] an individual living and working in central London could be expected to inhale perhaps 0.001-0.004 mg of fluoride per day. This might be increased by a factor of 5-10 on a very exceptionally foggy day of high pollution. In heavily industrialized English cities, Martin and Jones (loc. cit.)[1] consider the maximal inhaled intake to be of the order of 0.01-0.04 mg. Man ingests fluoride in his drinking water; water supplies range from 0.1 ppm or less to 3 or 4 ppm and occasionally higher in United States communities. All foods contain fluoride, sometimes in more than traces (e.g., sardines, 40 ppm). Fluoride intake in areas where drinking water contains little fluoride comes chiefly from food sources and ranges between 0.25 and 1.5 mg per day (Elliott and Smith, 1960;[2] Hodge and Smith, 1965;[3] Kramer et al, 1974;[4] Longwell, 1957;[5] Osis et al, 1974.[6] In areas using a fluoridated water supply, the total daily intake from foods, beverages and water usually varies between 2 and 3 mg F (San Filippo and Battistone, 1971;[7] Longwell, 1957;[5] Kramer et al, 1974.[4] It has been estimated that leafy vegetables grown in areas contaminated by fluoride-containing industrial effluents, on the average increase the total fluoride intake about 1.7% or 1% in nonfluoridated or fluoridated areas, respectively (Jones et al, 1971).[8] Edible products from cattle kept near a factory producing hydrogen fluoride showed an increase in fluoride concentrations, but these were insignificant so far as human health is concerned (Oelschlager et al, 1972).[9]

Air Quality

Minute traces of fluoride are found in the air of rural communities and of cities. Sources of these fluorides are varied, and include effluvia from volcanoes, dust generated by the weathering of fluoride-containing soils and outcroppings of fluoride-containing minerals, smoke from the burning of coal, and effluents from a variety of industrial processes. Obviously, the importance of these different sources varies from location to location. Analyses from water-soluble fluoride in particulate samples collected over a three-year period indicated that 88% of measurements made at urban stations contained less than 0.05 $\mu g/m^3$, the lower limit of detection (Thompson et al, 1971).[10] Only 0.2% of the urban samples exceeded 1.00 $\mu g/m^3$; the maximal concentration found was 1.89 $\mu g/m^3$. It should be noted that these urban sampling sites are characterized as center-city business-commercial, and are not industrial locations. Over 98% of measurements at nonurban sites, more than 90% of the combined urban and nonurban samples showed no detectable fluoride. Data collected in six different U.S. cities during a more intensive two-year program showed the proportion of samples containing no detectable (water-soluble) fluoride to range from 42% in St. Louis to 84% in Cincinnati (loc. cit.). Samples collected at urban sites in Cleveland during 1972 contained an average of 0.02 μg F/m^3; samples collected near certain industrial locations ranged up to 0.230 $\mu g/m^3$ (King et al, 1976).[11]

In view of the difficulties in adequately distinguishing between gaseous and particulate fluorides, it is not surprising that very little data of this nature are available. In 1974, Israel[12] reported that airborne fluorides in the vicinity of an alumina reduction plant consisted of 13% gaseous components, 64% particulates and 23% gaseous forms absorbed on aerosols. Other investigators have found total fluorides sampled near aluminum plants to contain 20-44% gaseous fluorides, with the remainder particulate in nature (Hluchan et al, 1968;[13] Okita et al, 1974).[14] The gaseous fluorides most frequently encountered are HF and SiF_4. Elemental fluoride is not a common air pollutant, though it may be encountered in the glass industry and in rocket engine test firings. Fluorine reacts rapidly with moisture to form HF, O_2 and small amounts of O_3, though at concentrations of a few ppm or less, free elemental fluorine may persist for 20-30 minutes (Rickey, 1959).[15] Common particulate fluorides are cryolite, fluorspar, aluminum

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fluoride and fluorapatite. The biological activity of all of these forms in the airborne concentrations usually encountered, should be directly related to the availability of the fluoride ion, i.e., to their respective solubilities and dissociation in biological systems. Collings et al (1951, 1952)[16 17] reported that fluoride in the particulates generated in the phosphate fertilizer industry is as readily available biologically as the fluoride in HF. Rye (1961)[18] did not find this to be the case in his study on fertilizer workers.

The remainder of this review will be directed to the effects of airborne fluoride on man.

EFFECTS OF AIRBORNE FLUORIDE: INDUSTRIAL HEALTH

Acute Episodes: Lung and Skin Injury

Pulmonary exposures to either elemental fluorine or to HF may occur independently or simultaneously with skin exposures. The violent reaction of gaseous F_2 with the skin produces a thermal burn; in contrast, solutions of HF produce painful slow-healing chemical burns (Stokinger, 1949).[19] Treatment of HF burns involves efforts to fix the fluoride in a chemical complex (for example, with calcium or magnesium) as well as the usual therapy for burns (Finkel, 1973;[20] Carney et al, 1974;[21] Gosselin et al, 1976).[22] The delicate tissues of the lung may be intensely, even fatally irritated by high concentrations of F_2 or of HF (Greendyke and Hodge, 1964).[23] For predictable exposures of workers, the TLVs are applicable. The current OSHA occupational and health standards, i.e., concentrations that can be inhaled for an 8-hour day for a 5-day week with little or no adverse effect, are 0.1 ppm (0.2 mg/m^3) for elemental fluorine, and 3 ppm (2 mg/m^3) for hydrogen fluoride (Department of Labor, Occupational Safety and Health Administration, 1971).[24] The American Conference of Governmental Industrial Hygienists (1976)[25] recommends threshold limit values of 1 and 3 ppm for fluorine and for HF, respectively. The NIOSH criteria documents recommend a standard of 2.5 mg/m^3 both for "inorganic fluorides" (1975),[26] and for HF (1976);[27] no document on fluorine has appeared.

Largent (1950)[28] lists the increasing intensity of acute effects with increasing concentrations of gaseous fluorides for human subjects as follows: (1) 3 ppm — no local immediate systemic effects are noted; (2) 10 ppm — many persons experience discomfort; (3) 30 ppm — all persons complain and object seriously to staying in the environment; (4) 60 ppm — brief exposures — definite irritation of conjunctiva, nasal passages, tickling and discomfort of pharynx, trachea; and (5) 120 ppm — highest concentration tolerated less than 1 min. by two male subjects; smarting of skin as well as above effects. Some persons describe a transient irritation, reddening and itching of exposed skin on exposure to 3 ppm.

The National Academy of Sciences-National Research Council Advisory Committee on Toxicology have presented Emergency Exposure Limits (EELs) for fluorine and for hydrogen fluoride. It is considered that these concentrations can be inhaled for the periods specified without disabling the individual or interfering with his performance, that such exposures will be rare, and that the individual will not be placed in a position where a second emergency exposure could occur until the responsible physician authorizes such placement (Smyth, 1966).[29] The limits are

	Exposure		
	10 min	30 min	60 min
F_2, ppm	3	2	1
HF, ppm	20	10	8

These limits are intended for military and space agencies for use in contingency planning for plant accidents or breakdown, not for normal operations or the general public.

Chronic Effects

It is a matter of record that fluoride exposures of severe proportions (some were natural phenomena such as volcanic eruptions, or dust blown from exposed rock phosphate outcroppings and reefs; some were man-made industrial effluents) have, on occasion, caused large-scale damage to plants, to animals, and sometimes to man. The kinds of injuries produced by excessive fluoride in plants have been discussed by Leonard Weinstein (1977);[30] in animals by John Suttie (1977).[31] We will limit our comments to the effects of excess fluorides on man with particular attention to occupation-related exposures, in-plant and neighborhood, especially (a) the effects on bone, lung, kidney and skin, and (b) the validity of the proposed air quality standards, giving weight to the published reports of exposures in the aluminum and rock phosphate industry.

Industrial Sources of Fluoride. — Fluoride-containing pollutants are released to the atmosphere by a variety of industrial processes, including grinding, drying and calcining of F-containing minerals, acidulation of these minerals, metallurgical processes involving fluoride fluxes or melts, kiln firing of brick and ceramic materials, melting of raw materials in glass making, and the use of fluoride-containing materials in cleaning, etching, and electroplating (National Academy of Sciences, 1971).[32] NIOSH recognizes 92 occupations with potential exposure to fluorides, and has estimated that approximately 350,000 workers in the U.S. are exposed to fluorides; 57 occupations and 22,000 workers are considered to have potential exposures to hydrogen fluoride (National Institute for Occupational Safety and Health, 1975, 1976).[26 27]

Fluoride emissions from major industrial sources are listed in Table 1.

Table 1. — Estimated Total Fluoride Emissions from Major Industrial Sources in the United States in 1968.*

Source	Atmospheric Emissions, tons/year
Manufacture of normal superphosphate fertilizer	9,700
Manufacture of wet-process phosphoric acid	3,000
Manufacture of triple superphosphate fertilizer	300
Manufacture of diammonium phosphate fertilizer	100
Manufacture of elemental phosphorus	5,500
Manufacture of phosphate animal feed	100
Manufacture of aluminum	16,000
Manufacture of steel (open-hearth furnace)	16,800
Manufacture of steel (basic-oxygen furnace)	8,400
Manufacture of steel (electric furnace)	14,900
Welding operations	2,700
Nonferrous-metal foundries	4,000
Manufacture of brick and tile products	18,500
Manufacture of glass and frit	2,700
Combustion of coal	16,000
Total	118,700

*From National Academy of Sciences (1971).[32]

Air Concentrations vs. Urinary Concentrations of Fluoride. — Fluoride absorbed into the body is handled in two ways, viz., by deposition in the skeletal system, and/or by excretion in the urine. The former process represents the principal threat of chronic exposure to excessive fluoride, and is discussed later. The urinary excretion of fluoride is prompt and is closely related to the amount absorbed; it has long been utilized as an index of fluoride exposure. However, this very rapidity of excretion, and the variations in nature and magnitude of exposures encountered in the course of a working day make it impossible to assess general working conditions from a single spot urine sample from a single individual. Consequently, the National Institute for Occupational Safety and Health (NIOSH) (1975, 1976)[26] [27] has recommended that for workers exposed to inorganic fluorides or to hydrogen fluoride, end-of-shift urine samples shall be taken after four or more consecutive days of exposure. If the individual's postshift sample contains more than 7.0 mg F/l, a preshift sample is to be taken within two weeks at the start of a workshift at least 48 hours after the previous occupational exposure, and a repeat postshift sample shall be taken at the conclusion of that workweek. If the preshift sample exceeds 4.0 mg F/l, or the second postshift sample exceeds 7.0 mg F/l, the individual's dietary sources and personal hygiene, and basic work practices and environmental control are to be evaluated. Should the median postshift urinary F concentrations for all members of the shift exceed 7.0 mg/l, the working environment is to be evaluated through an industrial hygiene survey. Preshift samples are considered to be a measure of the worker's body (skeletal) burden of fluoride, while the postshift sample is taken to be representative of exposure conditions during that shift.

Literature Review of Industrial Fluoride Exposures. — The literature contains reports, varying in thoroughness, of the results of industrial hygiene surveys of most industries or industrial operations with real or potential fluoride exposure. More than 40% of such papers appearing during the past 25 years have dealt with the production of aluminum, and another 17% with the manufacture of phosphate fertilizers, phosphorus, and phosphoric acid from fluoride-containing rock phosphate. These industries together account for approximately 30% of all fluoride emissions. Other significant sources of fluoride emissions include the combustion of coal, production of steel, and the manufacture of brick, tile and glass products. A disproportionately small amount of literature has appeared describing these industries.

In Table 2 are shown published data describing conditions of fluoride exposure experienced in the aluminum industry and in the processing of rock phosphate. Included also are comments upon the effects of these conditions upon the workers. All of these reports deal with human exposures. For the most part, in-plant conditions in both of these industries have been kept below the recommended threshold limit value of 2.5 mg F per cubic meter of air. At times these limits have been exceeded, but in the aluminum industry, at any rate, the occasions when excessive concentrations were reported have included instances during the war years when optimal conditions were more difficult to attain (Agate et al, 1949;[33] Kaltreider et al, 1972).[34] In only a few instances have the proportions of gaseous and particulate fluorides been determined (Agate et al, 1949;[33] Kaltreider et al, 1972;[34] Barboric et al, 1969).[35] Gaseous fluorides were reported to range between 13 and 74% of the total airborne fluoride in the aluminum industry, and from 13-40% in the processing of rock phosphate. Airborne fluorides are not the sole pollutants to which the worker is exposed. Atmospheres in the aluminum industry may also contain ammonia, carbon monoxide, carbon dioxide, sulfur dioxide, and the distillation products of tar, pitch and coal, as well as cryolite, alumina, aluminum trifluoride, hydrogen fluoride and silicon tetrafluoride. The processing of rock phosphate involves exposure to sulfur dioxide as well as to hydrogen fluoride and to fluosilicic acid. Urinary fluoride concentrations frequently are below the limits recommended or mandated today, and in other instances exceed these limits. Excessive concentrations were sometimes encountered in the aluminum industry during the war years (Agate, 1949;[33] Kaltreider et al, 1972).[34]

The use of fluoride-containing fluxes in welding may lead to excessive exposures (Krechniak, 1969;[36] Pantucek, 1975),[37] but effects uniquely attributable to fluoride (other than fluoride in urine) have not been reported (Mangold and Beckett, 1971;[38] McCann, 1964).[39]

OSTEOSCLEROSIS AND THE FLUORIDE AIR STANDARD

Industrial fluorosis of crippling severity, described by Møller and Gudjonsson (1932)[40] and investigated thoroughly by Roholm (1937)[41] has been seen since the original identification, in only a few isolated workmen. Roholm reproduced in animals the painful, economically disastrous, debilitating disease repeatedly observed in many parts of the world in animals grazing on contaminated forage down wind from F-emitting industries. The importance of this disease is not disputed. Ventilation and industrial hygiene practices in the U.S. have prevented the occurrence of the crippling disease in the past; the purpose of the discussion that follows is the assessment of the probability that the proposed air standards will prevent the development of any detectable bone changes.

