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FLUORIDE

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ABSTRACTS

EDITORIAL

FLUORIDE VERSUS SULFUR OXIDES IN AIR POLLUTION

For several decades, extensive investigations have been under way regarding airborne sulfur oxides and their effects on human health. Sulfur oxides are a major atmospheric contaminant derived from the burning of fossil fuels, particularly of soft coal.

In the two London, England,smoke disasters in 1940 and in 1952, sulfur oxides received understandably much attention because the smoke could be seen coming out of the many chimneys of London homes where soft coal was being burned. Furthermore, their characteristic odor, their bluish-white color, and the relative ease of demonstrating their presence in the air accounted for their identification with coal smoke. Nevertheless, some investigators (1-3) questioned the role of sulfur oxides in smoke disasters, because the officially reported concentrations in the air were not sufficiently elevated to induce serious damage to health. In the 1952 London disaster, the average concentration of sulfur dioxide was 1.7 ppm which is well within the industrial threshold limit of 5 ppm (4).

In contrast to the London disaster, in the Donora, Pennsylvania (1948), and the Meuse Valley (1930) pollution episodes,where zinc smelters and fertilizer plants contributed significantly to the atmospheric contamination,sulfur oxides played a minor role. These industries are notorious sources for fluoride emission. Indeed, the official investigators failed to establish a major contaminant to which the disastrous effect could have been attributed since knowledge on airborne fluorides was very sparse at that time. Independent studies in both areas, in Donora by Sadtler (5) and in the Meuse Valley in retrospect by Roholm (6) produced considerable evidence indicating that fluoride was primarily responsible for illness and death in these two disasters.

In reviewing the effects of the two pollutants on vegetation and domestic animals there can be no doubt that airborne fluoride is far more harmful than sulfur oxides. Guinea pigs exposed to sulfur oxides continuously for one year at a concentration of 5 ppm failed to develop respiratory disorders (7). Fluoride, on the other hand, reaches the blood stream both through inhalation and by ingestion with contaminated food. Similarly, in plants the translocation of fluoride throughout the plant structure and its damaging effect on leaves, blossoms and fruit is much more pronounced than that of sulfur oxides (8). In comparing the effects of sulfur oxides on plants with that of fluorides, Bohne (9) showed that greater amounts of fluoride had accumulated and that fluoride had caused more damage than sulfur oxides.

In humans,more than 90% of inhaled sulfur oxides are absorbed in the airways above the larynx (10). With the moisture of the air, they form sulfuric acid and sulfates which, although irritating to the respiratory membranes, are of low toxicity.

Thus sulfur oxides irritate, primarily, the upper respiratory tract. They

rarely, if ever, enter the distal portions of the lungs and the alveolar system. They never enter the blood stream. Fluoride, on the other hand – a systemic poison – is promptly absorbed into the blood stream from the upper respiratory tract. It affects primarily the calcified tissue but can also induce considerable damage to many other organs, especially the arteries and the heart.

In the London episode, the delayed effects and subsequent deaths from respiratory diseases differed materially from effects in Donora and in the Meuse Valley where heart failure played a major role in the afflicted persons. Sulfur compounds are associated with a general increase in the total white male mortalities (11). These authors were not aware that sulfur oxides are not likely to reach beyond the respiratory tract. The simultaneous presence of fluoride and other toxic agents in coal and other fossil fuel could well account for their findings.

Recent studies by Dässler and others (see page 223), from the German Democratic Republic, tend to shed considerable light on the explanation of the cause of casualties in the London disaster. They found that the fluoride content of soft coal may reach a level as high as 1400 ppm (ashed) and that between 70 and 100 percent of gaseous fluoride is airborne when coal is burned. In other words, where there is smoke from burning coal there is also fluoride. Thus, the systemic damage to humans believed to have been induced by sulfur oxides is likely to be primarily brought on by fluoride in conjunction with such other toxic agents as arsenic, cadmium and mercury present in coal (4). Further studies on this problem are indicated.

Bibliography

1. Anderson, D. O.: The Effects of Air Contamination on Health, Part I, Canadian Medical Association Journal, 97:528-536, 1972.

2. Amdur, M. O. and Underhill, D. W.: Response of Guinea Pigs to a Combination of Sulfur Dioxide and Open Hearth Dust. J. A. P. C. A., 20:31-34, 1970.

3. Alaire, Y., Ulrich, C. E., Busey, W. M., et al: Long-Term Continuous Exposures to Sulfur Dioxide in Cynomolgus Monkeys. Arch. Env. Health, 24:115-127, 1972.

4. Waldbott, G. L.: Health Effects of Environmental Pollutants. C. V. Mosby Company, St. Louis, 1973.

5. Roholm, K.: The Fog Disaster in the Meuse Valley: A Fluorine Intoxication. J. Industr. Hyg. Toxicol., 19:126-137, 1937.

6. Sadtler, P.: Fluorine Gases in Atmosphere as Industrial Waste Blamed for Death and Chronic Poisoning of Donora and Webster, Pennsylvania Inhabitants. Chemical and Engineering News, 26:3692, 1948.

7. Alaire, Y., Ulrich, C. E., Busey, W. M., et al: Long-Term Continuous Exposure of Guinea Pigs to Sulfur Dioxide. Arch. Env. Health, 21:769-777, 1970.

8. Garber, K.: Effects of Air Contamination. Gebrüder Bontraeger, Berlin, 1967.

9. Bohne, H.: Fluorides and Sulfur Dioxides as Causes of Plant Damage. Fluoride, 3:137-142, 1970.

10. Frank, N. R.: Studies on the Effects of Acute Exposure to Sulfur Dioxide in Human Subjects. Proc. Roy. Soc. Med., 57:1029-1033, 1964.

11. Schwing, R. C. and MacDonald, B. G.: Measures of Associations of Some Air Pollutants Ionizing Radiation and Cigarette Smoking with Mortality Rates. Presented at the International Symposium on Recent Advances in the Advancement of Health Effects of Environmental Pollutants, Paris, France, Jan. 24-28, 1974.

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EVIDENCE OF MUSCLE FIBER DEGENERATION IN RABBITS TREATED WITH SODIUM FLUORIDE

by

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SUMMARY: The levels of phosphocreatine kinase (CPK) in the sera of rabbits treated with sodium fluoride were biochemically determined. The results indicate an enhanced level of serum CPK. Such an increase of CPK in the serum constitutes an index of degeneration of muscle fibers and of the highly permeable plasma membrane. The findings from the current investigation indicate that degeneration of muscle fibers results from fluoride toxicity.

The phosphocreatine content in skeletal muscles is much greater than in all other tissues in the body (1). Phosphocreatine is concentrated in mitochondria muscles where the enzyme creatine phosphokinase (CPK) is localized (2). This enzyme is responsible for accelerating the reversible transfer of the phosphate radicle between adenosine-di-phosphate and phosphocreatine (3). Creatine phosphokinase (CPK) therefore plays an important role in phosphorylating the high energy substances in muscles.

It is known that degeneration of muscle fibers and defects of plasma membranes raise the CPK level in serum (4). The CPK level in the serum is considered an index for assessing the healthy state of the muscle fiber as well as that of the muscle membrane. Determination of the CPK concentration in the serum is, therefore, one of the methods to assess the functional status of the muscle fibers and of the plasma membranes.

In the current investigation, sodium fluoride has been administered to rabbits and serum CPK has been biochemically determined at varying time intervals.

Materials and Methods

Healthy, adult male rabbits weighing 1.1 to 1.4 kg were used.

The animals were segregated into 2 groups - Group A and Group B. The rabbits of Group A comprising six animals were given 50 mg/kg body weight of sodium fluoride dissolved in 1 ml of water through the intra-gastric route with the aid of a fine polythene cannula 1 mm in diameter and 15 cm in length. The administration of fluoride was carried out daily up to a maximum period of 30 days. Group B comprising 8 rabbits served as controls. Both groups of animals were kept under identical laboratory conditions.

The animals of both groups were bled on day 10, 20 and 30 by puncture of the marginal vein of the right pinna. The serum collected was utilized for the estimation of creatine phosphokinase activity which was measured by the method adapted by Hughes (5) and later modified by Pearce, Pennington and Walton (6). This method is based on the quanti-tation of creatine formed by the interaction of creatine phosphate (CP) and adenosine-di-phosphate (ADP) as a result of creatine phosphokinase activity (CPK).

Procedure: The following were pipetted into 5 ml centrifuge tubes:

    1. Serum................................. 0.1 ml
    2. Tris buffer (0.1 M; pH 7.35).......... 0.2 ml
    3. Creatine phosphate (12mM)............. 0.3 ml
    4. Cystein hydrochloride
            (0.15 M; pH 7)................... 0.05 ml
    5. De-ionized water .... 0.05 ml

The test tubes were grouped into sample (I) and blank (B) and were equilibrated for 3 minutes at 37°C in a water bath. After equili-brating for 3 minutes, a solution of 0.2 ml (10 mM) was added to the sample tubes; to the tubes marked B, 0.2 ml of de-ionized water was added. These tubes were then incubated for 30 minutes. The reaction was stopped by the addition of 0.2 mg of 5% zinc sulphate and 0.2 mg of 0.3 N barium hydroxide.