Roholm, in his classic monograph (1937),[41] described the skeletal abnormalities of crippling fluorosis of workers in the dusty Danish cryolite factory, especially the diagnostic triad: (a) osteosclerosis (a radiological diagnosis, (b) exostoses, and (c) calcification of ligaments, with signs and symptoms referrable to bones, ligaments and joints. Nonskeletal complaints and signs included chronic respiratory disease, and a number of common nonspecific disorders. The daily fluoride exposures to bring about the bony changes were roughly estimated by Møller and Gudjonsson (1932)[40] to range from 20 to 80 mg F (or more) taken into the body daily for 10 to 20 years. In a later study with Brun and Buchwald (1941),[42] Roholm estimated that air concentrations ranged from 15 to 20 mg F/m^3. These exposures exceed any known industrial condition in the United States; the estimated intakes may have been approached by certain residents of Morocco (1936),[43] India (1937),[44] and China (1950),[45] whose fluoride sources and intakes are not known but whose severity of skeletal changes was as great or greater than that seen in Denmark.

Roholm described three sequential phases of the development of crippling fluorosis on the basis of the radiographic findings in cryolite workers. Bosworth et al (1941)[46] added estimates of the duration of exposures (Table 3).

Characteristic histological changes of increasing degrees of abnormality accompanied the three phases defined radiographically (Roholm),[41] including increased formation of osseous tissue both from periosteum and endosteum, irregular and abnormal hypercalcification and abnormally wide *seams* of organic matrix. Johnson (1965)[47] traced the histogenesis of osteofluorosis in tissues of animals with known histories of excessive fluoride exposures. Johnson found mottled bone, analogous to mottled enamel, in grossly normal bone tissue as well as in bone with abnormal organic matrix. He defined four sorts of histological changes in the

Table 2. — Responses in Man Exposed to Airborne Fluorides in the Work Place.

Subjects	Exposure Conditions	Comment	Reference
Aluminum Production			
Group 1: 232 males 12 females	Furnace rooms 0.14-3.43 mg F/m³ 15-74% gaseous 26-85% particulate	Mean urinary F: Grp. 1 males exposed full-time and with normal x-ray findings, 9.08 mg/24 hrs; with abnormal x-rays, 9.36 mg/24 hrs. Group 1 males exposed part-time, with normal and abnormal x-ray findings, 3.89 and 3.09 mg/24 hrs, resp.; Grp. 2 males with normal and abnormal x-ray findings, 1.90 and 1.46 mg F/24 hrs, resp.; Grp. 2 females, 1.42 and 5.10 mg/24 hrs. resp. Grp. 3 males with normal and abnormal x-ray findings, 0.80 and 0.86 mg/24 hrs., resp.; Grp. 3 females, 0.84 and 1.10 mg/24 hrs, resp.	Agate et al (1949)[33]
Group 2: 44 males 25 females	Other areas of plant 0.015-0.141 mg F/m³ 13-74% gaseous 26-87% particulates		
Group 3: 25 males 52 females	Residents nearby villages outside air concns. dropped precipitously to 0.27 mg F/m³ at 200 yds (1.42 mg F/m³ in furnace room). Some further decline out to 1 mi.	Incidence of cough: 12.83% in Group 1, 6.9% in Group 2, 3.9% in Group 3 Dyspnoea upon exertion: none in any group Complaint of aches, pains in back: 5.3% in Group 1, 4.4% in Group 2, 6.5% in Group 3	
	Control areas 0.033-0.048 mg F/m³	Digestive complaints: 14.7% in Group 1, 10.1% in Group 2, 5.2% in Group 3	
		Radiological findings: x-rayed 189 workers in Group 1 and found "abnormal x-ray appearance" in 25.4% ("abnormal x-ray appearance": covers gamut from minor abnormalities not explainable by any other disease, to true skeletal fluorosis, and is not synonomous with "skeletal fluorosis"). For men of given age, some increase in incidence of abnormalities with increasing length of exposure. For those with equal periods of exposure, the incidence of abnormalities was higher in the older workers. Some workers were partially exposed and the data suggest (not significantly) a lower incidence of abnormalities in this group. Partially exposed workers included 24 women, 1 of whom showed abnormal findings. Urinary fluoride excretion not significantly different in those persons with abnormal x-ray findings. X-rayed 60 Group 2 workers, 5 of whom (8.3%) showed "abnormal x-ray appearance." X-rayed 75 Group 3 villagers, 3 of whom (4%) showed "abnormal x-ray appearance." None of the children examined showed changes. Skin, renal effects: None were reported. Full occupational and medical histories were taken, and complete physical examinations were done.	
Mfg. of AlF_3	Airborne concns: HF 3.72-37.2 mg/m³ dust 97 - 126 mg/m³ both exceed MPC		Alekperov et al (1970)[122]
24 cryolite workers employed 1-34 yrs.; 8 plant mechanics with less exposure; 6 former cryolite workers last exposed 2-11 yrs. ago; 30 controls		Urinary excretion: controls 0.30-1.60 (av. 0.92) mg F/l cryolite workers 2.41-43.4 (av. 16.05) mg F/l mechanics 1.78-11.67 (av. 4.81) mg F/l 4 ex-cryolite workers with osteosclerosis, 2.81-7.42 mg F/l 2 ex-cryolite workers without osteosclerosis 0.92 mg F/l (9 yrs. post-exp.) 2.54 mg F/l (11 yrs. post-exp.)	Brun et al (1941)[42]
Anode men and potmen Prebake reduction process in 2 plants	Av. airborne exposures: Plant A anode men 1.14 mg F/m³ pot men 0.73 Plant N anode men 2.19 pot men 1.96	Urinary F: 24-hr. excretion correlates well with air concns; about 38-43% of inhaled F is excreted per 24 hrs. Preshift data show slow increase with time, evident after 12-18 mos.	Dinman et al (1976)[58 60 89 123]

Table 2 (cont.)

Subjects	Exposure Conditions	Comment	Reference
		Average concn, mg F/l Plant A anode men / pot men Preshift 1.31 / 1.23 7-day work 5.49 / 3.31 Corrected to sp. gr. 1.024 Plant N anode men / pot men 2.45 / 1.77 7.79 / 5.69	
		Samples taken after 3rd day of work representative of group exposure; because of individual variability should limit data to group basis.	
		Radiological findings: Films made in 1974 of 56 workers who showed no x-ray evidence of bony fluorosis in 1960 and 1966. No evidence in 1974 of increased bone density, alterations in trabecular patterns, or ligamentous calcification. Age in 1974, 42-61, av. 52.1 yrs; exposure in 1974, 10-43, av. 25.2 yrs. Conclude av. group postshift urinary F of <8 mg/l, or preshift concns. <4 mg/l are not associated with enhanced risk of bony fluorosis.	
		Renal effects: Proteinuria not associated with urinary F of at least 10 mg/l	
Plant using prebake or Söderberg process 457 potroom workers 228 controls		Pulmonary findings: Prevalence of chronic pulmonary disease 4.9% in workers, 5.3% in controls (ratio, 0.92). No influence by process, degree of exposure, present or past employment. Criteria: questionnaire; forced expiratory vol. (FEV); total forced vital capacity (FVC).	Discher and Breitenstein (1976)[88]
Portroom workers 190 men	Concentrations not given. Exposure to cryolite dusts, fumes, Al_2O_3 + AlF_3 dust, HF, CO, CO_2, distillation products of tar, pitch, coal	Incidence of bronchial asthma 12 times greater in potmen than in community. Thought to be an allergic asthma. Allergen not identified but believed to be among the distillation products or perhaps result of several combined factors.	Evang (1938)[77]
		Radiological findings: x-ray examination of vertebral column and pelvis of 26 workers with an average employment of about 20 years revealed no clear-cut evidence of fluorosis. One of the 26 was considered "suspicious;" ligmental deposits of "uncertain" nature were described in another.	
Aluminum smelter		Skeletal fluoride: one individual sampled 7 yrs after terminating 18 yrs. exposure, 300 ppm F (rib ash) Franke et al noted longer exposure for development of fluorosis than did Roholm, and suggest this is because Roholm's cryolite workers had a more severe exposure.	Franke et al (1975);[50] Franke and Auermann (1972)[53]
Electrolysis rooms	Airborne concns. of HF often >0.5 mg/m³, the Polish MAC	Nasal mucosa: 30% of workers showed chronic inflammatory changes, e.g., hypertrophic or atrophic rhinitis.	Golusinski et al (1973)[124]
Aluminum smelter 1 man Died at age 64 yrs. Employed from 38-62 yrs of age		During last 2 yrs of life, hospitalized, repeatedly with signs attributed to chronic bronchitis, emphysema, gross cardiac enlargement. Skeletal x-ray changes attributed to fluoride, were noted. Cause of death: cor pulmonale, diffuse pulmonary fibrosis, fluorosis.	Great Britain H. M. Chief Inspector of Factories (1969)[125]

Table 2 (cont.)

Subjects	Exposure Conditions	Comment	Reference
		Radiological findings: Increased density of vertebral bodies. Some osteolytic foci, mainly osteoplastic foci in cranial vault. Cortical hyperostoses with some cystic degeneration at the proximal ends of radius and fibula; later, increased spondylosis and increased osteophytosis. Dorsal spine showed marked increase of density, with spurs at the articular surfaces of the lower vertebrae; in one instance the spurs joined to form a bridge. In pelvis and long bones of the limbs, findings included increased density with loss of normal trabecular graining, abnormal roughening, exostoses. Findings attributed to fluorosis probably sustained during employment in aluminum smelting.	
Söderberg pots. Primary Al_2O_3 used to clean effluent gases from pots. This secondary Al_2O_3 can be returned to the pots Potmen, anode men, truck men exposed to pots using only primary Al_2O_3 or to pots using primary plus secondary Al_2O_3	Airborne concns., av. mg F/m³ primary Al_2O_3 potmen 0.70 anode men 1.33 truck men 1.04 secondary Al_2O_3 potmen 0.79 anode men 1.49 truck men 1.82	Urinary F, av. mg F/l primary Al_2O_3 potmen 1.64 anode men 1.83 secondary Al_2O_3 potmen 2.11 anode men 1.93 Men exposed to secondary Al_2O_3 complained of irritation of mucous membranes, headache, nausea	Gylseth and Jahr (1975)[126]
44 potmen	Air concentrations not given. Dust samples from floors, beams, roof of potroom contained 11.8-22.6% F; one sample of dust contained 24.7% cryolite + Al_2F_6	None of these subjects had visited doctor prior to study. Five mentioned light symptoms of nausea, shortness of breath which they attributed to work. Found 3 cases of asthma possibly associated with work in potroom, plus 2 cases in persons in electrode plant Radiological findings: x-ray examination of 56 potmen with possibly up to 18 years exposure showed no signs of fluorosis in lumbar spine and pelvis. No x-ray changes attributable to fluorosis in spinal column of 70 year old worker who sorted and screened potroom sweepings for 13 years (always wore mask).	Hjort (1938)[85]
Comparison of Söderberg pots with ventilation, without ventilation, and hooded prebaked anode pots with ventilation.	Airborne concns., mg F/m³ special operations (adjusted anodes) Söderberg ventilated 5-20.5 (av. 10) Söderberg unventilated 2.5-8 (av. 5) hooded prebaked pots < 2.5 shift exposures mean concns. for all pots < 2.5 24-71.5 (av. 56.6) % of airborne F was HF general potroom atm. Soderberg ventilated ca 1.4 Soderberg unventilated ca 0.7 hooded prebaked pots ca 0.3	Urinary F: All mean values acceptable except for ladle cleaning (8 mg F/l) and bath tapping (6.5 mg F/l in Söderberg potrooms with ventilation. Urinary F and exposure less in hooded prebaked anode pots. Av. of postshift samples from workers on Söderberg pots with ventilation was 4.9 mg/l; for Söderberg pots without ventilation, 3.1 mg/l; for hooded, prebaked anode pots with ventilation, 2.3 mg/l. Urinary fluoride and fluoride exposure were correlated for workers in potrooms with prebaked anodes and with Söderberg pots with ventilation. Urinary F increased day to day during the week, but this was compensated during days off work.	Jahr et al. (1974)[73]

Table 2 (cont.)

Subjects	Exposure Conditions	Comment	Reference
		Lung function (FEV1) as % of total vital capacity showed neg. correlation with exposure. More respiratory complaints among workers in prebaked anode potrooms than among other workers.	
200 potroom workers	Airborne concns, mg F/m³: total 0.058-0.093 particulate < 0.02 gaseous 0.048-0.083 crusher operator 0.20-0.25 total ball mill operator 0.05-1.10 total filterpress operator 0.05-1.10 total cryolite plant	Urinary fluoride where airborne concns. are < 0.34 mg F/m³: preshift 2.0-2.8 (av. 2.35) postshift 3.2-6.5 (av. 4.8)	Johnson et al (1973)[72]
	particulate / gas / total		
	top floor filter bldg. < 0.02 / 0.093 / 0.103		
	ground floor < 0.02 / 0.045 / 0.065		
	ball mill bldg.		
	ground floor 0.068 / 0.037 / 0.105		
	ground floor near inoperative ball mill < 0.02 / 0.055 / 0.065		
	crusher bldg. 1st floor 0.314 / 0.025 / 0.339		
	3rd floor 0.283 / 0.026 / 0.309		
Niagara Falls Works: 107 potroom workers 27-65 yrs. old, av. 51.9 yrs. 2-40 yrs. exposure, av. 19.1 yrs 108 control subjects 22-70 yrs. old, av. 50.7 yrs.	2.4-6 mg F/m³ 36-50% gaseous	Urinary fluoride: 8.7-9.8 mg F/l. Controls, 0.7 mg F/l. Respiratory findings: Normal incidence of chronic obstructive pulmonary disease; normal forced vital capacity. Radiological findings: x-ray examination of 79 potroom workers showed 96% of these men to have varying degrees of skeletal fluorosis, without physical impairment or overt clinical signs. Skin findings: Minor burns from splashed hot metal; 2 instances ichthyosis, pruritic rash; normal incidence furunculosis; no skin cancers. Renal findings: No adverse effects.	Kaltreider et al (1972)[34]
Massena operations 231 potroom workers 21-64 yrs. old, av. 46 yrs. up to 40 yrs. exposure 152 control subjects 31-64 yrs. old, av. 48.8 yrs.	Airborne concentrations not given	Urinary fluoride (sp. gr. 1.024): After 5 days work, 1.4-4.6 (av. 3.0) mg F/l; after 48 hrs off, 1.0-1.6 (av. 1.4) mg F/l; after 72 hrs off, 1.0-1.6 (av. 1.5) mg F/l. Controls, 0.8-0.9 mg F/l. Respiratory findings: Insignificant increase in incidence of upper respiratory tract infections. Normal incidence chronic obstructive pulmonary disease. Radiological findings: x-ray examination of 231 workers showed no evidence of skeletal fluorosis. Skin, renal findings: Nothing unusual. "Chizzola" maculae not evident.	

Table 2 (cont.)

Subjects	Exposure Conditions	Comment	Reference
300 workers		Radiological findings: No evidence of skeletal fluorosis. No evidence for a so-called "peripheral form" of bone fluorosis of occupational origin which would precede vertebral osteosclerosis.	Lanyi (1969)[127]
smelting 61 workers	Av. airborne concentration in plant, 1.1 mg F/m³	Noted F in urine; dental gingival, digestive effects, arthropathies, all of which correlated with levels of pollution.	Leloczky and Orsos (1972)[128]
4 workers 46-59 yrs old; 7-11 yrs. exposure		Urinary F: 1.15-6 mg/24 hrs Radiological findings: slight to marked osteosclerosis, ligamentous ossification, occasional paresthesia, pain in hands, knees. Increased concns. of F in single teeth	Lezovic and Arnost (1969)[67]
Total of 61 cases of fluorosis in Swiss aluminum industry as of June 1973. Of these, 20 were investigated in detail. Age 60 ± 5 yrs; exposure, 29 ± 7 yrs. 20 controls, age 58 ± 6 yrs.		Radiological findings: Greater incidence of exostosis, apposition of new bone, and lesser incidence of osteoporosis, in workers than in controls. Great variations seen radiologically among cases with same concentrations of bone F.	Maillard et al (1975)[68] Boillat et al (1975)[55]
400 potroom workers	Usually 1-2 ppm F (1-2 mg F/m³); increased 2-fold over 4 month period. HF, organic tars, dust-borne F, AlF3, cryolite, Al2O3, SO2	When first employed in potroom, most developed nausea, headache, irritation of conjunctiva and respiratory passages; these usually passed off in a few days. Four instances of acute asthma developed immediately and these men left. Over 5 yrs, 54 cases of asthma developed; clinical details given. Many of these occurred during the 4 mos. of elevated air concns.; men were able to continue in potroom after concns. returned to usual levels. Average of 3 yrs. exposure before attacks developed. Considered to be allergic asthma and allergen to be an unknown F-containing compound.	Midttun (1960)[78]
417 workers in electrolytic shop; 63.8% constantly exposed (electrolysis workers, anode or ladle workers). 72% were 25-30 yrs. old. 37.4% exposed up to 5 yrs., 58.5% 5-10 yrs, 6.7% >10 yrs	Air concns. not given HF principal agent	All workers: cough, often dry 37.4%; local or indefinite chest pain 18.9%; dry or moist râles 33.6%; difficult breathing-29.5%; chronic tracheobronchitis or bronchitis 16.5%; pronounced bronchitis 9.1%; beginning emphysema + bronchitis 5.5%. Controls: no emphysema, 2% chronic bronchitis. Subjective and objective indications increased with increasing length of service, e.g., no râles with ≤ 2 yrs. work, 40.6% for those with 5-10 yrs., and rales in 43.2% of those constantly exposed, 24.3% in others. Little correlation between objective and subjective data in majority with chronic bronchitis. Generally, bronchitis caused by F was light. X-ray, roentgenographic exam. 270 workers constantly exposed indicated moderate chronic bronchitis most frequent change. Emphysema in 11.5% (moderate in majority), thickening of interlobar pleura in 21.5%, pleural adhesions region of phrenico-costal sinuses in 12.2%. Total lung capacity normal in 65% of 405 workers, increased or decreased in 35%; increased in 15 of 40 with chronic bronchitis.	Papoyan and Demirchoglyan (1963)[75]

Table 2 (cont.)

Subjects	Exposure Conditions	Comment	Reference
		decreased in 7 of 40. Increased rate of respiration, small increase in min, vol of respiration, some increase in O consumed/min, some decrease in coefficient of O utilization indidating moderate respiratory deficiency, clinically comparatively well compensated. Av. increase of 30.6% in BMR of those with chronic bronchitis. Tachycardia in 13.9% increasing when airborne F increased; feeling of suffocation, esp. at work. X-rays showed hypertrophy of left ventricle in 36.3%, both ventricles in 25.2%; attributed to phys. work. No electrocardiographically demonstrable damage to myocardium in 35 workers. Increased capillary permeability in 60.8%; seen more often in those fully exposed and with increasing service. In young (25-35 yrs age) workers, 30.7% showed incipient calcification of cartilage of 1st ribs, total calcification all rib cartilages in 15%. Dental caries, 3.8% (34% in controls). Early loss (without damage) and loosening of teeth in 18.9%, due to dental alveolar changes	
Production of Al2O3 from bauxite ore	Airborne concentrations: respirable fraction, 0.89 and 0.06 mg F/m3. Total, 0.48, 0.51, 0.89 mg F/m³	One individual exposed less than 1/3 day to cryolite. No symptoms suggestive of chronic fluorosis.	Ramos et al (1973)[129]
A 55 yr old male employed 20 yrs in electrolytic operations		Radiological findings: marked density of lumbar vertebra, pelvis; diffuse osteopetrosis remainder of skeleton. Slight calcuria (31-36 mg). Increased F in dental enamel. Renal pain	Roche et al (1960)[130]
170 workers in electrolysis process		Respiratory findings: Higher incidence of impaired nasal respiration. Changes in respiratory tract, ears dependent upon work experience, work place, age.	Rybicki (1970)[71]
61 cases of industrial fluorosis	Airborne concns. approx. 3 mg F/m³	Skeletal fluoride:	Schlegel (1974)[52]

	Normal	Stage 0-1	Stage 1	Stage 2	Stage 3
No	—	16	18	23	4
age, yrs					
range	—	45-70	50-67	51-75	66-73
av.	—	59	51.5	63	69
exposure, yrs					
range	—	9-39	12-45	11-49	30-43
av.	—	22	29	29	40.5
F in bone ash, mg/kg	1500	6900	5200	7500	8400

Thermal decompn. of AlF3·3NH4F	Airborne concn., 0.15-100 mg F-contg. dust/m³. NF, SiF4, NH4F, NH3, CO present in atmosphere. Temp. 25-40°C. Excessive noise, vibration, inadequate light	Incidence of bronchitis, pneumonia, nervous disorders, skin diseases more frequent in AlF3 workers than among other fluoride workers.	Solov'eva (1974)[131]
Three plants in Switzerland; Plants A and B are modern, Plant C is older	Airborne concns., av. mg F/m³. Gen. work areas of Plants A and B, 0.48-2.1 and 1.2-3.7, resp.		Sutter (1973)[132]

Table 2 (cont.)

Subjects	Exposure Conditions	Comment	Reference
	Personnel samplers on workers, mg F/m³ A B C oven operation (break crust, cover up) 0.86 1.6 1.5 ladling 0.50 1.7 1.5 Al2O3 charging 0.55 1.3 1.1 anode servicing (changing anode, raising traverses) 1.3 2.4 2.6 chiefs — 1.1 1.2		
10 potroom workers 7-30 years experience	4 ppm F in one plant 3 ppm F or less in another	X-ray examination showed generalized osteosclerosis (not incapacitating) in 2 workers, areas of localized densification in 3.	Tourangeau (1944)[64]
70 workers	Not given, but considered relatively high on basis of urinary F (3-5 mg F/liter)	Examinations made after 5 years employment indicated improvement in condition of respiratory passages, compared to results of examinations previous year. Low incidence of bronchitis.	Ulrich (1958)[133]
17 potroom workers, age 56-66 (av. 61) yrs. Employed 11-46 (av. 29) yrs.		Radiological findings: 9/17 showed increased density to x-ray on films of pelvis and lumbar spine. 17/17 showed ossification of spinal ligaments, outgrowth of bony spurs on vertebrae (bridging) not unique to fluorosis. 10/12 showed changes in elbows, forearms, most common being ossification of interosseous membranes, bony appositions, ossification of tendon insertions, free osseous bodies. 16/17 complained of vague pains, stiffness in extremities, shoulders, neck, lower back. Iliac crest contained 135-472 (av. 332) mg F/100 g dry fat-free bone	Vischer (1970)[65]
2 cryolite plants	Exposure to HF, cryolite dusts, NaF, AlF3, CaF2	Respiratory tract changes earliest signs of fluorosis; include inflammation of mucous membranes of nose, upper respiratory tract. Progression from hypertrophic to atrophic to possible perforation of nasal septum. Vegetative and vascular dysfunction as hyperhidrosis, bradycardia, hypotonia frequently with dystrophic changes in myocardium. Earliest gastrointestinal signs are ventricular and intestinal dyskinesia with secretory and motor changes. Even the earliest of these signs may be accompanied by bone and joint pains without detectable x-ray changes. Skeletal x-ray changes appear 5-7 yrs. after onset of bone pain. First such changes are thickening of periosteum and (less often) endosteum of tubular bones of shin, forearm. Many subjects with fluorosis show hypofunction of thyroid and adenohypophsis.	Zislin and Girskaya (1971)[74]
Phosphate and Fertilizer Production			
50 workers	ground floor particulate 2.7 mg F/m³ gaseous 1.7 first floor particulate 1.5 mg F/m³ gaseous 0.3 second floor particulate 2.6 mg F/m³ gaseous 0.4	70% showed atrophic changes in nasal mucosa; 74% showed hypertrophic changes in larynx. Comparison with other workers in same plant in manufacture H_2SO_4 and exposed to same pollutants except F, indicated this upper respiratory tract involvement mainly due to F. No subjective complaints characteristic of fluorosis. Serum Ca, P, acid and alk. phosphatase, liver function tests normal.	Barboric et al (1969)[35]

Table 2 (cont.)

Subjects	Exposure Conditions	Comment	Reference
		Radiological findings: The most valuable diagnostic tool. Periostosis in 28% of workers exposed an average of 13 years. Spongiosclerosis in 8% of workers after an average exposure of 20 years.	
1 man, employed 10 yrs.	0·2.4 mg F/m³	Urinary F, 3.2 mg/l	Collings et al (1952)[17]
5 workers employed 6-8 (av. 7) yrs.	2.5-4.9 mg F/m³	Urinary F, 5.1-10.4 (av. 7.3) mg/l	
4 workers employed 3-4 (av. 3.5 yrs.)	5.0-9.0 mg F/m³	Urinary F, 5.8-10.1 (av. 7.4) mg/l	
5 workers, of whom 4 employed 9 yrs. and 1 for 4 yrs.	> 10 mg F/m³	Urinary F, 10.0-19.0 (av. 15.1) mg/l	
74 workers age 30-66 yrs, av. age 45.3 69 controls	Dust as well as gas. Time weighted average exposure, 0.5-8.32 (av. 2.81) mg F/m³. 50% of samples > 2.5 mg/m³	Increased incidence (14.9%) of emphysema, non-specific fibrosis, costrophrenic adhesions, healed TB lesions in exposed workers (6.0%) Attributed by authors to irritating properties of acid gases. No disability attributed to F.	Derryberry et al (1963)[59]
		Radiological findings: Minimal or questionable bone density changes in 17 of 74 (23%). Ages 35-66, av. 48.4 yrs. Exposure 7.1-24.8, av. 13.7 yrs. Urinary F, 2.2-8.9, av. 5.18 mg F/l. Atm. concns., 1.78-7.73, av. 3.38 mg F/m³	
		No radiological changes in 57 of 74. Ages, 30-63, av. 44.4 yrs. Exposure, 4.5-25.9, av. 14.3 yrs. Urinary F, 2.1-14.7, av. 4.53 mg F/l. Atm. concns., 0.5-8.32, av. 2.64 mg F/m³.	
		Renal findings: Albuminuria in 4 of 17 showing skeletal x-ray changes.	
Undetermined number of subjects		Fluoride concns. were measured in urine, saliva and blood Mg % F Years exp. / Urine / Saliva / Blood 0 / 0.077 / 0.099 / 0.166 0-5 / 0.218 / 0.308 / 0.188 5-10 / 0.353 / 0.508 / 0.336 10-15 / 0.275 / 0.413 / 0.440 F in blood was considered a reliable indicator of exposure	Domzalska et al (1968)[134]
83 workers Employed several months to slightly over 4 yrs.	phosphoric acid areas total acidity as SO2 8.5 ppm HF + H2SiF6 1.58 ppm at filters HF + H2SiF6 1.81 ppm at vats HF + H2SiF6 1.57 ppm	Urinary F: 0.15-1.16 mg/l. Nearly all complained at some time of burning in nose, tickling in throat; a few had minor nasal hemorrhages. 80% had minor nasal irritation and inflammation, clearing rapidly on removal from exposure. Some irritation of nasal pharynx. Occasional transitory sensations of pain in chest, bouts of cough, retrosternal sense of constriction and weakness. Findings believed result of exposure to acid vapors. All objective examns. neg.	D'Onofrio et al (1954)[135]
		Radiological findings: x-ray examinations of the oldest workers did not reveal evidence of excessive fluoride absorption.	
		Skin findings: No skin manifestations of occupational origin were seen.	
20 workers 25-40 yrs. old, employed 3-8 yrs. in prodn. of $Ca_3(PO_4)_2$	0.5-2 mg F/m³ plus SO2 at < 5 mg/m³	Urinary F: 2.5-3.2 mg/24 hrs. Thyroid: normal uptake of ^{131}I.	Gabovich et al (1960)[136]

Table 2 (cont.)