The tubes containing the reaction mixture were shaken well by means of a Vortex Genie, allowed to stand for 10 minutes and then centrifuged at 3000 r.p.m. for 10 minutes. The supernatant was decan-ted and 0.7 ml of it was treated with 0.3 ml of p-chloromercuribenzoic acid (25 mM), 2.5 ml of distilled water, 1 ml of x-naphthol and 0.5 ml of 0.04% diacetyl. The tubes were then allowed to stand for 5 minutes and the optical density was read at 520 mμ in a Zeiss PMQ spectrophoto-meter with the use of quartz cells of 1 cm path length. The results are expressed as μ moles of creatine formed/hour/liter of at 37°C (Interna-tional Unit).

Results and Comments

The serum CPK values of normal rabbits, and those treated

with NaF, on day 10, 20 and 30 are reported in Table I. The results in-
dicate a considerable rise in the level of CPK. The serum CPK of the
rabbits treated with NaF were enhanced by 78%, 185%, and 276% on day
10, 20, and 30 respectively.

TABLE 1

Creatine Phosphokinase Activity in Sera of Rabbits
Treated With Sodium Fluoride

Duration of exposure to sodium fluoride	Amount of sodium fluoride admini- stered (average)	Creatine phospho- kinase level Mean $\pm$ S. D.	Rise in CPK level (%)
Untreated	Nil	153.578 $\pm$ 5.10 (8)	....
10 days	0.555 gm	247.267 $\pm$ 7.70 (6)	78
20 days	1.078 "	438.497 $\pm$ 7.30 (6)	185
30 days	1.390 "	578.735 $\pm$ 11.46 (6)	276

The numbers given in parenthesis indicate the number of
experiments carried out.
S. D. = Standard deviation.
The results are expressed in μ moles of creatine formed/
hour/litre of serum at 37°C.

Hitherto, no evidence has appeared in the literature that the
skeletal muscle is directly affected in fluorosis. The involvement of the
muscle has been considered to be a secondary effect resulting from the
compression of the spinal cord and of nerve roots because of narrowing
of the vertebral canal and the intervertebral foramina (7). The current
study, however, indicates that as early as 10 days after administration
of sodium fluoride, the creatine phosphokinase activity increases in the
serum by 78%. The rise in CPK has been found to be a gradual process and
the level shot up to 276% by day 30. This progressive increase in CPK in
serum proves that the direct involvement of muscle is due to fluoride tox-
icity. This conclusion is supported by the fact that our light microscopic
studies on the mammalian diaphragm have failed to disclose any structural
changes suggestive of neuronal degeneration in muscle (8).

It is noteworthy that the serum level of CPK is very high
during the onset and early phases of muscular dystrophy (9, 10) and that,
during this phase, the population of muscle fibers undergoes the maximum
structural damage. During the late stages of dystrophy, when the de-
generation of muscle fibers is almost complete, and when the muscle is
fully infiltrated with fat and connective tissue, the serum CPK levels
are known to be well below the normal range. This evidence supports the
view that the rise in serum CPK level could be due to degeneration of

muscle fibers.

It may be assumed that the increased levels of CPK in serum could be due to atrophy of muscle fibers of the neuronal type. But the rise in the level of serum CPK is recorded only during the late stages of neurogenic atrophy, not during the early phase of the disease (10). The changes in serum CPK recorded in the NaF-treated animals is not likely to be related to neuronal involvement because a 30 day period is too short a time to produce such a high % rise. Moreover, as indicated above, our light microscopic studies have not revealed any evidence of neurogenic atrophy of muscle tissue.

Our recent histochemical and ultrastructural studies on rabbit diaphragm exposed to toxic doses of sodium fluoride constitute additional evidence that degeneration of muscle fibers and destruction of mitochondria occur in fluoride toxicity even at very early stages (8). The current experimental study, therefore, indicates that degeneration of muscle fibers in 'Fluorosis' is most likely due to the direct action of fluoride on the skeletal muscle rather than to secondary action which is the result of compression upon the spinal cord.

Bibliography

1. Ennor, A. H. and Rosenberg, H.: Determination and Distribution of Phosphocreatine in Animal Tissues. Biochem. J., 51:606-610, 1952.

2. Bokdawalla, F. D. and George, J. C.: Histochemical Observation on Creatine Phosphokinase Activity in the Red and White Fibers of Normal and Denervated Pigeon Breast Muscle. J. Neurol. Sci., 9:443-448, 1969.

3. White, A., Handler, P., and Smith, E. L.: Principles of Biochemistry. McGraw-Hill Book Co., New York, 1964, 3rd edition, page 260.

4. Ebashi, S., Toyokura, Y., Momoi, H. and Sugila, H.: High Creatine Phosphokinase Activity of Sera of Progressive Muscular Dystrophy Patients. J. Biochem. (Tokyo), 46:103, 1959.

5. Hughes, B. P.: A Method for the Estimation of Serum Creatine Kinase and its Use in Comparing Creatine Kinase and Aldolase Activity in Normal and Pathological Sera. Clin. Chim. Acta., 7:597, 1962.

6. Pearce, J. M. S., Pennington, R. J., and Walton, J. N.: Serum Enzyme Studies in Muscle Disease Part I. Variation in Serum Creatine Kinase Activity in Normal Individuals. J. Neurol. Neurosurg. Psychiat., 27:1, 1964.

7. Singh, Amerjit and Agarwal, N. D.: Neurological Complications Observed in Endemic Fluorosis in Punjab and Management of Fluorosis Myelopathy. J. Bone and Joint Surg., 47-B: 184, 1965.

8. Kaul, R. D. and Susheela, A. K. (1974) under preparation for publication.

9. Richeterich, R., Rosin, S., Aebi, U., and Rossi, E.: Progressive Muscular Dystrophy. V. The Identification of the Carrier State in the Duchenne Type by Serum Creatine Kinase Determination. Am. J. Hum. Genet., 15:133, 1963.

10. Pearce, J. M. S., Pennington, R. J., and Walton, J. N.: Serum Enzyme Studies in Muscle Disease. Part. II Serum Creatine Kinase Activity in Muscular Dystrophy in other Myopathic and Neuropathic Disorders. J. Neurol. Neurosurg. Psychiat., 27:96, 1964.

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FLUORIDE DISTRIBUTION IN THE
SILVERBOW, MONTANA, AREA

by

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SUMMARY: This study describes the distribution of fluoride in a 16,000 acre contaminated area surrounding a chemical phosphate facility in Silverbow, Montana. The biological monitoring for fluoride was performed through field collection and laboratory analysis of indigenous vegetation of the area. The fluoroapatite ore reduction process in operation at the plant emits fluoroapatite dust and hydrogen fluoride causing the accumulation of amounts exceeding the Montana state maximum for fluoride in forage. The biological monitoring method is presented as a model for rapid determination of the relation between fluoride air pollution and its potential hazard to grazing livestock and wildlife.

Introduction

A fluoride-emitting phosphorus extraction facility has been in operation in Silverbow, Montana, since 1951. Complaints concerning the effects

of fluoride air pollution on local cattle (1) and request for governmental assistance in dealing with this problem (2) were first recorded in 1956 and 1957. Limited air pollution monitoring in the area initiated by Montana State Board of Health in 1957 (3), indicate that fluoride concentrations in the ambient air exceeded the current maximum allowable concentration, on an average of one part per billion in 24-hours (4). In October, 1972, Carlson (5) found concentrations of fluoride in vegetation in the area as high as 74 ppm. To date, no in-depth studies of air pollution in the immediate Silverbow area have been made.

Operation of the Plant

The phosphorus extraction process, at the Silverbow facility, employs the electric furnace method. Raw phosphate rock containing fluoroapatite, $Ca_{10}F_2(PO_4)_6$, is agglomerated by nodulizing at high temperature in a rotating kiln. Dust containing fluorides is emitted from this process. The nodulized material is cooled on conveyors and stored. Following storage, coke breeze and siliceous flux (sand) are added, and the mix is charged to the electric furnace. As the furnace is charged, gaseous and particulate materials again escape. Phosphorus is vaporized at high temperature, passed through electrostatic precipitators and condensed into water. After a final filtration, the phosphorus is stored under water and shipped.

Fluoride is also lost in slag in the electric furnace, primarily as CaF_2 mixed with other impurities. Periodically slag is drained from the furnace after it solidifies it is transported to the slag pile (6, 7). The chemical equation $2Ca_{10}F_2(PO_4)6 + 18SiO_2 + 30C$ $(18 \cdot CaO \cdot SiO_2 \cdot 1/9CaF_2) + 30CO + 3P_4$ (8) describes the high temperature reaction occurring in the electric furnace. The loss of gaseous and particulate fluoride, which occurs as the furnace is charged and during the preparatory heating in the nodulizing kiln, is not known.

A 1968 emission inventory submitted to the Montana State Board of Health listed fluoride emissions as 205 pounds of gaseous fluorides per day and 200 pounds of fluoride tied into the fluoroapatite mineral, $Ca_3(PO_4)_2 \cdot 1/2 CaF_2$. The plant operates continuously. Three hundred and sixty thousand tons per year of phosphate rock were utilized containing 26 percent equivalent phosphate listed as P_2O_5 and 2.6 percent fluoride listed as F (9). Recently, the phosphate rock consumption has increased from an annual use rate of 360,000 tons to 500,000 tons (10).