Subjects	Exposure Conditions	Comment	Reference
"Comparable" group in prodn. of granulated superphosphate, handling of NaF, SiF4	3-8 mg F/m³ plus SO2 at 10-70 mg/m³	Urinary F: 8.5-13 mg/24 hrs. Thyroid: possible slight depression of ^{131}I uptake	
"Comparable" group in H2SO4 prodn. (processing pyrites)	< 1 mg F/m³ plus SO2 at 50-110 mg/m³	Urinary F: 1-1.5 mg/24 hrs. Thyroid: decreased uptake of ^{131}I Conclude 50-110 mg SO2/m³ or 10-70 mg SO2/m³ plus sufficient F to achieve absorption of 0.1-0.2 mg F/kg body wt. will decrease uptake of ^{131}I by thyroid	
302 female workers, 80% being 20-40 yrs. old. Employed in manufacture of superphosphate. 309 control subjects	Conveyor area, 1.3 mg F-dust/m³; processing equipment platforms, 0.27 mg F-dust/m³; crushing dept. equipment area, 1.3 mg F-dust/m³; drying drum area, same; powdering, drying areas, 3.1 mg F-dust/m³. Generally F-dust of plain superphosphate > granulated and double superphosphate. Dust levels all work areas 4.9-56.6 mg/m³; 2-3% phosphorite and superphosphate.	Menstrual irregularities in 32.1% workers, 5.1% controls. Chief complaint, oligomenorrhea, 9.9% in workers, 2.3% in controls. Frequency of irregularities related to F concns. and yrs. of exposure: 21.9% in those exposed up to 1 yr; 22.3% in 1-5 yrs; 42.7% in > 6 yrs. Inflammation of uterus, cervix, vagina more frequent in workers and chiefly among those in plain and granulated superphosphate area. F in workers' menstrual blood, absence in that of controls. No pregnancies, miscarriages, births. Toxemia or pregnancy, hypotension and threatened abortion more frequent among workers.	Kuznetsova (1969)[133, 137]
123 workers, 100 control subjects		Leukocyte counts from the nasal mucous membrane were elevated in 52% of workers, being 3.9-7.4x above controls. Occurrence of desquamative epithelial cells 2x greater among workers in primary process. Effects seen more frequently as years of exposure increased. Anosmia present in 50% of workers. Immunological function decreased in workers	Rasskazova (1970)[138]
A 58 yr. old male employed 10 yrs (from 25-35 yrs of age) in Tunisia phosphate mines		Radiological findings: diffuse osteopetrosis of skull, spine, pelvis, extremities. Increased F in dental enamel. Laboratory data including urinary Ca normal Pain in elbows, knees, ankles	Roche et al (1960)[130]
28 men Employed 2-35 years	Grinding rock phosphate. No air concentrations given	Urinary F: concns. ≤ 4 mg F/l. Most were 0.5-1.5 mg/l X-ray examination of chest, lower spine, pelvis, upper femurs did not reveal significant alterations from normal radiological pattern.	Rye (1961)[18]
Not stated Employed 3 years	Production of phosphoric acid from rock phosphate. Air concentrations < 3 ppm as HF	General physical condition unaltered. Urinary F usually below 5 mg/l. No significant incidence of any particular type of gastrointestinal or respiratory complaint, no anemia, anorexia or other specific adverse effect. Substantially zero occurrence of nonspecific upper respiratory disease in this work force except during annual 2 week maintenance shut down. No evidence of x-ray changes.	
1 worker	Production of triple superphosphate from rock phosphate. 2-4 ppm F as HF, but approx. 60% dust, 40% gas.	No alterations in general health, well-being Urinary F in postshift sample after 5 days of work, 8-9 mg/l. Returned to 3-4 mg/l after 2 days off work.	

Table 3. — Radiographic Findings in Cryolite Workers.

Length of Employment (years) Roholm[41]	Length of Employment (years) Bosworth et al[46]	Condition of Osseous System as Seen Upon X-ray Examination	Dust Exposure (Roholm)[41] Slow	Medium	Heavy
			No. of Workers		
8	—	no change	2	9	11
9.3	2.5	1st phase: osteosclerosis in pelvis, vertebral column. Coarse and blurred trabeculae, diffuse increased density of bone	5	19	2
9.7	4.5	2nd phase: increased density and blurring of contours in pelvis and vertebral column, extended to ribs and extremities	1	18	5
21.7	11	3rd phase: greatly increased density of bone. Irregular and blurred contours. All bones affected, particularly cancellous bones. Extremities thickened. Considerable calcification of ligaments of neck and vertebral column	—	3	4

chalky, enlarged bones from severely poisoned animals: (a) diffuse bone sclerosis, (b) osteoporosis of the cortex with accelerated cortical remodeling, (c) osteomalacia with wide uncalcified osteoid seams, and (d) periosteal cortical reinforcements (new bone) streamers of woven bone and tendon bone.

Osteosclerosis and Bone Fluoride

The difficulties (a) in the differential diagnosis of early osteofluorosis, a rare disease, distinguishing the bone abnormalities radiographically from other bone diseases, on the one hand, and (b) in the assessment of the degree of severity of osteofluorosis when the ailment has been identified have led to determined searches for other diagnostic criteria. While the history of occupational exposure remains preeminent in early differential diagnosis, the calcification of the sacrotuberous and sacrosciatic ligaments when the disease has advanced to this stage is indisputable evidence of fluorosis, not seen in other diseases (Stevenson and Watson, 1957).[48] Evaluating the stage of osteofluorosis radiographically remains difficult except with long experience. When histological preparations and fluoride bone concentrations are also available, the task is easier and as more evidence of these sorts is accumulated, diagnostic reliability will be enhanced. The necessity of performing iliac crest biopsies to give samples for histological and chemical analysis stands as a serious drawback. Other possibly useful fluoride effects, especially biochemical indices, are under study and will be mentioned later.

Some years ago Fritz (1958)[49] recommended adding two earlier stages of fluoride-induced changes in bones: (1) "subtle signs", and (2) phase 0-I, both with slight radiological changes such as the enlargement of trabeculae in the lumbar spine. Recently, Franke et al (1975)[50] observed "vague symptoms" (nocturnal backpain, restriction of rotation of the trunk, slight x-ray changes) in workmen exposed for 11 years whose bone ash contained 3,500 to 4,500 ppm F. The validity of the "slight x-ray changes" can be challenged: some years ago it was suggested that osteosclerosis

Table 4. — Relations Among the Degree of Radiographic Changes, Years of Exposure and Bone Fluoride Concentration.

Osteosclerotic Phase	Av. Years Exposure Franke et al[50]	Av. Years Exposure Schlegel[52]	% F in Bone Ash Franke et al[50]	% F in Bone Ash Schlegel[52]
normal	—	—	0.05-0.10	—
Fritz pre-stages				
vague symptoms	11	—	0.35-0.45	—
0-I	12	22	0.5 -0.55	0.59
Roholm				
I	16	29	0.6 -0.7	0.52
II	18	29	0.75-0.9	0.75
III	20	40	>1.0	0.84

Table 5. — Presence of Osteosclerosis.

Authors	Air mg F/M³	Urine ppm F	No. of cases No. at risk
In Aluminum Industry			
Kaltreider et al (1972)[38]	2.4 -6	9	76/79
Agate et al (1949)[37]	0.14-3.4	9*	"a few"/?
	0.3 -0.9		
Tourangeau (1944)[44]	2.5 -3.5	—	2 or 3/10
Vischer et al (1970)[45]	—	—	9/17
Boillat et al (1975)[39]	0.5 -3.7†	—	18/20
Franke et al (1972, 1975)[51, 50]	—	—	28/?
Roche et al (1960)[130]	—	—	1/?
Lezovic and Arnost (1969)[47]	—	1.15-6*	4/50; 2 sl., 2 mod.
Schlegel (1974)[52]	2-3	—	61/?
Coulon‡	—	13 postshift	13/631
Roholm (1937)[41]; Brun et al (1941)[42]	15-20	16 av.	57/68
In Other Industries			
Largent et al (1951)[133]	1.2 -3.9	>10¶	5/16
Peperkorn and Kehling (1944)[40]	—	—	34/47
Dale and McCauley (1948)[36]	—	10.8	24/40
McGarvey and Ernstene (1947)[43]	—	23	1
Henderson (1975)[43]	0.06-8.2	2-6 preshift	1/4
		4-25 postshift	
Wilkie (1940)[52]	—	15	2
Derryberry et al (1963)[35]	3.4	0.5-44, av. 4.7	17/74
Bowler et al (1947)[36]	0.1 -0.7	0.5-7.5	1/54
Fritz (1958)[49]	—	—	57/156
Bishop (1936)[134]	—	—	1
Fourrier and Champiex (1956)[135]	—	—	4

*Mg/24 hr urine
†Data from Sutter (1973)[132]
‡Personal communication
¶In 4 of 5 with severe osteosclerosis

appears only when the bone contains more than 4,000 ppm, i.e., 0.4% F and probably is first detectable in bone containing 4,000 to 5,000 ppm F (Smith and Hodge, 1959).[51] Franke et al[50] also found the four stages of Fritz useful. A diagnostic scheme was proposed correlating clinical complaints, radiographic findings, histological evidence, bone F concentration and duration of exposure. The histological and analytical data were obtained on iliac crest biopsy samples.

Schlegel (1974)[52] correlated histologic findings, duration of exposure, and fluoride concentrations in bone ash with the four radiographic phases, namely, 0-I pre-stage of Fritz and the three phases of Roholm. His data and those of Franke et al, are compared in Table 4. Discrepancies in the fluoride percentages probably arose from the small number of samples, e.g., Schlegel had two samples of bone graded 0-I. With increasing degrees of osteosclerotic changes, the increasing years of exposure, the fluoride percentages in bone ash tend to rise; the ranges probably represent reasonable first estimates. To achieve roughly equivalent deposition of fluoride in bone in periods that are not far from half as long, the air concentrations in plants studied by Franke et al (1972, 1975)[50 53] may have been higher by a factor of about 2 than in the plants studied by Schlegel from whose discussion it can be guessed that the air contained perhaps 2 to 3 mg F/m³ and that the total intake per shift ranged from 20 to 30 mg F.

A still more involved system for expressing the radiographic findings in osteofluorosis was offered by Rouget (1974)[54] in the form of "scores". This numerical classification scheme awards 1, 2 or 3 points for no, moderate, or intense change, respectively, in the following observations: (1) increased osteosclerosis, (2) increased trabecular changes, (3) thickening of the cortex, (4) effects on periosteal bone, (5) exostoses, and (6) calcification of tendons. Boillat et al (1975)[55] examined 20 potroom workers and discovered a linear relation between the fluoride concentrations in iliac crest samples and the scores representing the phases of bone fluorosis. Around the central tendency, variability was marked in the radiographic appearance of bones with similar fluoride contents. X-ray scores averaged about 17 on this scale when bone samples contained upwards of 10,000 ppm F and about 9 when 5,000 ppm F were found in the bone ash.

The preceding discussion has centered on the effects of excess fluorides on bone in which considerable distortions in bone architecture may occur and ligaments may calcify. Only in a few instances have these processes advanced to a degree that has crippled the individual. It is important to stress as our attention is turned to the prevention of these bone changes that in man, short of crippling fluorosis, osteosclerotic bone appears to function normally both as a framework for muscle action and as a mineral storehouse.

Osteosclerosis with Air Fluoride Concentrations in Excess of 2.5 mg F per Cubic Meter; Urine Levels of 9 mg F per Liter or More

Osteosclerosis has been reported in aluminum smelter workers in 11 investigations (Table 5). As can be seen, only two of these reports (Kaltreider et al;[34] Agate et al)[33] have furnished data on the air concentrations plus data on the urinary fluoride excretion of potroom workers. Another (Roholm;[41] Brun et al)[42] gave these data on cryolite workers.

The reports of Kaltreider et al[34] and of Agate et al[33] agree only on the urinary F concentrations. Almost all of those examined by Kaltreider et al exhibited osteosclerosis; in the study of Agate et al, only "a few" of the workers showed any "abnormality". Air concentrations exceeded 2.5 mg/m³ in the Niagara Falls plant of Kaltreider's et al study but the scanty air data of Agate et al showed only air concentrations < 1 mg F/m³.

Table 6. — Absence of Osteosclerosis.

Authors	Air mg F/M³	Urine ppm F	No. of Workers
In Aluminum Industry			
Kaltreider et al (1972)*	≤ 2.5	3 av.	231
Johnson et al (1973)[32]	1	2.4 preshift 4.8 postshift	200
Dinman et al (1976)[18]	≤ 2.5	2.8 preshift 7.7 postshift	56
Cook and Hughes*	—	4.4 preshift 8.8 postshift	
Hjort (1938)[35]		9.0 postshift	62
Domesle (1969)[13]	—	—	400
Lanyi (1969)[37]	—	—	300
In Other Industries			
Rye (1951)[39]	≤ 4	5	—
Lyon (1962)[36]	0.3-1.4	1.1	61
Ramos et al (1973)[43]	1	"normal"	350
Leidell et al (1967)[31]	0.85	0.6-4.5, av. 1.9 preshift 1-27, av. 3.4 postshift	305

*Personal communication

Looking at all the potroom data available, a certain coherence appears. Air concentrations usually exceeded 2.5 mg F/m³. Urinary fluorides generally equalled or exceeded 9 ppm F. The incidence of detectable osteosclerosis was often high. When air F concentrations exceed the proposed standard (e.g., at airborne F levels averaging perhaps twice the standard or more) years of exposure do eventually cause osteosclerosis. With higher air F concentrations and with long-continued employment, osteosclerosis develops more rapidly, the extent and the degree of abnormality are greater, the stage of osteosclerosis tends to be higher, and the percentage of exposed workers showing osteosclerosis increases. The incidence of osteosclerosis (1/10) in lifetime residents of a community with 8 ppm F in the drinking water whose urines contained about 9 ppm F stresses the consonance of urinary values and osteosclerosis (Leone et al, 1955).[56]

Absence of Osteosclerosis with Air Concentrations Less than 2.5 mg F/m³; Urine Levels Less Than 5 mg F per Liter

In a total of eight reports, radiographic examinations of aluminum smelter workers have given negative evidence, i.e., no osteosclerosis (Table 6). In only three reports were air concentrations given; these did not exceed 2.5 mg F/m³. In five reports, urinary fluoride concentrations were given: in four of them the fluoride concentrations preshift were less than 5 ppm. Four additional studies in other industries reported air concentrations and urinary fluoride concentrations: in three, air concentrations were less than 2.5 mg/m³; in none did urinary fluoride levels exceed 5 ppm.

When air concentrations are maintained near or less than the proposed standard, years of exposure in potrooms do *not* produce osteosclerosis. The urinary fluoride concentration serves as a useful guide to exposure conditions. Valuable supplementary information can be drawn from the fact that in communities where the drinking water concentrations are about 4 ppm, no osteosclerosis ever develops. In such communities, average

urinary F concentrations are roughly comparable to those of the occupationally exposed group (i.e., < 5 ppm), indicating a comparable magnitude of absorbed fluoride.

The standard is therefore seen to serve as a useful guide. Individual variations call for a safety factor, and as an example, in the Massena population of 231 potroom workers (Kaltreider et al),[34] some presumably had larger total F intake from air, from food, and from water than others. The uniform absence of osteosclerosis stands, therefore, as evidence that the standard includes some margin of safety. There is another, more practical factor of safety in the standards. Irwin of ALCOA reported years ago on an empirical basis, that workmen never developed osteosclerosis if their exposures were controlled sufficiently that urinary F concentrations did not exceed 5 mg/l (ppm) for prolonged periods (Hodge and Smith, 1970).[57] The validity of this limit is reinforced by the data in Table 5. When postshift urinary F values recorded semiannually have exceeded 5 mg/l (e.g., Dinman et al, 1976)[58] regularly for three years, still osteosclerosis has not been detected.

This constitutes no cause for alarm or for precipitous action. No illness has been identified accompanying the earliest stage of osteosclerosis and a considerable length of time is required for the next stage to appear (Table 4), e.g., from stage 0-I to stage I might take four years (Franke et al),[50] or seven years (Schlegel),[52] allowing ample opportunity to correct conditions and reduce exposure. Urinary F analyses semiannually or annually and, *when indicated*, radiographs at longer intervals should guarantee that osteofluorosis will not develop. One study of employees in a fertilizer manufacturing plant, Derryberry et al (1963),[59] has stood for years at variance with the generalities relating air fluoride and urinary fluoride concentrations to osteosclerosis. Three specific points at which their data do not conform can be cited: (1) bone density increased in workers with low urinary fluorides (9/17 averaged less than 5 mg/l); (2) bone density increased in workers with low atmospheric fluoride exposures (5/17 with time-weighted atmospheric exposure of less than 2.5 mg/m³); and (3) little tendency appeared for bone density to increase with years of exposure. We suggest that the explanation for the apparent aberrations lies in, (a) generally low air fluoride concentrations in the plant as reflected, (b) in the generally low urinary fluoride excretions, and (c) the acceptance of "questionable or minimal changes" in bone density as uniformly real.

Derryberry et al[59] reported the health status and morbidity experience based on clinical studies together with time-weighted atmospheric exposures and urinary fluoride data compiled over periods of years. Two groups were selected for study: (a) *Exposed Group*; from all areas of the plant having fluoride exposure, 74 workers were chosen on the basis of "consistently high urinary fluoride excretion"; (b) *Control Group*; 67 matched employees with no "potential fluoride exposure." Individual data for the exposed group are given in their Appendix C, specifically "bone density changes", urinary fluoride excretion, and environmental fluoride weighted exposure. Evidence of increased bone density was drawn from chest and pelvic radiographs for each subject, plus pelvic films made prior to the study of each worker in the exposed group. Urinary F concentrations were estimated on postshift specimens collected after five consecutive workdays. The fluoride exposures for each worker were expressed as time-weighted averages based on average air F concentrations at each job location and the periods of time a workman spent on that job.

The roentgenographic examinations revealed "minimal or questionable degrees of increased bone density . . . in 23% of the fluoride-exposed group" (17 workers). A recent statistical treatment of these data (National Institute for Occupational Safety and Health, 1975)[26] gave "significant" increases in bone density with "exposure to higher atmospheric concentrations" of fluoride. We question the clinical reality of the osteosclerosis: The challenge is based on (a) the radiologist's prior knowledge of each individual's potential fluoride exposure, (b) the radiologist's statements that (i) "none of the radiographs showed sufficient increase in bone density to be recognized as such in routine radiological practice," and that (ii) "in no case was the bone change clear-cut," and (c) on the anomalous distribution of bone density changes when urinary fluoride values of selected individuals of the exposed group are compared as functions of the intensity or of the duration of fluoride exposure. This latter point will be explored in some detail.

Of the 57 exposed workers without bone density changes there are 14 whose average urinary F concentrations exceeded 5 mg/l (Table 7, Part A); in 13 of the 17 exposed workers *with* increased bone density, urinary F levels averaged ≤ 6.1 mg/l (Table 7, Part

Table 7. (Part A) — 14 of 57 Workers Without Bone Density Changes With Urinary F > 5 mg/l.

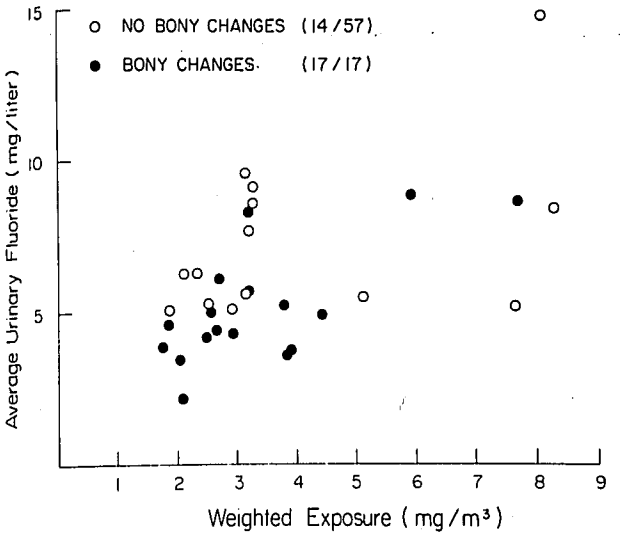
Worker Code No.	Years of Exposure	Urinary F Av (mg/l)	TWE* (mg/m³)
119	18.5	14.7	8.16
0	8.4	9.6	3.19
41	15.8	9.1	3.29
120	16.7	8.6	3.29
148	10.5	8.4	8.32
29	17.0	7.7	3.24
14	14.3	6.3	2.33
115	15.2	6.3	2.11
51	14.9	5.6	3.18
94	16.2	5.5	5.12
217	7.4	5.3	2.54
114	10.4	5.2	7.66
A-7	7.8	5.1	2.91
308	11.9	5.1	1.89

*Time-Weighted Exposure

Table 7. (Part B) — 17 Workers with Increased Bone Density 13 with Urinary F <6 mg/l.

Worker Code No.	Years of Exposure	Urinary F Av. (mg/l)	TWE* (mg/m³)
147	9.6	8.9	5.98
54	17.0	8.6	7.73
314	14.4	8.3	3.24
A-10	10.3	6.1	2.72
A-4	7.1	5.7	3.22
284	7.8	5.2	3.79
301	15.2	5.0	2.56
241	17.0	4.9	4.48
231	16.3	4.6	1.88
203	18.2	4.4	2.66
249	15.0	4.3	2.95
A-8	24.8	4.2	2.50
250	9.8	3.9	1.78
200	14.0	3.8	3.92
A-6	8.4	3.6	3.85
88	15.5	3.5	2.06
325	11.8	2.2	2.10

*Time-Weighted Exposure



Average urinary fluoride concentration vs weighted airborne exposure.

B). These data along with time-weighted exposures and years of exposure are taken from Appendix C of the original publication of Derryberry et al.[59] When average postshift urinary F concentrations are plotted against TWE (Fig 1), only three of those designated as showing questionable or minimal bone density increase are found, together with seven individuals without bone changes, among workers excreting urine containing on the average >6.1 mg/l. The basis for the statistical trend can be visualized; however, such a computation assumes equal validity for each point. Irwin's rule-of-thumb that osteosclerosis does not develop when urinary fluoride concentrations do not exceed 5 mg/l has been buttressed by all available information (see above). Fourteen of the 17 points fall at urine F levels ≤ 6.1 mg/l; for most of them the roentgenologic diagnosis is doubtful indeed. Only 6/17 cases would be suspect: those with urinary F values of 8.9, 8.6, 8.3, 6.1, 5.7 and 5.3 mg/l. Eleven instances of osteosclerosis from occupational F exposures may be found in the earlier literature summary (Table 4) in which urinary F data are given (some averages, some fragmentary): 9, 9, 10, 11, 13, 15, 15, 16, 23, ≤ 25 mg/l. In only two instances of osteosclerosis urine fluorides ranged below 9 ppm. Three of the workmen in the study of Derryberry et al[59] with average urinary F concentrations of 8.9, 8.6 and 8.3 mg/l may well have had minimal osteoporosis; it is improbable that any of the others did.

When the data from Table 7, A and B are grouped by the years of exposure, more workmen with or without bone density change had exposures of more than 15 years. Duration of employment apparently was not a key factor in the roentgenographic diagnosis.

Duration of Exposure (yrs.)	No. with Bony Changes	No. without Bony Changes
5-9	4	3
10-14	4	3
≥15	9	8

Finally, exposures of the 17 workers identified as exhibiting increased bone density were not uniformly excessive, in fact 9 had TWE below 3 mg/m³.

In summary, the radiographic examinations together with the other data reported by Derryberry et al[59] justify the diagnosis of "questionable or minimal changes," i.e., increased bone density, in only a few of the workers.

Research Needs

1. Additional data are urgently needed, such as those presented in Tables 5 and 6, specifically to support or amend the proposed relation between air F concentrations, urinary F concentrations and the presence or absence of osteosclerosis. To be most useful, the evidence should be collected on the same worker population over sufficient periods of employment to establish generalities like those foreshadowed in Table 4.

2. To understand and therefore to be in a position to control the effects arising from excess fluoride intake in workmen, additional data are needed on the metabolic fate of fluorides. In a recent publication, Dinman et al (1976)[60] offered a "whole body fluoride transfer model" with provisional assignments of fractions of inhaled fluoride (a) retained or exhaled in the respiratory tract, (b) absorbed in the gastrointestinal tract or excreted therefrom, (c) taken into the blood, (d) deposited in the bone, (e) lost through the sweat, or (f) eliminated in the urine. This model attempts to analyze and account for the known relations between air F concentrations and urinary fluoride excretion in workers who after several consecutive days of exposure have reached an approximate "steady state" of fluoride intake and excretion. No small part of the value of this model can be found in the emphasis directed toward several factors needing further study.

3. The potroom worker inhales a mixture of gaseous fluorides (HF, SiF_4) and particulates (cryolite, aluminum fluoride, aluminum oxide, dust). The particulates presumably bear adsorbed gaseous fluorides. Only scanty information is available on the relative proportions of gaseous and particulate fluorides in the potroom air.

4. One of the unresolved anomalies of fluoride absorption from industrial exposures is found in the studies of Collings et al (1951).[16] Fluoride inhaled as solid particulates was shown to be excreted in the urine as promptly and as quantitatively as followed inhalation of gaseous HF. Dinman et al (1976)[60] calculated the correlation between total F dose (gaseous plus particulate) assuming the workman breathed 10 m³ of air in an 8-hour shift, and total 24-hour urinary F excretion, estimating how much F would be excreted during the working hours, and adding this amount to the total F in the 16-hour urine collection beginning with the shift end. The correlation coefficient was high ($R^2 = 0.957$), perhaps but not necessarily implying that whatever gaseous and particulate fluorides were inhaled, the metabolic pattern was stable and not a function of the relative quantities. Dinman et al inferred that the gaseous (HF) part of the smelter air was "behaving as a particulate as regards pulmonary deposition." The total urinary F (mg/24 hr.) was linearly related to the total atmospheric F dose. By interpolation it appeared that those inhaling air containing about 2.5 mg F/m³ would excrete 9 or 10 mg F per 24 hours.

5. Dinman et al, for the first time indicated fractional deposition of fluorides in the naso-pharyngeal and tracheobronchial portions of the respiratory tract (particle size not stipulated) as well as alveolar deposition of 1-5 μm and of <1 μm particles. More evidence of particle size distribution is needed; to date not a single determination of the mass median aerodynamic diameter of potroom dust has been reported.

6. The number tentatively assigned in the model of Dinman et al to fluoride excretion in the sweat cannot be supported by any analyses. Workmen in the potroom engaged in strenuous work in a heated environment, may drink from 4 to 6 liters of water per

shift. Dinman et al (1974)[61] in discussing heat disorders in these workmen pointed out that usually only small changes of body weight occur, on the average about 0.3% loss during a 7-hour shift although electrode men during a 7-day week lost about 1.7% body weight, mostly in the first day. If sweat contains only F ion at serum concentrations (0.01 ppm), very large volumes would account for negligibly small fluoride losses.

Incidence of Arthritis

The earliest description of occupational fluorosis listed stiffness, restricted motion of the spine and "rheumatic pains" especially in the back and extremities (Møller and Gudjonsson,[40] Roholm,[41] Wilkie).[62] Recent writings often confirm these findings (e.g., Franke et al, 1975;[50] Domesle, 1969),[63] although sometimes no difference in the frequency of back or rheumatic pain is observed (Tourangeau, 1944;[64] Agate et al, 1949).[33] Hjort (1938)[65] found signs of spondylosis deformans of the spinal column in 37.5% of a group of 56 workers none of whom had osteofluorosis; the frequency corresponded with "that ordinarily met with in this age group (average 42 years)." Understandably, it is not uncommon to find reference to arthritic changes, (Derryberry et al, 1963;[59] Vischer et al, 1970;[66] Lezovic and Arnost, 1969;[67] Kaltreider et al, 1972)[34] if for no other reason than the difficulty of distinguishing them from certain fluoride effects on bone (Maillard et al, 1975).[68] Derryberry et al[59] compared the incidence of rheumatic and joint conditions in exposed workers with that in a control group (11% vs. 4%, resp.), and of hypertrophic arthritis (2 vs. 1, resp.). Kaltreider et al[34] recorded several observations indirectly or directly bearing on the arthritic status of potroom workers. They found in the 1945-46 survey of potroom workers in the Niagara Falls works, 11 of 107 workmen with "restricted motion of elbows" whereas, in the control group only one of 108 showed this condition. "None of the potroom workers complained of back pain, even though many had rather marked restriction of the dorsolumbar spine due to hypertrophic arthritis, osteosclerosis and calcification of these spinal ligaments. It is believed that the restriction of the motion of elbows in potroom workers is due to traumatic arthritis rather than to fluoride absorption because roentgenograms do not show the generalized increase in bone density that is characteristic of fluorosis. The use of sledge hammer and long metal bar by these workers results in repetitive jarring to the arms." In the survey by Kaltreider et al[34] of the Messina operations in 1960-67, "A fair number (4.7%, 11 of 231 potroom workers) . . . have definite bony involvement of the elbows, resulting in restriction (both flexion and extension) of the forearm, a condition which was painful in some cases." Three of the control group of 152 had similar degenerative changes. Symptomatic degenerative arthritis was found in 4.3% of the exposed group as compared with 5.9% of the control group.