This study was to establish through biological monitoring the distribution and concentration of fluoride in the area and its relation to the operation of the phosphorus extraction facility. The concentration of fluoride was determined by the chemical analysis of indigenous vegetation and soils, with particular emphasis being placed on a forage grass species very common to the area.

Literature Review

Metabolism of Fluoride in Plants: Injury to vegetation has recently

become of significant economic concern owing to the phytotoxicants produced in photochemical smog (11). Biological monitoring,particularly concerning the distribution and effects of sulfur dioxide,has been carried out (12). Detailed studies have often involved the evaluation of many physiological aspects other than visual foliar damage, such as general effects upon growth rate (13), metabolic changes (14), root growth (15), and many others.

With the development of modern aluminum smelting processes and increased demand for the production of phosphate fertilizer, the atmospheric emission of fluoride compounds (gaseous and particulate) has rapidly increased. Other major sources of atmospheric fluoride emissions include the manufacture of steel, brick and tile products, and the combustion of coal (16). Fluoride enrichment in the foliage of various plants,exposed to atmospheric contamination in the field,has been demonstrated by Knabe (17).

Leaves accumulate more fluoride than any other plant part (18) because of their large surface area and because of structural features which facilitate gaseous exchange.

The correlation between leaf injury and fluoride content is better for washed leaves than for those which are unwashed. Washing does not necessarily remove all fluoride from the leaves. Some is leached from the leaf interior.

Most residual particulate forms of fluoride on the leaf surfaces are insoluble and non-toxic to vegetation. Current evidence indicates that fluoride must exert its toxic effects after penetrating the cytoplasm (19). The manner in which atmospheric fluorides affect the metabolism of the plant is not clear.

Various levels of fluoride tolerance have been established for plants: Gladiolus is one of the most sensitive (20). Environmental parameters,other than the relative sensitivity of plants,seem to modify fluoride concentration and effects: Forage plants exposed to intermittent HF fumigation accumulate more fluoride than those exposed continuously to low concentrations (21). The rate of air flow past the plant alters the susceptibility of alfalfa to fluoride (22). Furthermore, plants seem to be more susceptible during the growing season to accumulation from gaseous sources. However, this susceptibility varies with the stage of growth,with the relative age of foliage,and with nutritional and moisture stresses (23).

Once gaseous fluoride begins to be absorbed and concentrated by the plant, continuous processes of translocation and dilution begin. Fluoride loss results from the diluting effects of weathering, plant growth, and foliar abcission. There seems to be no translocation of absorbed HF into new growth (24). Injections of NaF^{18} into tomato plants revealed that the F^{18} moves primarily to the leaf margins and tips, none going to the roots (25). A large loss of accumulated fluoride in spruce occurred when the trees were

removed from the polluted atmosphere (26).

Fluoride in Food Chain Biological monitoring of the movement of fluoride through the food chain has provided valuable information. Both, the accumulation of gaseous fluoride compounds in plant tissue and the deposition of particulate fluoride compounds on foliar surfaces, have led to toxic effects in grazing wildlife and domesticated animals. The natural fluoride contents of forage are about 5 to 10 ppm (mg/kg dry weight), but few extensive or systematic compilations of analysis are available. The major source of fluoride in the rations of livestock in contaminated areas is the ingestion of high fluoride vegetation (27).

Gordon (28), Carlson (28a), and Dewey (29) have analyzed the distribution and concentration of fluoride effluents from an aluminum smelter in plant and animal populations in a nearby national forest and national park. Gordon examined vegetation histologically and determined the fluoride content of bones from many species of birds and mammals.

In the same area, Carlson and Dewey utilized 10 radial sampling routes for chemical analysis of vegetation and histological examination of conifer needles. Fluoride content in herbivorous and carnivorous insects was determined, along with observations of species diversity relative to the degree of pollution. Carlson used his data to construct an isopol map which displayed acreages contaminated by various concentrations of fluoride. The main timber species in this area, lodgepole pine, showed significant effects from increased foliar fluoride concentrations, due to increased insect infestation (29a) and reduced tree growth (29b).

In another area of western Montana, near a phosphate rock reduction facility, Gordon (30) and Kay (31) made similar surveys. They utilized the Specific Fluoride Ion Electrode as a method of chemical analysis which is a rapid, specific, efficient, and inexpensive method (32, 33, 34) for the determination of fluoride in environmental media.

Methods

The Area: The Silverbow, Montana, chemical facility is located in a prairie basin at the northern termination of a north-south valley (Fig. 1). The valley is enclosed by three mountainous barriers which rise to elevations of 8,000 feet above sea level. The valley floor in the vicinity of the plant, slightly above 5,300 feet high, extends approximately eight miles due south where it is terminated by the Continental Divide. The northern end of the valley opens in two directions -- to the northwest where Interstate highway 90 descends in the direction of Anaconda, Montana, seventeen miles to the west and to the east where Interstate 90 ascends in the direction of Butte, Montana, seven miles away.

The construction in 1957 of that section of Interstate 90 which connects Butte and Anaconda utilized slag material from the chemical factory as a fill for the roadbed. Because the slag contains about 3 percent CaF_2

Fig. 1

Topography Surrounding Silver Bow, Montana Study Area
From U.S.G.S. Map

1 - Chemical Company   2 - Plant Slag Pile   3 - Bull Moose Fluorspar
Deposit 4 - Wrong Front Fluorspar Deposit   5 - Anaconda Company
Smelter   6 - U.S. Highway 10 Road Fill   7 - Butte Airport Weather
Station

Contour Interval 1,000 ft.

(35), this project constitutes a man-made fluoride deposit.

The construction of Interstate 90 also covered some surface exposures of naturally occurring fluorspar deposit (CaF_2), namely the Bull Moose deposit 1 1/2 miles northeast of the chemical plant and the Wrong Front deposit (36) 1 3/4 miles northeast of the phosphorus plant. The presence of fluorspar in the area could cause higher background fluoride concentration in the soils. However the low solubility of fluorspar, 0.0016 parts per gram in 100 cc. of cold water (37), should tend to make fluoride from this source unavailable for plant uptake.

Climatological Factors: The yearly normal precipitation* is 12.67 inches, two thirds of which is measured during the growing season - April through September; May and June are the wettest months. In summer, maximum temperatures infrequently reach 90° F (32° C); the hottest month is July followed by August. Zero minimums have been recorded as early as October and as late as April, with an average of 43 yearly zero readings. Freezing temperatures can be expected at any time of the year with an average of 120 days between the last temperature of 28° F (-2° C) in the spring and the first in the fall. The mean speed and direction of the wind are 7.9 mph and northwest, respectively (38).

Inversions: Mountain valleys in this area are particularly subject to intense and long-lasting inversions which are caused by: 1) the atmosphere being less dense at these higher elevations than at lower altitudes and generally dry, 2) winter nights being relatively long, 3) surrounding mountains acting as a barrier to strong winds, and 4) snow cover during the colder months reflecting away solar energy and constituting an excellent radiator of heat at night. Furthermore cool air, because of its greater density, gradually sifts to lower elevations and thereby causes deeper and more intense inversions in a valley than would occur on level ground.

Table 1 illustrates the inversion frequencies for this general region of the United States. Protected mountain valleys, similar to the one in which Silverbow is located, have even higher percentages of inversions.

TABLE 1

Inversion Frequencies

Season	Percent of Total Hours
Winter	45 - 55
Spring	30
Summer	30 - 35
Fall	40 - 50

Annual 40

Plume Behavior: Plume behavior and ground concentrations of air pol-
lutants are greatly affected by topography, inversions, and wind directions.
It follows that a plume of air pollution is confined by a valley or will follow
valley walls. Because of the "valley effect," high ground concentrations can
occur at a greater distance downwind from the source than in flat terrain (39).

Vegetation: The relatively low annual precipitation, high altitude, and
resultant short growing season are the main natural modifying factors govern-
ing the indigenous vegetation. The valley bottom grasslands usually become
dormant in mid-July due to lack of soil moisture. Of the many species of range
grasses, bluebunch wheatgrass (Agropyron spicatum) was the most frequently
observed. Other grasses observed were crested wheatgrass (Agropyron crista-
tum), foxtail barley (Hordeum jubatum), and giant wild rye (Elymus cinereus).
Scattered throughout the range grasses, the bitterbrush (Purshie tridentata)
and rose (Rosa spp.) shrubs may also be found. The three species of trees
on the valley floor were widely scattered Rocky Mountain juniper (Juniperus
scopularum), Douglas fir (Pseudotsuga menziesii) and lodgepole pine (Pinus
contorta). Few trees exceeded a height of 15 feet. In the vicinity of the
chemical plant, the vegetative cover was 50 percent or less, leaving much ex-
posed soil.

On the slopes of the surrounding mountains there is an abrupt transi-
tion to forest composed almost entirely of Douglas fir. In the few wet areas
near creek beds, isolated stands of willow (Salix spp.) and black cottonwood
(Populus trichocarpa) are found as well as quaking aspen (Populus tremuloides)
in some of the mountain side ravines.

Field Collection: On October 6, 1972, a study group began two days of
field collection of vegetation and surface soil samples. Twelve collection
routes were established which extended radially from the property of the
chemical facility (Fig. 2).