Some support for the contention that sclerosis does not predispose to arthritis can be found in the studies by Leone et al (1955)[56] of persons whose drinking water supply contained 8 ppm F and who developed osteosclerosis in about 10% of the population, but without unusual incidence of arthritis. Stevenson and Watson (1957)[48] also reported no unusual incidence of arthritis in 23 patients with histories of long continued intake of drinking waters containing 4 to 8 ppm F.

LUNG EFFECTS AND THE STANDARD

Irritancy

Irritation of the eyes and nose by about 35 ppm hydrogen fluoride was reported by Machle and colleagues (1934-35)[69] and respiratory irritation at 67 ppm (1934). Elkins (1959)[70] described nose bleeds and sinus trouble from high HF exposures. These were all excessive concentrations in comparison with the modern emergency exposure limits. Recent reports described impaired nasal respiration (Rybicki, 1970),[71] and wheezing and discomfort in the nose and throat of workers in a cryolite plant (Johnson, 1973).[72] Jahr et al (1974)[73] found a 42% incidence of pharyngitis in Söderberg potroom workers (all smokers) against 17% in control subjects (all but one smokers); there was no pharyngitis in nonsmoking workers. Zislin and Girskaya (1971)[74] described a remarkable and progressive sequence beginning with inflammation of the upper respiratory tract and nose, progressing from membrane hypertrophy to atrophy, even perforation of the nasal septum. The exposure was described only as "elevated in level." Papoyan and Demirchoglyan in 1963[75] commented that the "industry is free of conditions which would cause the gross pathology that was observed formerly — perforation of the septum nasi, pronounced pneumofibrosis, etc."

Shortness of Breath

Shortness of breath was a common complaint, afflicting 50% of the Danish cryolite workers and accompanied by a high incidence of pulmonary fibrosis (Roholm).[41] Industrial dyspnea in potroom workers has been described by Frostad (1936),[76] Evang (1938),[77] Hjort (1938),[65] Midttun (1960),[78] Johnson (1973),[72] Jahr et al (1974),[73] and others.

Asthma

Asthma, noticeably common, was first related to potroom exposures by Frostad (1936),[76] an observation repeated and discussed by Evang (1938),[77] Hjort (1938)[65] and others. In Evang's study, 18 of 190 in-plant personnel complained of "bronchial" asthma whereas only 32 of 1,800 residents of the nearby district suffered from such attacks. Hjort attributed to better ventilation, the lower incidence he observed, five asthmatic patients among 89 workers. Both Evang and Hjort suspected there was an allergic basis for the illnesses; Evang suggested that possibly a component of the tar smoke, "a motley mixture", might be responsible. Midttun (1960)[78] found 55 asthmatic workmen among approximately 400 examined during 1955 to 1960; some exhibited atopy and eosinophilia. An occasional individual suffered an asthmatic attack immediately on first exposures to the potroom atmosphere; a familial history usually was presented. In a plant with air concentrations of HF and of particulate fluorides generally below the TLV, Johnson et al (1973)[72] located 13 asthmatic individuals (eight with familial histories) among 2,125 examined. Guthe (1976)[79] in a note on respiratory disorders in potroom workers quoted two investigations rejecting an allergic basis for the asthmatic responses in potroom workers (Bruusgaard, 1960;[80] Glømme et al, 1961).[81] Under the exposure conditions of the Massena plant, Kaltreider et al[34] commented that "the incidence of chronic obstructive pulmonary disease among the employees in the potroom was little different from the control" (13.8% vs. 11.8%, resp.). Their diagnosis included chronic bronchitis, bronchiectasis, emphysema and intrinsic asthma, in each case based on clinical history and physical findings. Papoyan and Demirchoglyan (1963)[75] commented on the "comparatively light course" of chronic bronchitis most often observed in potroom workers, 9% of whom were so diagnosed and changes noted roentgenologically. Over one-third of these workers complained of cough and one-fifth of chest pain. Râles were not found in those employed less than two years but did occur in 40% of the potroom workers employed 5-10 years as com-

pared to 24% of others in the plant. On x-ray examination about 10% exhibited emphysema of moderate degree and pleural thickening in over one-fifth of the employees.

Upper Respiratory Infections

A small difference in the frequency of upper respiratory infections (two or more per year) between potroom employees (24%) and the control group, in the opinion of Kaltreider et al,[34] although not significant, "warrants further evaluation". Blaming the dustiness of the air as well as the components, Miller and Gotlib (1973)[82] characterized upper respiratory infections as "extremely common" and named them and bronchitis as responsible for most temporary disabilities.

Chronic Respiratory Disease

No difference in the numbers of respiratory illnesses of 698 potroom workers and of unexposed employees appeared in their medical histories during a 4-year period, according to Tourangeau (1944).[64] "Not normal" respiratory conditions were discovered by Derryberry et al[59] more frequently in the exposed group of phosphate fertilizer workers than in the controls by both medical histories (26% vs. 12%, resp. — pneumonia, pleurisy, influenza) and by physical examinations (11% vs 8%, resp.). Tsunoda (1970)[83 84] commented that trouble in pulmonary function was "not serious." Kaltreider et al[34] diagnosed five cases of chronic obstructive lung disease in 107 potroom men as compared with four cases in 108 control group employees. Productive cough accompanied by sputum production was higher in the furnace room employees examined by Agate et al (1949)[33] than in men and women with lesser exposures.

Spirometry measurements have been used on a number of occasions to evaluate the incidence of chronic obstructive lung disease. In two reports, the tests confirmed the diagnosis of obstructive airway change in a few workmen known to suffer from respiratory disease (Glømme et al, 1975;[81] Johnson et al, 1973).[72] In the program of tests of one aluminum smelter Jahr et al (1974)[73] measured the FEV_1 before and after work for the same workers and correlated lung function with fluoride exposure and with postshift urinary F concentration. A tendency appeared, not marked, for FEV_1 to decrease during the shift as atmospheric fluorides increased. No correlation between FEV_1 and urinary fluoride was found, FEV_1 measurements remained unchanged before and after work, and from day to day in three plants, but decreased over the weekend in 25 workmen from a hooded prebake potroom; the averages were 80.4 before and 75.3 after the weekend (Jahr et al, 1974;[73] compare Jahr and Wannag, 1972).[85] In four other applications of spirometry (Bowler et al, 1947;[86] Leidell et al, 1967;[87] Kaltreider et al, 1972;[34] Jahr and Wannag, 1972),[85] which based the diagnosis on a combination of two tests (the standardized respiratory symptoms questionnaire, and forced expiratory spirometry), the conclusions were clear-cut: In the words of Discher and Beitenstein,[88] "potroom workers do not incur a major risk of chronic pulmonary disease." Papoyan and Demirchoglyan (1963)[75] found normal total lung capacity in two-thirds of the employees. The studies of S. G. Yeramyan were quoted: 50 workers who showed chronic fluoride effects (bronchitis?) showed increased respiration rate, small increases in minute volume, some increase in oxygen consumption, decrease in the coefficient of oxygen utilization, and an increased basal metabolism.

The smoking habits of employees in fluoride-exposed and control groups have been recorded in a few studies (Jahr and Wannag, 1972;[85] Jahr et al, 1974;[73] Discher and Breitenstein, 1976);[88] some, not disastrous, adverse effects accompanied smoking.

No meaningful differences were observed by Kaltreider et al[34] in the incidence of a number of other pulmonary diseases when potroom workers were compared with control groups: bronchitis, bronchiectasis, emphysema, pneumonia, carcinoma, pneumothorax and lung abscess.

KIDNEY EFFECTS AND THE STANDARD

Acutely toxic fluoride doses can cause severe kidney injury. Chronic exposures of experimental animals to excessive amounts of F, e.g., 100 ppm F in the drinking water of rats for a few months, produce detectable structural and functional changes. Although the chronic effects have never been seen in man, the possibility of kidney injury from prolonged industrial exposures has been explored several times. Cryolite exposures under very dusty conditions were not accompanied by albuminuria or glycosuria (Roholm);[41] autopsies of two long-term employees revealed slight chronic nephritis in one and normal kidney tissues in the other. Tourangeau (1944)[64] found no evidence of differences in renal disease between potroom workers and a control group. A question of a fluoride injury was raised by Derryberry et al (1963)[59] on the basis of a higher incidence of albuminuria in fluoride-exposed workmen (12% of 74), as compared with a control group of employees (4% of 67); all other "not normal genitourinary conditions" occurred with approximately equal frequency in the two groups. The suspicion was reinforced by distribution of albuminuria between the groups of fluoride-exposed workmen (a) "with increased bone density" — 24% and (b) "without increased bone density" — 9%, and led to the suggestion "of a relationship between fluoride exposure and increased excretion of albumin in the urine," no such relation can be found in the data of Kaltreider et al:[34] In the Niagara Falls plant albuminuria was reported in 5 of 107 potroom workers as compared with 3 of 108 controls; in the lower exposures at the Massena plant the corresponding data were 3 of 231 and 5 of 152, respectively. The hypothesis that protein levels in the urine increase with increasing urinary fluoride concentrations was tested specifically by Dinman et al (1976)[89] using data from over 16,000 urinalyses, 4652 on control employees, 11,793 on potroom workers. A chi-square statistic was applied to the data presented in two ways: (a) incidence by cumulative fluoride concentration groups, i.e., in those with average concentrations $\geq$ 10 ppm, $>$ 9 ppm, etc., (b) incidence in groups with average F concentrations 3 to 3.99 ppm, 4 to 4.99 ppm, etc. No significant differences appeared. The conclusion thus can be safely drawn that urinary fluoride concentrations do not contribute to proteinuria in these potroom workers.

SKIN DISORDERS

A relative high frequency of skin rashes (12%) occurred in the cryolite workers examined by Roholm.[41] Tourangeau (1944)[64] included skin disorders with a considerable list of other diseases showing no differences in incidence between potroom workers and a control group of workers. A marked increase in the incidence of dermatitis in potroom workers followed a malfunctioning of equipment which released large quantities of fluorides (Midttun, 1960).[78] Rybicki (1970)[71] mentioned skin irritation of the ears. A report of careful skin examinations by Kaltreider et al[34] listed a few disorders of various sorts. In the Niagara Falls plant, scars from minor burns were common, two cases of ichthyosis and two of pruritic rash were found. In the Massena plant, dermatologic lesions of potroom and control workmen were

tabulated; the conditions were "essentially the same in both groups." No skin cancers were found at Niagara Falls, one "questionable basal cell carcinoma of the left ear" at Massena. Chizzola maculae were absent (see below). On reexamination of 66 of the 231 potroom workers five to seven years later, one man had developed an allergic-type dermatitis, "skin tests were all negative except for rare tars." Skin diseases in general were "similar to those one might expect in any group of workers with similar background."

PREGNANCY

The health hazards for the pregnant woman and for the fetus have not in the past been a routine consideration in the selection of TLVs. Evidence on fluoride effects can be drawn from animal toxicity studies and from a few observations on human exposures.

Animal toxicity studies show effects from large doses on reproduction, and on the fetus: (1) Fluoride crosses the placenta and deposits in the calcified tissues of the fetus (Gedalia, 1970).[90] (2) The estrus cycle of rats, not altered by dietary fluoride levels nearly high enough to inhibit growth, ceased when 2.5 mg/kg body weight was taken daily. Equivalent restriction of the amount of control diet to that of the fluoride diet voluntarily consumed had similar effects (Phillips et al, 1933).[91] (3) Fluoride in concentrations over 60 ppm (in dairy cows) interferes with reproduction (see review by Hodge and Smith, 1965)[92] (one report at variance described decreased breeding efficiency when drinking water contained > 5 ppm F (Van Rensberg and de Vos, 1966)).[93] (4) Embryotoxicity (abortion, dead fetuses, necrotic placentae) followed doses to rats of 3-12 mg F/kg/day (Devoto et al, 1972).[94] (5) Abnormal fetal tooth and bone structures were produced by dosing the pregnant dog or rat with one or more mg NaF/kg/day (Knouff et al, 1935-36;[95] Glock et al, 1940;[96] Paynter and Grainger, 1956).[97] (6) Treating ova of the mouse, sheep and cow *in vitro* with F concentrations ranging from 250-4000 ppm gave rise to detectable alterations in meiotic division and in chromosomes. (7) Repeated *in vivo* doses ranging from 2.5-7.5 mg F/kg/day in mice did not interfere with meiosis except for one test in which 500 μg F per mouse intravenously produced several cells with abnormal-appearing chromosomes (Jagiello and Lin, 1974).[98] On a weight for weight basis, these toxic doses in animals exceed an estimated occupational fluoride intake for a 50 kg woman employee by at least 10 to 200-fold.

Clinical reports of industrial medical experience with pregnant women exposed to fluorides are nearly non-existent. Møller and Gudjonsson (1932)[40] discovered osteosclerosis in two women employed in a dusty cryolite factory for six years and Roholm[41] reported a total of five children born to women who worked before or during pregnancy in that factory.

Data are available from a single epidemiological study of gynecologic problems in female workers in a superphosphate manufacturing plant (Kuznetsova, 1969).[99] The exposed group comprised 302 women mostly 20-40 years old and the control group 309 office employees and housewives not exposed to F. Dust concentrations in the superphosphate plant ranged from 5 to 57 mg/m^3; F concentrations ranged from about 0.3 to 2.8 mg/m^3. Irregularities of menstruation were considerable more frequent (five or six times) in the workers; the frequency increased with dustiness, not with age, but markedly (two times) with employment over six years. Inflammation of the uterus, cervix and vagina occurred four times as frequently in workers, mostly in women exposed to plain and granulated superphosphate.

No differences were noted between exposed and control groups in the numbers or the courses of pregnancies, miscarriages, and births. During pregnancy, the plant workers more frequently showed (a) toxicosis with hypotension and threatened abortion, and (b) "untimely" discharge of amniotic fluid and "weakness of birth activity" (Kuznetsova, 1969).[99] Additional epidemiological studies are needed.