Among the forage grasses, BLUEBUNCH WHEATGRASS was most com-
monly collected. By cutting through the base of the plant, one inch above
ground level, the current year's growth was obtained as well as that of the
previous year which is matted down near the base of the bunch or crown area
of the plant. NON-BUNCH GRASSES were cut one inch above ground level; this
procedure yielded only one year's growth.

Samples of CONIFEROUS TREE were obtained by clipping terminal seg-
ments of at least three branches from each tree. Attempts were made to ob-
tain foliage representing the last five years of growth. JUNIPER collections
were made without consideration of foliage age, since separation of this foliage
by year of growth is very difficult. Foliage representing only the current
year's growth was obtained readily from deciduous trees. The SHRUB species
found in the area were generally deciduous and were collected as such. In addi-
tion to the shrubs noted, a few samples of CURRANT (Ribes spp.) and MOUN-
TAIN MAHOGANY (Cercocarpus spp.), rare to the collection area, were taken.

Fig. 2

Illustrating the Radial Collection Routes
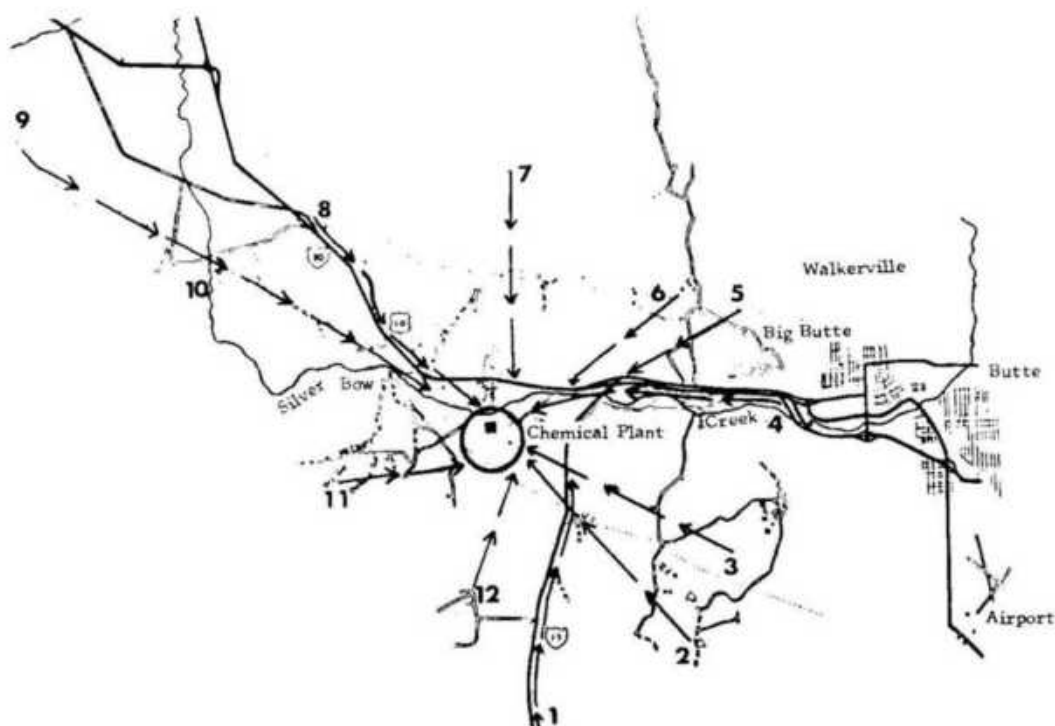
Soil samples were collected less frequently than vegetation samples. The collector chose an area devoid of vegetation or organic debris and removed the upper half inch of soil. Immediately upon collection, all samples were placed in paper bags which were sealed with rubber bands and labeled as to sample type and location.

Laboratory Analysis: Vegetation was analyzed for fluoride according to the Gordon (40) method, soils according to Ficklin's procedure (41). Analysis was performed on 14 species of vegetation with 387 samples, including 25 reanalyses to assure accuracy. Soil analyses were also performed, including reanalysis.

### Graphic Display Method for Fluoride Distribution

Each collection site was plotted along the 12 radial collection routes. This location, in conjunction with the results of chemical analysis, established isopols for each sample site. For bluebunch wheatgrass, two isopol maps (Fig. 3) were constructed in order to illustrate the fluoride concentrations in the two age classes grown in summer 1972 and in "1971 and older".

In addition, the fluoride concentrations in bluebunch wheatgrass were graphed along each collection route as they relate to the topography.
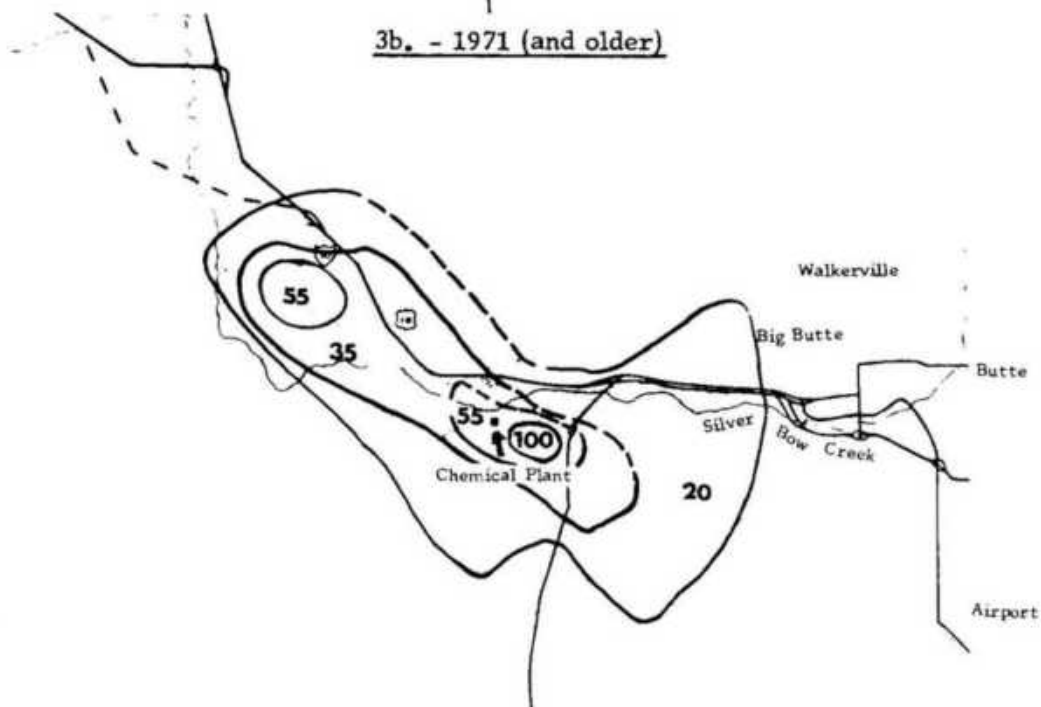
FLUORIDE

Fig. 3

Isopol Maps Showing Fluoride Concentrations (in ppm) in Forage (Bluebunch Wheatgrass)

3a. - 1972
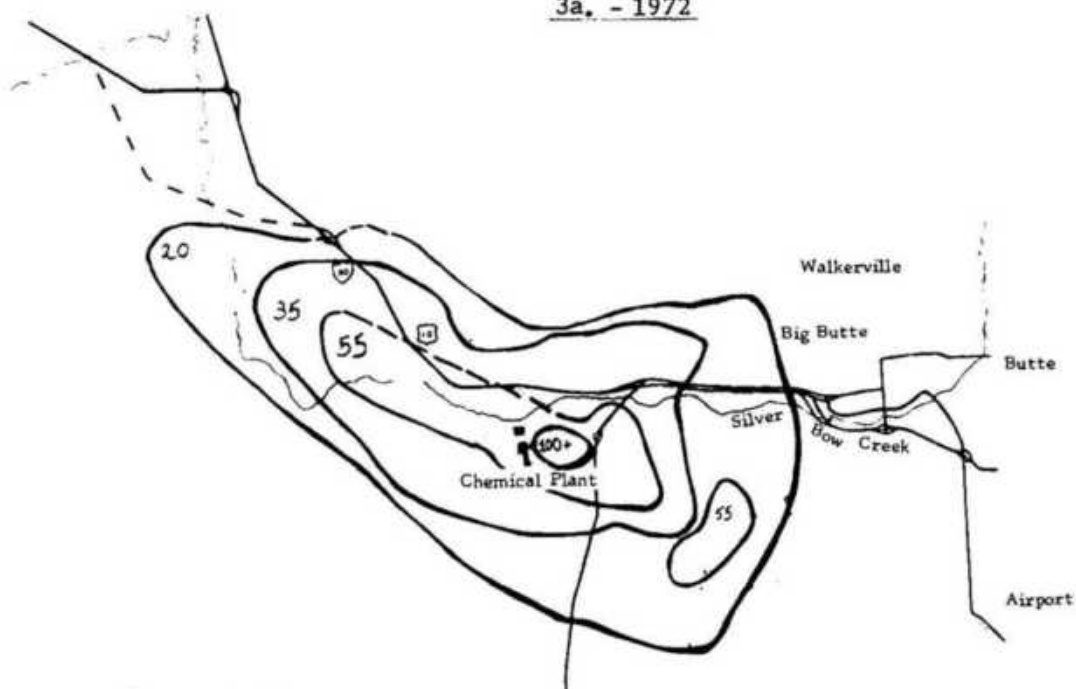
3b. - 1971 (and older)

——————— Boundaries of equal concentrations
-------- Sampling inadequate

Results

Fluoride Concentrations in Forage

Isopols: The isopols show greater fluoride concentrations in older bunchgrass (Fig. 3b) than in new grass (Fig. 3a) which had been exposed to the ambient atmosphere for only five months. Nevertheless, the patterns were similar for both age classes.