No reports of unusually high spontaneous abortion rates, nor of elevated birth rates of abnormal fetuses have come from U.S. communities in which the drinking water supplies naturally contained 4 ppm fluoride or more.

The risks from occupational exposures to fluorides at concentrations maintained at or below 2.5 mg F/m^3 is judged to be small: the standard predictably will protect the pregnant woman and her fetus.

INDICES OF FLUORIDE INTOXICATION

The diagnosis of early industrial fluorosis depends on the appearance of identifiable radiologic bone changes. The difficulties attendant are generally recognized and have stimulated searches for other criteria. Some of the growing list of possibly or demonstrably useful indices will be cited:

1. The history of fluoride exposure stands out as a key factor.

2. Medical histories and physical examinations often bring out evidence of restricted rotation of the trunk, and stiffness. The complaints repeatedly reported from factory groups outside the U.S. include back pain, headache, vertigo, tinnitus, anorexia, dyspepsia, constipation, nausea, cough, dyspnea, and occasionally autonomic disorders (increased gastric acidity, hyperhidrosis, bradycardia, myocardial changes), endocrine responses to skeletal change (hypothyroid, hypopituitary function), and suspected neurologic effects (anterior horn cell lesions in the spinal cord). The authenticity of these complaints, i.e., their relation to fluoride exposure, is doubtful unless the exposure conditions exceed those typical of U.S. operations.

3. Urinary fluoride concentrations are widely accepted as trustworthy indices of exposure and their trend a dependable prognosticator.

4. Grades of x-ray changes are evaluated as described in the discussion of osteosclerosis.

5. Histologic abnormalities in preparations from bone biopsies offer valuable guidance, at a serious cost.

6. Fluoride concentrations in bone ash from bone biopsies are accepted as useful confirmatory evidence of the status of the exposed worker especially after prolonged periods of employment. The cost, of course, is high. Tooth fluoride levels may be a substitute, but are not at present established.

7. Blood fluorides are promising indices; preliminary evidence points to a simple relation between bone fluoride and blood fluoride concentrations.

8. Disturbances in other blood constituents offer attractive possibilities. None has reliably demonstrated diagnostic value; a growing number has been reported. The list includes: INCREASED cobalt (Sidorkin and Nikolaev, 1971),[100] glutathione (Shirinova and Rubinskaya, 1973),[101] cholesterol (Veretel'nikova and Kornilova, 1968),[102] lactate, enolase, pyruvate kinase, ATPase (Guminska and Sterkowicz, 1975),[103] and alkaline phosphatase (Franke et al, 1975);[50] DECREASED manganese (Nikolaev and Kas'yanova, 1970),[104] catalase and peroxidase, (Shirinova and Rubinskaya, 1973),[101] lecithin, calcium, sodium (Vetel'nikova and Kornilova, 1968),[102] and β-globulin, glucose (Guminska and Sterkowicz, 1975).[103]

HEALTH EFFECTS OF FLUORIDE EMISSIONS IN THE SURROUNDING COMMUNITY

When compared to investigations of effects in factory workers, it is evident that far fewer studies have been reported of persons residing in the vicinity of fluoride-emitting industries. The data available have been assembled in Table 8. It is evident that most such investigations have been directed to communities in the neighborhood of either aluminum or fertilizer manufacturing plants, with the former outnumbering the latter 3 to 1.

There appears to be no uniformity of findings among the results summarized in Table 8. Fluoride from either industry has been found by some investigators to cause mottling of the enamel of children's teeth, while this effect has not been noted by others. Effluents from the aluminum industry have been credited by some investigators with reducing the incidence of dental caries in children, but others have seen no such protective action. In two instances the concentration of fluoride in teeth was increased. Skeletal changes detectable upon x-ray examination were reported in two studies, but were not demonstrable in four others. Urinary excretion of fluoride also was reported unaffected more often than not. On the other hand, hematologic and other blood changes were described in two studies, but were not seen in a third. Afflictions of the respiratory tract were found in three studies. Examining the data on drinking water, airborne fluoride, and urinary excretion reported in the several studies gives the impression of mostly fairly "normal" values. The origin of the abnormalities described in skeletal, dental, hematological, pulmonary and other systems is not clear; if fluoride is a factor, other important sources must be unrecognized.

Several other reports of population studies can be cited. Call et al (1965)[105] did not find unusually high concentrations of fluoride in soft tissues obtained at autopsy of residents of Utah who were subjected to industrial effluents; however, the fluoride exposure of these individuals was unknown. Murray and Wilson (1946)[106] reported elevated urinary fluoride concentrations and the presence of bone and joint pains in members of a farm family residing near an ironstone works, but osteosclerosis was not evident upon x-ray examination. Claims of fluoride injury by residents of a farm 1.5 miles from an aluminum plant in Oregon were upheld by the courts. However, an investigation by a Royal Commission (1968)[107] into the possibility of damage to residents near a phosphate fertilizer plant in Haldimand County, Ontario found the air concentrations were not such as to cause fluorosis and that food and water supplies were not contaminated, nor was there radiological evidence of exostoses or evidence of elevated urinary fluoride in those persons who felt they were suffering from fluorosis.

The evidence assembled here suggests that industrial emissions of fluoride have little, if any, significant effect upon the health of nearby residents. The data also suggest that the definitive study has not yet been done, and that it will require careful planning and execution. For example, only two of the several criteria used in the above listed studies are specific for fluoride, viz., urinary excretion of fluoride, and the concentration of fluoride in teeth. Skeletal changes seen upon x-ray examination may also be considered pathognomonic of fluorosis. Each of these criteria, however, may be affected by fluoride received from other than airborne sources. Consequently, it will be necessary that the study group and the control group be closely matched as to nonairborne sources of fluoride intake. Indeed these should be quantitatively measured, not assumed to be equivalent because of similar socio-economic backgrounds. Also, the level of dental care enjoyed by the two groups must be closely similar. Changes in blood indices, and nature and frequency of respiratory complaints are not unique to fluoride. They do reflect many of the minor childhood illnesses to which the two populations will be subject, and, therefore, may be expected to confuse comparisons between the groups with positive responses not related to fluoride exposure.

Chizzola maculae

The Mori aluminum smelter located near the village of Chizzola in Trentino, Italy, began operation in 1929. Not long thereafter, the effluents damaged nearby trees and vines, and within two years cattle and goats developed the skeletal changes associated with chronic fluorosis. In 1932 and 1933, an epidemic of skin lesions christened "Chizzola maculae" appeared in persons living in the neighborhood, diminished in prevalence in subsequent years, although lesions were occasionally (Table 9) seen until 1937 (Cristofolino and Largaiolli, 1966).[108] The lesions, round areas, often about the size of a dime, dark-blue, brown to red, or grey in color, sometimes disappeared after four or five days, sometimes persisted for a few weeks. Frequently during the first days or at the time the skin lesion appeared, those afflicted suffered transient arthralgia, asthenia, anorexia, and rarely fever. The spots were similar to ecchymosis or to erythema nodosum; differentiation between a spot and ecchymosis was difficult. These "Chizzola maculae" were observed in children, sometimes in women, rarely in men, and not in smelter workers nor in their families. Steinegger (1969)[109] described the same condition in the village children of Bolzano near another aluminum factory. Several subsequent reports have dealt with the description, distribution and history of the lesions (Largaiolli, 1968;[110] Colombino et al, 1967, 1969;[111] [112] Cerquiglini-Monteriolo et al, 1967;[113] Ricci, 1967;[114] Olivo et al, 1968).[115] In 1969, Waldbott and Cecilioni[116] discovered Chizzola maculae on the skin of 10 individuals among 32 residents near fertilizer plants in Ontario and in Iowa, and an iron foundry in Michigan. The concensus attributed the spots to fluoride exposures.

The table (based on the excellent summary of Cavagna and Bobbio (1970))[117] shows that in Chizzola children from 1933 to 1937 many cases were reported in the early years (1933-35) and only three in 1937. In the nearby villages, Serravalle and Santa Margherita, more distant from the aluminum plant at Mori, there were fewer cases. The incidence peaked in 1934 in each village and thereafter subsided. For reasons unknown, despite continuing aluminum production with the consequent contamination of the neighborhood air, no cases were reported between 1937 and 1965.

In 1967, a new epidemic appeared in which 38% of the children examined in Chizzola had maculae (Table 9).[117] Olivo et al[115] cast doubt on the accepted etiology by pointing out that in the village of Pilcante, 7 km from Chizzola, 23% of the children were affected although fluoride contamination must have been very much less than in Chizzola. The urinary fluoride concentrations near the factory were not different from urinary fluoride values in the uncontaminated area, a finding reinforcing the doubt of a causal role of fluoride. A survey of Chizzola and other school children beginning in 1965 by a Health Commission of the Ministry of Health showed in 1967 (Table 9) that 49% of the Chizzola children were afflicted which compared well with the incidence of spots in seven nearby communities where the air bore no effluents from aluminum factories. In these communities, 22 to 58 children were affected in the groups of 55 to 126 examined, or 36 to 52% of those examined.

Selected examples of other supporting evidence give additional

Table 8. — Responses in Neighborhood Residents Exposed to Fluoride Emissions.

Subjects	Exposure Conditions	Comment	Reference
Aluminum Production			
26 men, 51 women; most lived within 1 mile of plant, a few at 2 miles 29 boys, 24 girls aged 5-12 yrs. 34 boys, 25 girls aged 5-17 yrs. Nearly all of these children lived within 1-1.5 miles of plant	Drinking water for these populations contained 0.07-0.18 ppm F. Ambient air concns. on one calm day were 0.045-0.048 mg F/m^3	Urinary F: Av. excretion for adults 0.84 mg F/24 hrs, about 40-60% that of general factory workers. Av. excretion for children 0.32-0.45 mg F/24 hrs. Blood hemoglobin and RBC and WBC counts unaffected in adults or children. Teeth of children: Slight increase in incidence of very mild to mild mottling compared to children elsewhere (5.6% vs. 0.6 or 3.1% in two control areas). Teeth of children nearer plant appeared less prone to caries. No correlation between urinary F and occurrence of mottled enamel.	Agate et al (1949)[33]
46 school children 5th grade Most live downwind from alumina refinery	Plant effluents contain cryolite, fluorspar, SiF_4, H_2SiF_6, small amt. HF. Also CO, CO_2. Water supply contained 0.8 ppm F. 34 children had used this water >3 yrs; 3 used it <3 yrs.	Urinary F: Av. for all children 0.97 ppm. Av. for the 34 longer term residents, 1.01 ppm; for the others, 0.85 ppm. Conclude respiratory intake of F did not affect mean urinary concn., though range was skewed to right. No evidence of any major source of F ingestion.	Archer et al (1975)[147]
Children aged 6-14 yrs. Lived near aluminum plant up to about 12 yrs.	Study began after plant had been operating 5 yrs and continued for 8 yrs. Calcd. daily intake was 1.4 mg F from diet, 0.4-0.7 mg inhaled. Dietary intake in control area, 0.8 mg F; negligible amts. in air. Water supplies both areas, 0.1-0.3 mg F/l. Airborne concns. averaged 0.14 mg F/m^3 in zone around factory, (5x the MPC of 0.03 mg/m^3), and reached 1.13 mg/m^3; gaseous forms (HF, SiF_4) 39% of total, particulates (CaF_2, NaF, AlF_3) 31%. At 8-9 km, gaseous 85%, particulates 15%.	No significant differences in clinical observations between exposed and control groups. No skin spots. Av. F concns. mg F/100 g, for the exposed and control population were: hair, 0.7-4.7 (av. 1.6) vs 0.75; finger nails, 20.9 vs 14.3; teeth, (fresh wt) 13.5-131.4 (av. 45.02) vs 9.2-25.4 (av. 15.71). Urine, mg F/l, 0.14-0.86 (av. 0.32) vs 0.00-0.80 (av. 0.36). Decrease of hemoglobin, increase of erythrocytes in blood of exposed children. Populations were relocated to other areas, and 6-10 yr old children who had lived in the new area up to 10 yrs were examined as before. Erythrocyte counts were unchanged, hemoglobin was greater, F concns. in hair and urine were less, compared to the children who had lived near the plant.	Balazova (1971);[148,149] Hluchan et al (1968);[13] Balazova et al (1970);[150] Balazova and Lipkova (1974);[151] Lezovic and Balazova (1969)[152]
School children 9-10 yrs. old, 13-14 yrs. old living near aluminum plant; controls of comparable ages. Dental exams on 132 girls, 112 boys in this area, and on 99 girls, 85 boys in control area.	Water samples from the area contained 0.30-0.35 ppm F over a 3 yr. period, indicating no effect of emissions. Samples from 1 area contained 0.45-0.47 ppm F. Vegetables contained surface F concns. 5-10x above normal but easily removed by washing. F concns. normal in foods of animal origin.	Urinary F concns.: 9-10 yr. old exposed and controls, av. 0.64 and 0.50 mg F/l.; resp. 13-14 yr old exposed and controls, av. 0.68 and 0.54 mg F/l., resp. exposed and control adults 0.44-1.10 (av. 0.63) and 0.42-0.91 (av. 0.58) mg F/l, resp. Control adults using water containing 0.95-1.10 ppm F, 0.7-1.3 (av. 1.1) mg F/l in urine.	Demole and Held (1963)[153]
13 adults 22-65 yrs. old living near the plant; 8 comparable control subjects.		Caries incidence, concn. of F in teeth of children were normal. Skeletal effects: No instances of sacrolumbar pain, vertebral rigidity. X-ray examns. of 10 residents 30-65 yrs. old showed no signs of fluorosis.	
Children residing near aluminum foundry in Inata, Hungary	Airborne concns. 0.03-0.06 mg F/m^3	Children had slightly less caries than normal and excreted ≤ 6.6 mg F/liter urine	Leloczky (1970)[154]

Table 8 (cont.)