The radial collection route method reveals a general increase in fluoride content as the chemical plant is approached from all directions (Fig. 4).

Superimposition of the isopols on a U.S. Forest Service map of the area reveals acreages at various levels of contamination. Table 2 depicts the amount of acreage contaminated by fluoride at selected levels of fluoride concentration.

Compilation of fluoride concentrations found in all forage samples collected within each isopol area made it possible for averages to be determined (Table 3).

TABLE 2

Acreage Contaminated by Fluoride

Age of Forage	ppm Fluoride Concentration			
	≥ 20 and < 35	≥ 35 and < 55	≥ 55 and < 100	$= 100$
1971 (and older)	16,704	11,520	4,736	448
1972	16,448	5,184	1,536	384

TABLE 3

Mean Fluoride Concentration in Each Isopol Area

Isopol Area	1972 Forage	1971 (and older)
20 ppm	30 samples 22 ppm	35 samples 23 ppm
35 ppm	18 samples 36 ppm	23 samples 39 ppm
55 ppm	11 samples 59 ppm	15 samples 55 ppm
100^+ ppm	5 samples 201 ppm	9 samples 342 ppm

Topographic Profiles: The series of topographic profiles (Fig. 5) illustrate the concentrations of fluoride in ppm in forage (bluebunch wheatgrass),

FLUORIDE

Fig. 5

Topographic Profiles
Fluoride Levels Related to Elevation of Routes

Fig. 5 (cont.)

Route 7   Direction N

Route 8   Direction NNW

Route 9   Direction NW

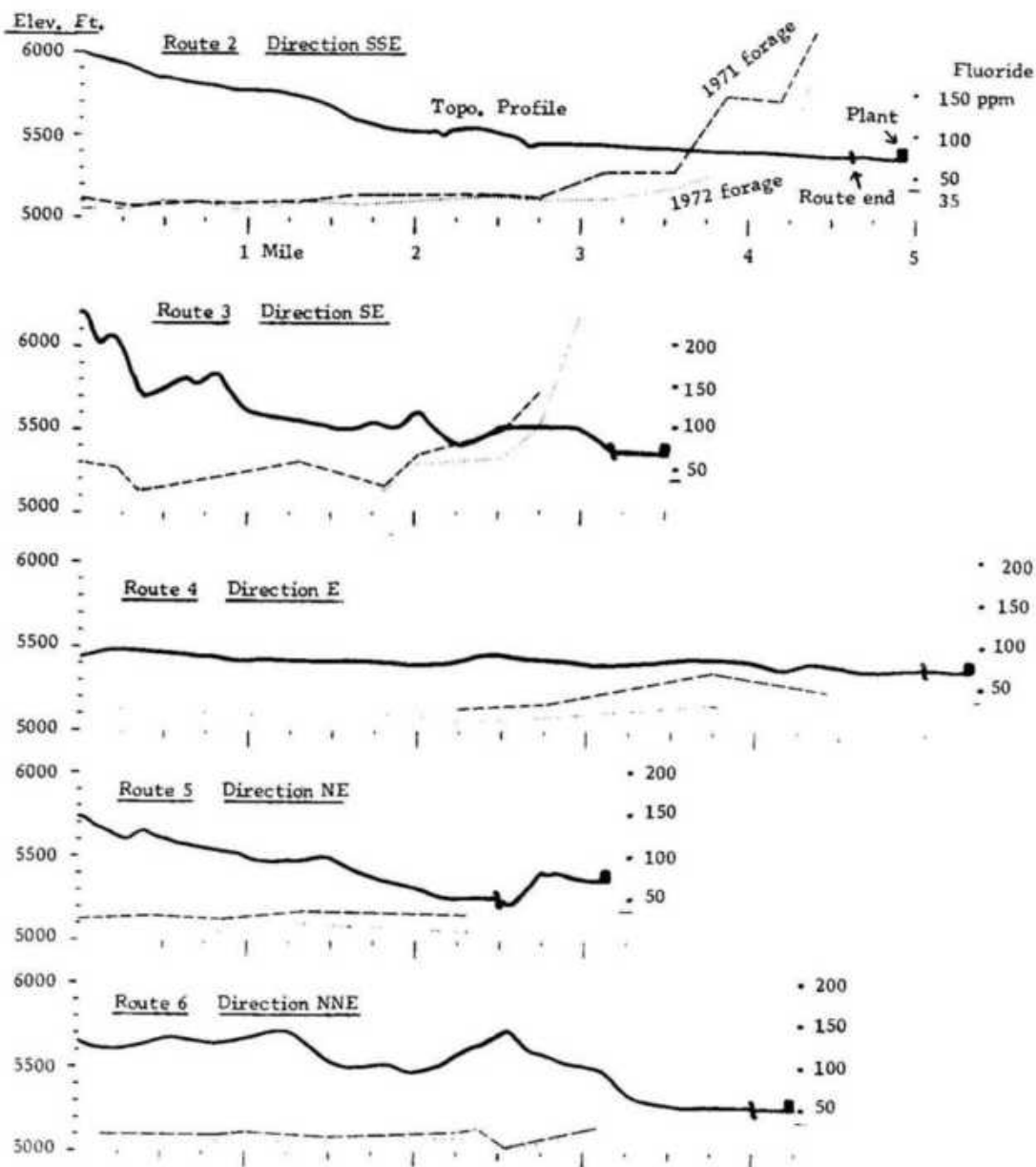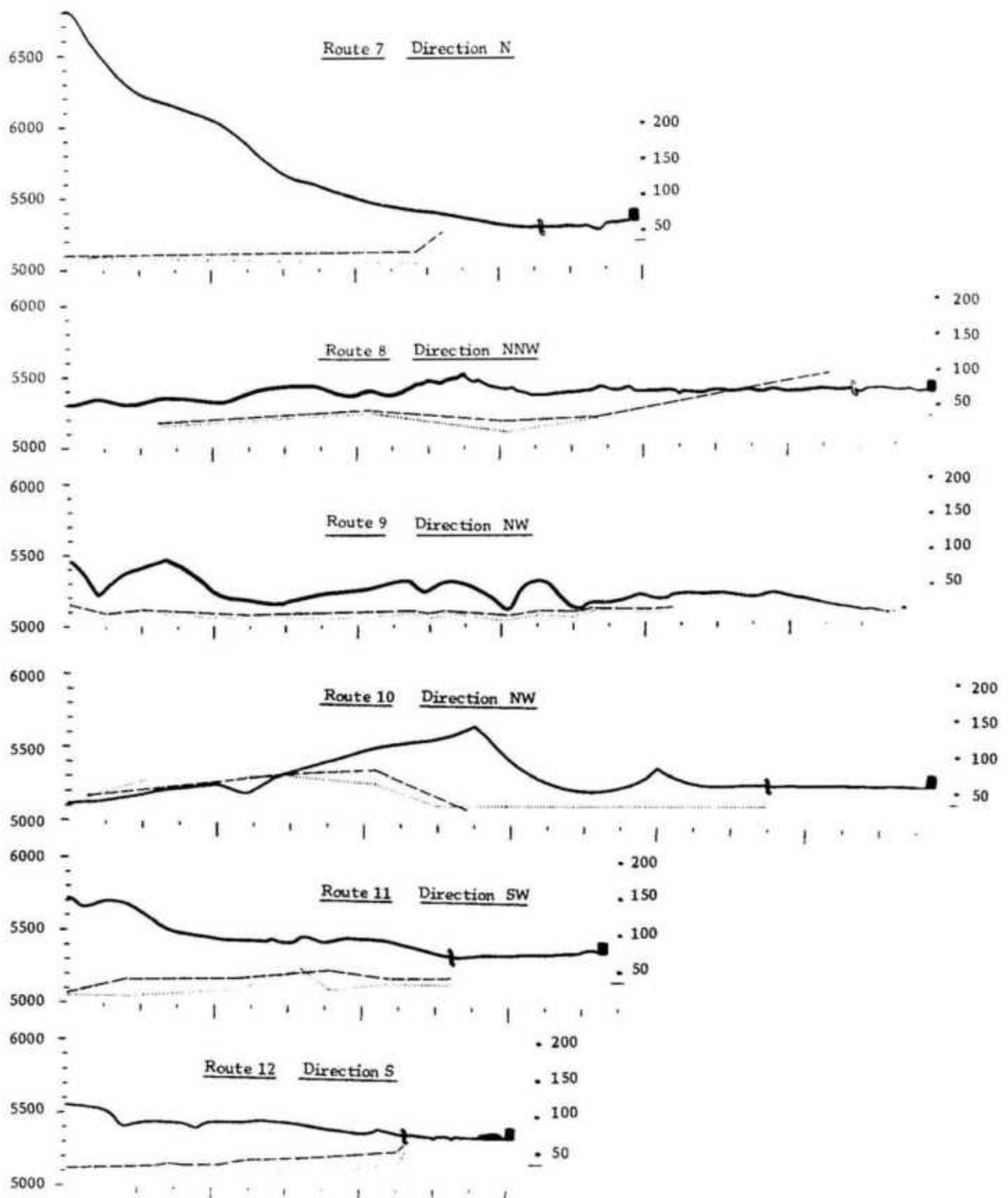Route 10   Direction NW

Route 11   Direction SW

Route 12   Direction S

FLUORIDE

to the distance and elevation of the sample site relative to the chemical factory. Again, a trend of increasing concentrations as the source is approached from many directions is evident.

Collection Route 1 was omitted because it entailed samplings from alternate sides of a highway, thereby contrasting the straight line-of-sight travel of the other routes. Collection Routes 9 and 10 are joined to form a single line of travel extending approximately 10 1/2 miles in the direction of the smelter in Anaconda, Montana. The prominent ridge Route 10 approximately 3 1/2 miles northwest of the chemical plant yielded forage with high fluoride content in an area facing away from the plant. The remainder of Routes 9 and 10 indicate a reduction of fluoride content from this point to a point within a few miles of the distant smelter. Along these two collection routes, fluoride content in forage drops to near control levels between the area of Silverbow and Anaconda.

Detailed air flow patterns for this valley system are unknown. However, the general deposition of airborne fluorides as shown by the graphs indicate that fluoride concentrations increase within 1 1/2 miles of the chemical plant in several directions: S, SSE, SE, NNE, N, and NNW. Several prominent hillsides facing the plant appear to be zones of plume impingement e. g., Route 3 (1 1/2 miles, 2 1/4 miles, and 3 1/4 miles southeast of the plant) and Route 11 (2 miles southwest of the plant). Other patterns of fluoride deposition are seen on Routes 6 and 10, where higher concentrations are found on hillsides facing away from the chemical plant. This phenomenon implies that local air movements are affected by various topographic features.

Fluoride Concentration in Juniper: Rocky Mountain juniper, the most commonly sampled tree in the study area, yielded fluoride concentrations as high as 420 ppm, about 40 times greater than control values (Fig. 6). The pattern of fluoride distribution found in juniper was similar to that in forage grasses, though the range of concentration was not as great.

Fluoride Concentration in Soils: Results of fluoride analysis from 46 surface soil samples collected in the study area are shown in Figs. 7 and 8. Localized high concentrations of fluoride occurred in the area of the plant. By following the concentrations on each collection route it appears that there was less measurable widespread pollution of surface soils than of vegetation.

Discussion

The fluoride emission problem in Silverbow, Montana, is common in many industrial operations which extract phosphate from phosphate rock for use as a fertilizer or for livestock feed supplemnnt. The high temperature necessary to purify the fluoroapatite content of the raw ore invariably results in defluorination. The final step in the production of phosphorus is the

Fig. 6

Thirty-One Samples of Fluoride Concentrations (in ppm)
in Juniper Plotted on Collection Routes
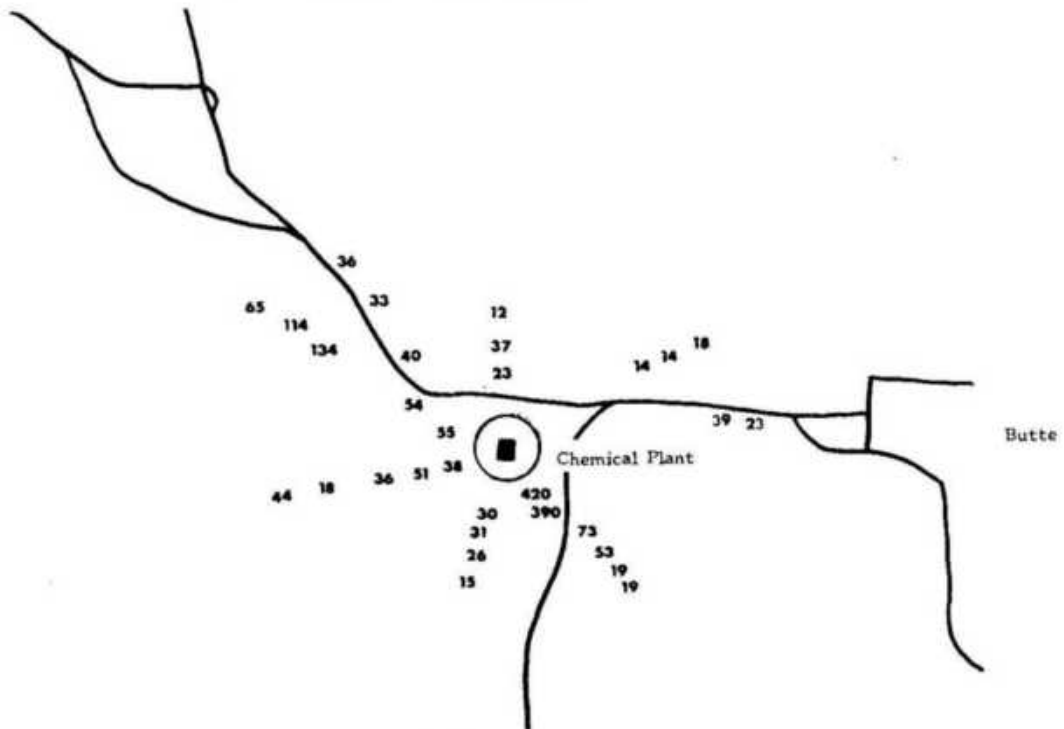
Fig. 7

Fluoride Concentrations in Soils Plotted on Collection Routes
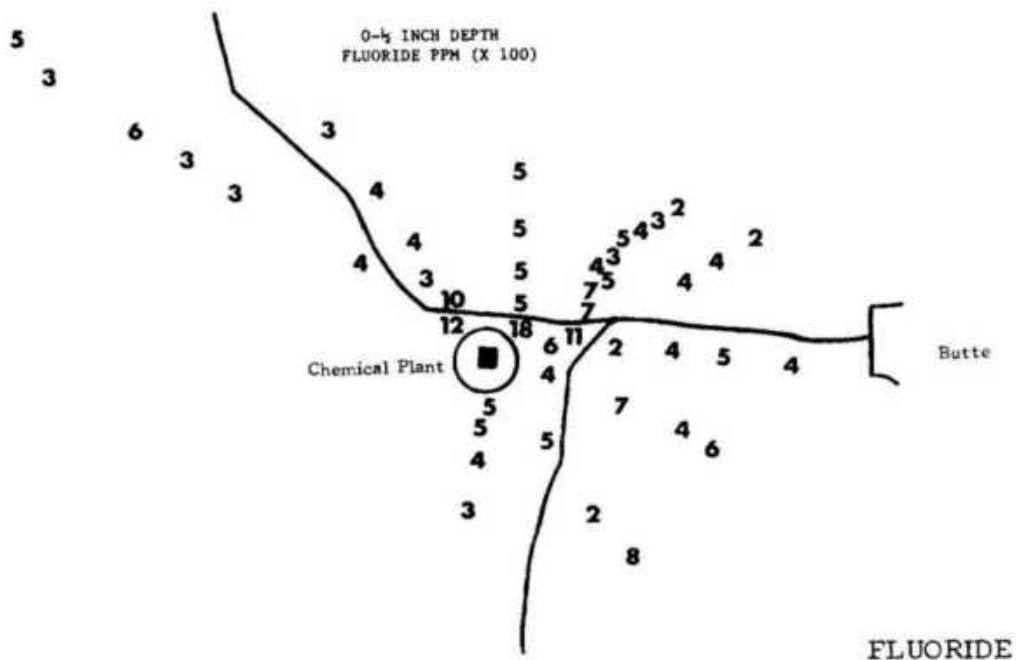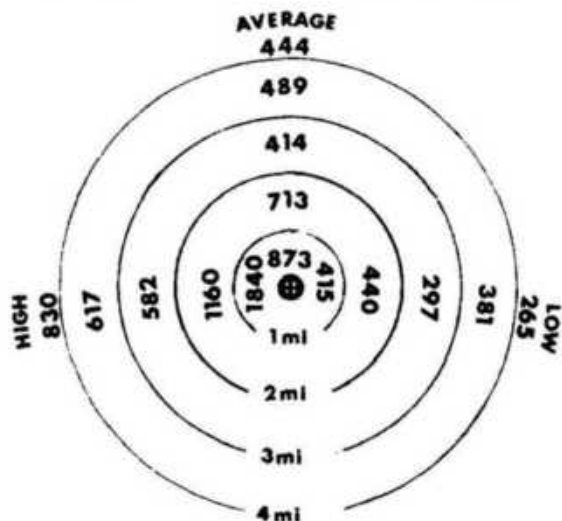

FLUORIDE

Fig. 8

Fluoride Concentration in Soils as a Function
of Distance from the Chemical Plant

electric furnace catalytic reaction of phosphate to phosphorus. Fluoride com-
pounds, P_2O_5, combustion products, and numerous unidentified compounds
common to the crude ore are either emitted into the atmosphere, collected
as slag, or flitered and washed into the settling pond. The airborne efflu-
ents are primarily vented through several 85-foot stacks, though the plant
has other emission points. Gaseous and particulate fluoride may also be emit-
ted from the settling pond near the plant.