Subjects	Exposure Conditions	Comment	Reference
145 children aged 6-14 yrs. living at least 6 yrs. in the fall-out area of an aluminum plant in Czechoslovakia Control subjects	Plant in densely populated area, inadequately ventilated valley, high humidity, calms prevailing 30% of time, frequent temp. inversions.	Av. hemoglobin concns. were decreased, erythrocyte counts elevated; leucocyte counts elevated in 6-8 yr olds but lower in older children (differences not significant). Differential white cell counts not significantly different. Measurements repeated 2 yrs. later showed hemoglobin did not increase in 12-14 yr olds as it did in younger children; leucocyte counts were lower, except in 9-11 yr olds, but differences not significant. All ages showed decrease in neutrophil non-segmented granulocytes, increases in lymphocytes. Urinary F, av. mg F/l, at first examn.: 6-8 yr olds, 0.8; 9-11 yr olds, 0.85; 12-14 yr olds, 0.4. Corresponding concns. at second examn. were 0.75, 0.84 and 0.45. Max. concns. for exposed children were in 1959, 1960, 1961 and 1962, 4.5, 4.75, 1.72 and 1.1., resp. X-ray of lumbar spine, hip joint, shoulder, arm + elbow showed no changes indicative of fluorosis. Dental caries index was 0.272 for exposed, 0.673 for controls. Mottling evident in 29% of exposed, (0.3% of controls).	Macuch et al (1963)[155]
Area residents near aluminum factory 15 "disputed" cases between Sept. 1960-Oct. 1967	Max. 0.059 mg/m³, av. 0.016 mg/m³ "in plot next to factory"	Medical survey showed symptoms such as cough, phlegm, nausea, throat irritation; similar effects seen in other, similar areas. No clear-cut ophthalmologic or otolaryngologic effects. High ratio of reddish pharynx and an abnormal respiratory sound, in infants. No immediate or serious concern, but steps should be taken since factory emissions will continue.	Osaka Prefecture (1970)[156]
Children 6-17 yrs. old Total of 2483 from 4 villages near Al or cryolite plants; 1380 from control village	Airborne concns. near plants, 0.03-0.56 mg/m³ Water fluoride, 0.17-0.54 mg/liter for 3 villages, 0.8 mg/liter for fourth Air- and waterborne F negligable for control village	Teeth: 31.0-37.5% incidence of mottled enamel and 10.8-24.5% incidence of dental caries. Percentages were 2.1 and 37.5%, resp. for controls.	Sadilova (1957)[157]
54 children 3-19 yrs old resident on island >3 yrs. 12 control children, resident ≤ 3 yrs. Sauvie Island, Oregon. At junction of Columbia and Willamette Rivers about 1 mile NW of aluminum plant in Vancouver.	During 1941-45, av. emissions of F as HF was 7000 lb/day; 1945-49, 3600 lbs/day; after 1949, 1100 lbs. Most of vegetables, meats grown locally. Water from private wells; < 0.1 ppm F	No evidence of mottling. Intraoral x-rays indicated slightly accelerated calcification and eruption of permanent teeth. Normal calcification of enamel. X-rays of wrist, hand, elbow, knee showed no changes attributable to fluoride. Body weights somewhat above av..	Savara et al (1954)[158]
School children of either sex from grades 5 and 6, primary school and years 2 and 3, secondary school Subjects resided within 2 km of aluminum plant	Concentrations of airborne fluoride were 3-5 ppb. F in soot, 100-230 kg/km²/month	X-rays of right hand and wrist of children living near plant indicated retarded skeletal development of carpal bone among boys in 5-6 grades of primary school, girls of 6 grade. Development was accelerated in carpal bones of girls in yrs 2 and 3 of secondary school.	Tajima et al (1968)[159]

Table 8 (cont.)

Subjects	Exposure Conditions	Comment	Reference
Control subjects resided in another town about 6 km from the plant		Conclude atmospheric fluoride pollution in these circumstances does not have important effect on skeletal development.	
Adult residents (35-64 yrs old) near Al refinery, and a control village	Not given	Noted subjective symptoms of F poisoning, e.g., bone x-ray changes, F in urine, cardiac pulmonary function changes, blood changes. Discomfort obviously more frequent among residents of polluted area, but little differences between the 2 villages as to irritation of skin, eyes, joint pain, pulmonary and cardiac function tests. Radiological findings: See above. Osteosclerosis was more frequent among men and women of the polluted area only for the knee joints. Skin effects: See above.	Tsuji and Tsunoda (1970)[160]
Residents living in vicinity of aluminum factory	—	At concns. of 1-1.9 ppm there was no conclusive evidence of skin or eye response, dental effects or osteomalacia; possible slight effect on pulmonary function.	Tsunoda F. (1970)[94]
Residents living near aluminum factory in Fukushima Prefecture	Airborne concns. within 1 km of the factory were 5.2-14.0 mg F/m³	Daily F intake is 4.2 mg; av. Japanese intake is 3.5 mg F/day. Evidence of dental, skeletal fluorosis, crippling fluorosis.	Tsunoda H. (1970)[93]
Phosphate and Fertilizer Production			
314 children in grades 3-7, living within 1 km of superphosphate plant	An older plant, located between two settlements; max. distance to further settlement, 200-300 m. Airborne concns. at varying distances were: 100 m, 0.90 mg F cmpds/m³ 400 0.44 700 0.40 1000 0.19 1500 0.09	Slight dental fluorosis seen in 183 children, moderate fluorosis in 26, and severe fluorosis in 4. No changes seen in children living in the area < 1 yr.	Khnygin and Shamsutdinova (1970)[161]
1375 children living 0.5-1.7 km south or 0.5-3 km west of superphosphate factory 678 children from control village 10 km distant	500 m from plant F concn., 16 x MAC SO2, 9.5 x H2SO4 aerosol, 27.9 x NOx, 33.9 x 3000 m from plant F concn., 3.3 x MAC SO2, 1.7 x H2SO4 aerosol, 3 x NOx, 1.2 x	High percentage of exposed children had enlarged lymphatic glands, Catarrhal condition 10.4-17.4 times that in controls; greater frequency with age, length of residency. Pulmonary x-ray changes (presumably of TB origin) were 2.68-3.76 times that in controls. (Lower figures for catarrhal and TB changes and the higher figure for non-TB changes are for children living in the further village).	Lindberg (1960)[162]
707 school children ages 7-14 yrs. Continuous residents of Khouribga, Morocco	Principal phosphate mining areas of Morocco located here. Drinking water contained 0.18-0.53 (av. 0.38) ppm F.	Nearly all children showed dental mottling. Community index of dental fluorosis was 1.5-2.7; lowest in 7-9 yr olds, highest in older age groups. Severity of dental fluorosis was inversely correlated with distance from phosphate factory out to 2 km. Conclude dental mottling seen in these children is caused primarily by F-containing phosphate dust.	Møller and Poulsen (1975)[163]
School children residing in vicinity of fertilizer operations		No indications of dental fluorosis	Specht and Calaceto (1967)[164]

Table 9. — Incidence of Chizzola Maculae.
(After Cavagna and Bobbio, 1970)[117]

Community	1933	1934	1935	1936	1937	1938-1965	1967	1968
	No. of cases in population							
Chizzola	248	149	8	26	3	0	38%*	98/100†‡
Serravalle	65	126	4	11	18	0		
Santa Margherita	18	58	1	1	1	0		
Pilcante (7 km from Chizzola)							23%*	
Chizzola school children							39/79 ~ 49%	
School children of 7 communities of same region, but free of aluminum plant effluents							22 to 58 of 55-126 examined (36-52%)	
Opatovce, Czechoslowakia 200-800 meters from aluminum plant in Ziar nad Hron				School children studied 1953-1968. Absorbed 2.5 mg F/day, chiefly in food. Dental fluorosis, low hemoglobin but no skin spots attributed to fluoride				

*Percent of population examined
†School children examined
‡Emission controls instituted

weight to the conclusion firmly drawn by Cavagna and Bobbio[117] that Chizzola maculae are not fluoride effects. (a) In Bratislava, the village of Opatovce lies 200-800 m from the aluminum smelter, Ziar nad Hron (see Hluchan et al, 1968;[13] Balazova and Rippel, 1968).[118] The children of the village absorbed something like 2.5 mg of fluoride daily from contaminated, locally grown items of their diets. These children were anemic and exhibited dental fluorosis but never developed skin spots. (b) A Royal Commission in Ontario (1968)[107] conducted a thorough environmental and medical survey of residents in the neighborhood of the fertilizer factory, including some of the residents diagnosed by Waldbott and Cecilioni as suffering from fluoride poisoning on the basis of a group of symptoms including Chizzola maculae. The Commission found no evidence of fluoride poisoning in any of the people examined. (c) Animals exposed to fluoride under various conditions have not developed skin lesions comparable to Chizzola maculae. (d) Skin lesions of this sort have never been observed in areas where fluorosis from drinking water is endemic nor in workers with occupational exposures to fluorides, e.g., in aluminum smelters, superphosphate plants, and steel mills.

Table 10. — Comparison of Fluoride Effects In Man and Animals.

Daily Intake by Man Inhaling 10 M^3 of Air Containing 2.5 mg F/M^3 (8 Hr. Work Day): 25 mg F			
	Man	Animal	Factor
Certainly lethal dose	2500-5000 mg F	—	100-200
Renal injury	[450]	Rat, mos.	18
Anemia	[450]	Rat, mos.	18
Impaired reprodn.	[250]	Cattle, yrs.	10
Thyroid interference	[200]	Many species, yrs.	8
Weight loss	[175]	Cattle, yrs.	7
Crippling fluorosis	> 25	—	2
Dental fluorosis	2 ppm in water		

AIR QUALITY STANDARDS FOR MAN

The three major, well-studied toxic effects of fluoride in man are listed in Table 10 along with five well-studied toxic effects of fluoride in animals. This tabulation emphasizes (1) the cumulative nature of the chronic fluoride effects, (2) the magnitudes of the associated doses or concentrations, and (3) the numbers of times greater each dose is (except that for dental fluorosis, i.e., mottled enamel) than the probable daily intake from air containing 2.5 mg F/m^3. A word about dental fluorosis is in order because comments often appear on the absence of mottled enamel in adults occupationally exposed. Mottled enamel cannot occur in adults regardless of fluoride dose. Mottling is the end product of a developmental injury. Fluoride impairs the function of the ameloblasts which form dental enamel in such a way that the surface enamel is imperfect, giving rise to the various degrees of severity of fluorosis. These functional changes precede the eruption of the tooth, consequently chronic fluoride exposures that would lead to mottling in children under the age of five to eight years can be tolerated without effect in the adult.

Some forms of vegation are so sensitive to fluoride exposures that to avoid injury air concentrations must be maintained below 1 ppb (see Weinstein,[30] this issue). It is inconceivable that the amount of fluoride inhaled by a man at this concentration could be detected, e.g., in the daily urinary excretion.

Domestic or wild animals grazing down wind in the neighborhood of a fluoride-emitting industrial plant have on many occasions been poisoned by fluoride deposits on the vegetation. The species most susceptible to fluoride effects appears to be cattle and in particular the dairy cow. In these animals, signs of intoxication, e.g., unthriftiness, appear after four or five years when the diet contains 40 ppm F. Factory effluents bearing about 1 ppb F will build up concentrations of about 30 ppm on foliage down wind. Thus, air concentrations kept below hazardous levels for sensitive plants offer no risk to grazing animals. Limited evidence of the magnitude of fluoride exposures to nearby residents who consume garden vegetables grown down wind is reassuring; practices of food preparation and eating habits tend to keep the daily fluoride intake from this source on a long-term basis below injurious amounts.

Ambient rural air usually gives "no detectable" fluoride by methods currently employed to assay it. City air contains only traces (≤ 1 $\mu g/m^3$) in most samples. Residents who breathe 20 m^3 in a 24-hour period would take into their lungs about 20 μg which if all were retained would increase the daily intake of fluoride (500-2500 μg) by an insignificant quantity. The absence of any fluoride analyses of smog during one of the tragic smog disasters leaves unanswerable the question of a fluoride contribution to the pulmonary irritation and injury believed to be the proximate cause of illness and death.

In the Soviet literature, considerably lower air fluoride concentrations have been recommended as maximal permissible concentrations (MPC) for industrial exposures. Miller (1955)[119] calculated from the accepted drinking water fluoride concentrations to improve dental health (1-1.5 ppm F) with water intakes of 1.5 to 2 liters/day, that equivalent fluoride from contaminated air would be inhaled by an individual breathing in 15 to 20 m^3/day of air containing 0.15 mg/m^3. Subsequently, Sadilova (1967)[120] found human responses, specifically, the threshold concentrations for odor detection, and for response to light in the dark adapted eye, to exposures of 0.03 mg F/m^3 (as HF). These studies were followed by five month-long rat inhalation exposures to atmospheres containing 0.10, 0.03 and 0.01 mg F/m^3 which revealed irreversible destructive changes in nerve cells, changes in conditioned reflex response patterns and lengthened chronaxie of knee flexors, changes in calcium and phosphorus metabolism, increased fluoride in bone, and histological changes in teeth, bone and several internal organs at the two higher concentrations but no evidence of any effect at 0.01 mg F/m^3. The average daily HF exposure according to Sadilova should therefore not exceed 0.01 mg/m^3. This concentration is quoted as the Maximal Permissible Concentration (MPC) for exposures to combined gaseous and other fluorides (Pavlov, 1970).[121] Different MPCs for fluoride compounds depending on such properties as volatility and solubility have been considered.

Mixtures of fluoride may require MPCs not identical with those of the components.

A review of the evidence bearing on the air quality standard of fluoride to protect the health of industrial workers, particularly in the aluminum and rock phosphate processing industries (vide infra) shows that the TLV has been effective, and justifies the OSHA standard of 2.5 mg F/m^3. This conclusion is buttressed by a few generalities.

1. No osteosclerosis develops when air fluoride concentrations (TWA) in the work place remain below 2.5 mg/m^3, accompanied by urinary fluoride concentrations that do not exceed 5 mg/l. The NIOSH Criteria Documents specify preshift concentrations not exceeding 4 mg/l and postshift concentrations not exceeding 7 mg/l.

2. Osteosclerosis develops when air concentrations exceed 2.5 mg/m^3 and urinary fluoride levels exceed about 9 mg/l for prolonged periods.

3. The incidence and character of lung disease reflects no fluoride contribution when air concentrations are held at ≤ 2.5 mg/m^3 with the possible exception of the frequency of upper respiratory infections in potroom workers.

4. In plants operating with air fluoride concentrations ≤ 2.5 mg/m^3, neither kidney injury nor lasting skin injury has occurred.

We conclude that the OSHA standards for occupational exposures to airborne inorganic fluorides and to hydrogen fluoride will be tolerated without injuring human health during a working lifetime.

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