The fluoride compounds, released into the atmosphere from this source,
behave in a somewhat different manner: The gaseous effluent is primarily hy-
drogen fluoride (HF), and the particulate mainly fluoroapatite dust. The at-
mospheric transport of these fluoride effluents is modified by certain charac-
teristics of the source such as height of the point of release, velocity of air
movement in the stack, and temperature of the stack effluent. Hydrogen flu-
oride gas is more widely dispersed by atmospheric transport than the particu-
late. The particulates emitted, depending on their size and density, will either
settle out rapidly on the surrounding terrain or may be carried further down-
wind. Since the air movements in this valley have never been studied, clima-
tological information has been used from the Butte weather station situated
on the other side of the Highland Mountains. The elevations of the site of the
chemical plant and of the weather station are very similar. However, the
wind directional data cannot be relied upon because mountains create a barrier
which isolates the Silverbow area from the weather station.

Intense atmospheric inversions result in high rates of gaseous fumiga-
tion and localized particulate fallout. Although air movements are greatly

confined by the structure of the valley, small scale topographic features with-
in the valley may channel air movements causing very high concentrations of
fluoride in some areas distant from the source, whereas other areas close to
the source may suffer little contamination. Vegetative cover on the valley
floor and slopes can also modify the speeds of surface wind and cause a filter-
ing effect of the pollutants.

Due to the higher dispersion potential of the gaseous effluents, it
should be possible to define the range of particulate fallout within the con-
taminated zone by washing the vegetation samples at different locations from
the source. This procedure was not utilized in this study. The literature in-
dicates that separation of particulate and gas-induced fluoride compounds is
difficult.

Fumigation experiments with hydrogen fluoride on spruce trees (24, 26)
demonstrate a natural loss of fluoride which is independent of washing, leach-
ing, and growth dilution. These experiments imply that fluoride uptake and
fluoride loss occur concurrently in living vegetation. Such findings do not ap-
ply to the accumulation of fluoride as a particulate surface deposit. Particu-
lates respond to washing only to a limited extent and are considered to be far
more cumulative. Whereas gaseous uptake in plants appears to occur primari-
ly during the growing season, particulate deposition occurs at all times of the
year on active, dormant or dead vegetative surfaces. Our data reflects the to-
tal accumulation of fluoride and its retention on vegetation subject to all na-
tural biological and climatological influences.

Climatological Influences

During the months of November through February, precipitation aver-
ages one half inch or less, primarily in the form of sleet or snow. Monthly
precipitation gradually increases to nearly two inches of rainfall during May.
At this time, the soils become warmer and the new growth begins to emerge
from the dormant bluebunch wheatgrass. During this period, the uptake of
HF gas is high and particulate accumulation begins on the new growth. The
heavy rainfall and the diluting effect of vegetative growth actively reduces
accumulation of fluoride. Rainfall is highest in June, averaging 2 1/2 inches.
Though the growing season in the area lasts until October, growing conditions
necessary for bluebunch wheatgrass often cause the onset of dormancy dur-
ing July because of high temperatures and rapid loss of soil moisture. As
dormancy occurs, the absorption of HF gas will dissipate, but particulate
deposition will continue through September until October when the rainfall
average drops below one inch per month. Our field collections were made on
October 6, the end of the greatest foliar washing period, and at the end of
a month of dormancy, which allowed gaseous accumulations to decline. In ad-
dition, this collection period followed the 90-day labor strike which probably
reduced the amount of fluoride emissions during that period. Therefore, the
fluoride concentration and distribution displayed by the isopol map (Fig. 3a

p. 189) is believed to be a very conservative evaluation of contamination of the Silverbow area during summer of 1972.

The forage collections representing vegetative remains of previous years' growth (1971 and older) have been subject to year-round contamination for possibly five years. To estimate the cumulative effects of HF induced contamination at this time is difficult. However, the accumulated highly insoluble fluoroapatite particulate is certain to comprise the majority of the fluoride found in these samples.

Juniper samples were not separated by age class. These composite samples have simply served to support the pattern of fluoride distribution found in the bluebunch wheatgrass.

Soil samples collected in the area do not display fluoride distribution patterns as clearly as the samples of vegetation probably because of higher background levels of fluoride naturally occurring in the soils, especially in fluorspar deposits. To determine control levels for soils,therefore,would not clearly establish the range of contamination which originates at the source of air pollution. However, the rapid rate at which fluoride increases in the surface soils within a radius of two miles from the source does indicate a heavy fallout zone of particulates.

As particulate concentrations increase on the surface of exposed, uncultivated soils another problem arises: During dry periods, surface air movements may transport these particulates and deposit them on foliar surfaces (42). They can thus become a long-lasting insidious source of future fluoride contamination for forage crops in the area.

Under normal range conditions, the consumption of juniper by wild and domestic herbivores is minimal. On the other hand, cattle, horses, sheep, deer, and elk show a preference for bluebunch wheatgrass in many areas (43, 44, 45) which is very abundant and highly contaminated in the area.

Bibliography

1. Hurry, J. J.: Report of Disease Investigation; Fluorosis in Cattle. Montana Livestock Sanitary Board, from the files of the Montana State Board of Health, 1956.   2. Spangler, H. L.: Letter to the Honorable Mike Mansfield from the Silverbow Fluoride Committee, from the files of the Montana State Board of Health, 1957.   3. Wake, B. F.: Air Pollution Study, Silverbow Area. Victor Chemical Works (Memorandum), from the files of the Montana State Board of Health, 1957.   4. Montana State Board of Health: Ambient Air Quality Standards, Montana State Board of Health, Helena, Montana, 1967.   5. Carlson, C. E.: Fluoride in Vegetation Near a Phosphorus Manufacturing Plant in the Vicinity of Butte, Montana. Northern Region U. S. D. A. Forest Service, Insect Disease Report No. 73-3, Missoula, Montana, 1973.   6. Montana State Board

of Health: Description of Process - Variance Recommendation, Stauffer Chemical Company. Montana State Board of Health, Helena, Montana, 1970.
7. Shreve, R. N.: Manufacture of Phosphorus and Phosphoric Acid in the Chemical Process Industries, McGraw Hill, N.Y., N.Y., pp. 352-355, 1956.
8. National Academy of Sciences: Fluorides. National Academy of Sciences, Wash., D.C., p. 11, 1970.   9. Montana State Board of Health: Emission Inventory Questionnaire - Stauffer Chemical Company. Montana State Board of Health, Helena, Montana, 1968.   10. Montana State Board of Health: Personal communication from staff, September, 1973.   11. Heck, W. W.: The Use of Plants as Indicators of Air Pollution. International Journal of Air and Water Pollution, 10:99-111, 1966.   12. Linzon, S. N.: The Influence of Smelter Fumes on the Growth of White Pine in the Sudbury Region. Ontario Department of Lands and Forests, and Ontario Department of Mines, Toronto, Canada, 1958.   13. Lathe, F. E. and McCallum, A. W.: The Effect of Sulfur Dioxide on the Diameter Increment of Conifers. Effect of Sulfur Dioxide on Vegetation, National Research Council of Canada, Ottawa, Canada, 1939.   14. McCune, D. C., Weinstein, L. H., and Mancini, J. F.: Effects of Hydrogen Fluoride on the Acid Soluble Nucleotide Metabolism of Plants. Contribution from Boyce Thompson Institute, 24:213-225, 1970.   15. Benedict, H. M., Ross, J. M., and Wade, R. W.: The Disposition of Atmospheric Fluorides by Vegetation. International Journal of Air and Water Pollution, 8:279-289, 1964.   16. United States Department of Health, Education and Welfare, Public Health Service, Environmental Health Service: Control Techniques for Fluoride Emissions. Department of H. E. W., Wash., D.C., 1972.
17. Knabe, W.: Experimental Study of the Fluoride Concentration in Needles and Leaves of Plants as a Function of Their Height Above Ground. Translation; The Franklin Research Institute Laboratories, Science Information Services. Landesanstalt für Immissions und Bodennutzungsschutz des Landes Nordrhein, 1969.   18. Hill, A. C.: Air Quality Standards for Fluoride Vegetation Effects. Journal of the Air Pollution Control Association, 9:331-336, 1969.   19. Jacobson, J. S., Weinstein, L. H., McCune, D.C., and Hitchcock, A. E.: The Accumulation of Fluoride by Plants. Journal of the Air Pollution Control Association, 16:412-417, 1966.   20. Spierings, F.: Injury to Gladiolus by Fluoridated Water. Fluoride, 3:66-71, 1970.   21. MacLean, D. C., Schneider, R. E., and Weinstein, L. H.: Accumulation of Fluoride by Forage Crops. Contribution from Boyce Thompson Institute, 24:165-166, 1971.   22. Hitchcock, A. E., McCune, D. C., Weinstein, L. H., MacLean, D. C., Jacobson, J. S., and Mandl, R. H.: Effects of Hydrogen Fluoride Fumigation on Alfalfa and Orchard Grass; A Summary of Experiments from 1952 through 1965. Contributions from Boyce Thompson Institute, 24:363-385, 1971.   23. Hill, A. C.: Air Quality Standards for Fluoride Vegetation Effects. Journ. Air Pollution Control Association., 9:331-336, 1969.   24. Hitchcock, A. E., McCune, D. C., Weinstein, L. H., MacLean, D. C., Jacobson, J. S., and Mandl, R. H.: Effects of Hydrogen Fluoride Fumigation on Alfalfa and Orchard Grass; A Summary of Experiments from 1952 through 1965. Contributions from Boyce Thompson Institute, 24:363-385, 1971.   25. Ledbetter, M. C., Maurodineau, R., and Weiss, A.

J.: Distribution Studies of Radioactive Fluorine-18 and Stable Fluorine-19 in
Tomato Plants. Contributions from Boyce Thompson Institute, 20:331-348,
1960.   26. Knabe, W.: Natural Loss of Fluorine from Needles of Norway
Spruce (Picea abies). Staub-Reinhalt. Luft, 30:29-32, 1970.   27. see ref.
8, p. 133-135.   28. Gordon, C. C.: 1970 Glacier National Park Study. Uni-
28 a. Carlson, C. E.: Fluoride Pollution in Montana. Fluoride, 6:127-137,
1973.   29. Carlson, C. E. and Dewey, J. E.: Environmental Pollution
by Fluorides in Flathead National Forest and Glacier National Park. U.S.
D.A. Forest Service, Missoula, Montana, 1971.   29a. Carlson, C.,
Bousefield, W., and McGregor, M.: Division of State and Private Forestry.
(Bulletin) Region I, U.S.F.S., 1974.   29b. Carlson, C. and Hammer,
B.: Division of State and Private Forestry. Region I, U.S.F.S. (manuscript
in preparation).   30. Gordon, C. C.: Fluoride Accumulation in Plants
and Animals in Garrison, Montana 1966-1969. University of Montana, Mis-
soula, Montana, 1971.   31. Kay, C. E.: An Inquiry Into the Distribu-
tion of Fluoride in the Environment of Garrison, Montana. Fluoride, 7:7-29,
1974.   32. Sun, M.: Fluoride Ion Activity Electrode for Determination
of Urinary Fluoride. Amer. Ind. Hyg. Assoc. J., 30:133-136, 1969.   33.
Singer, L., Armstrong, W. D., and Vogel, J. J.: Determination of Flu-
oride Content of Urine by Electrode Potential Measurements. Journ. of La-
boratory and Clinical Medicine, 7:354-357, 1969.   34. Elfers, L. S. and
Decker, C. E.: Determination of Fluoride in Air and Stack Gas Samples by
Use of an Ion Specific Electrode. National Center for Air Pollution Control,
U.S. Department of Health, Education and Welfare. Presented at the 154th
National Meeting, American Chemical Society, Chicago, Illinois, 1967.
35. Johns, W.: Personal Communication. Geologist, Montana School of Mines,
Butte, Montana, July, 1973.   36. Sahinen, U. M.: Fluorspar Deposits in
Montana. Montana School of Mines Bulletin, No. 28, Butte, Montana, 1962.
37. Weast, R. C. (ed.): Physical Constants of Inorganic Compounds. Hand-
book of Chemistry, 51st edition, The Chemical Rubber Company, Cleveland,
Ohio, p. B-77, 1970.   38. U. S. Department of Commerce: Local Climato-
logical Data, Butte, Montana. U. S. Dept. of Commerce Weather Bureau,
Washington, D.C., 1960. 39. U. S. Department of Health, Education and
Welfare: Powell County, Montana, Air Pollution Abatement Activity. U.S.
Dept. of H.E.W., Washington, D.C., 1967.   40. Gordon, C. C.: 1970 Gla-
cier National Park Study. University of Montana, Missoula, Montana, 1970.
41. Ficklin, W.: A Rapid Method for the Determination of Fluoride in Rocks
and Soils, Using an Ion-Selective Electrode. U.S. Geological Survey, Profes-
sional Paper 700, C186-189, 1970.   42. Gordon, C. C.: Cominco American
Report II. University of Montana, Missoula, Montana, 1969.   43. U.S.
Forest Service: Range Plant Handbook. U.S. Forest Service, Department of
Commerce, Washington, D.C., p. G-6, 1937.   44. Berwick, S. H.: Obser-
vations on the Decline of the Rock Creek, Montana Population of Bighorn
Sheep. University of Montana (thesis), Missoula, Montana, 1968.   45. Mor-
ris, M. S. and Schwartz, J.: Mule, Deer and Elk Food Habits on the National
Bison Range. Journal of Wildlife Management, 21:189-193, 1957.

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CIRCULATING PLASMA IMMUNREACTIVE PARATHYROID HORMONE LEVELS (IPTH) IN ENDEMIC SKELETAL FLUOROSIS WITH SECONDARY HYPERPARATHYROIDISM

by

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SUMMARY: Studies on 5 patients with gross symptoms and signs of fluorosis provided evidence that hyperactivity of the parathyroid glands is a frequent consequence of skeletal fluorosis. The plasma IPTH levels were elevated in all cases and one patient exhibited an adenoma and hyperplasia of the parathyroid glands at surgery.

The hyperactivity of the parathyroid glands in skeletal fluorosis in the presence of decreased solubility of the bone mineral (fluoroapatite) strongly suggests that it is a compensatory attempt to maintain a normal extracellular ionized calcium equilibrium. The possible mechanism responsible for hyperfunction of the parathyroid glands is discussed.

In our previous communications (1-3) we have shown biochemical, radiological and histological evidence of parathyroid hyperfunction in patients with endemic skeletal fluorosis. The purpose of the current communication is to report further observations and to provide direct evidence for the hyperfunction of the parathyroid glands by surgical removal of glandular tissue and by determination of the plasma immunreactive parathyroid hormone levels in patients with endemic skeletal fluorosis.

Material and Methods

Thirty patients (22 males and 8 females) aged 15 to 68 years of proven endemic skeletal fluorosis were investigated for their parathyroid function. All were laborers who worked in the fields and had resided since birth in an endemic fluorosis area in the district of Rai Bareli, Uttar Pradesh, India. The radiological changes suggestive of hyperparathyroidism were observed in 8 patients but the additional investigations could only be carried out in 5 of them.

Laboratory tests included plasma calcium, phosphorus and alkaline phosphatase, blood urea, creatinine and phosphate clearance, tubular reab-

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sorption of phosphates, urinary calcium, and fluoride. The fecal excretion
of fat on a six day collection was estimated in each patient. Skeletal and
dental roentgenograms and histology of the biopsied iliac crest bone were
studied. The fluoride content of the bone, drinking water and urine samples
was determined by the specific fluoride ion electrode as detailed by Taves (4).

Results

Radiological Changes (Fig. 1 and 2): Diagnostic radiological features
were observed in each patient. They included osteosclerosis, particularly of
the spine, pelvis and thorax; irregularly outlined osteophytes; periosteal bone
formation; irregular exostoses; calcification of ligaments, of interosseous
membrane and of muscular attachments.

The radiological findings suggestive of hyperparathyroidism were ob-
served in all 5 patients namely 1) subperiosteal erosions in the fingers, 2) loss
of the lamina dura, 3) coarse trabeculations, microcystic expansion of bones,
metaphyseal erosions and thinning of the cortex, particularly in the bones of
the pelvis, knees and hands.

Fig. 1

Skiagram of Pelvis

Sclerosis, new bone formation and metaphyseal resorp-
tion of the bones.

Fig. 2

X-ray of Hand

Sclerosis and subperiosteal erosions
of the phalanges suggestive of hyperparathyroidism

Bone histology (Fig. 3): Osteoclastic resorption and irregular ero-
sions in the edges of the bone trabeculae were observed in all 5 cases. An in-
crease in the periosteocytic surface resorption area was observed in all biop-

Fig. 3

Iliac Crest Bone Biopsy
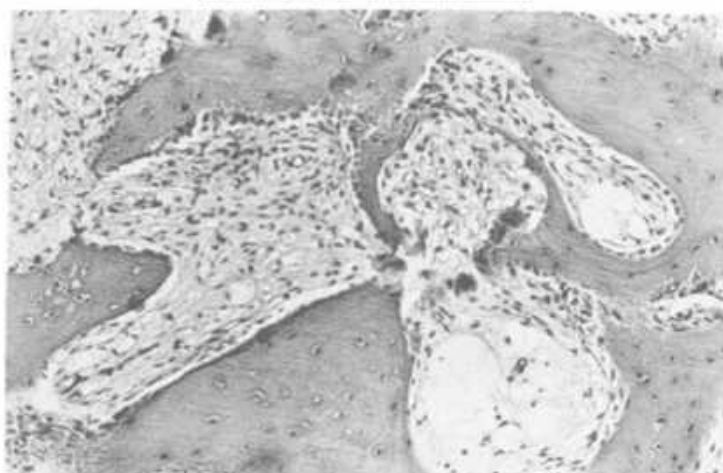
Osteoclastic resorption of the trabeculae and increased periosteocytic os-
teolysis suggestive of hyperparathyroidism (x 700)

sies. This feature strongly suggested overactivity of the parathyroid glands
(Table 1) induced by drinking water.

TABLE 1

Quantitative Histology and Composition of Bone (Ileum)

Patient No.	Histology *				Composition/100 g Dry Fat Free Bone Ash		
	O S (%)	C F (%)	R L (%)	P R (U 2)	Ca (g)	P (g)	F (mg)
1	25	95	22	83.0	12.8	5.5	575
2	30	88	18.4	77.0	12.0	5.0	420
3	27	78	17	70.0	13.0	4.8	472
4	22	85	15	68.0	12.0	5.0	365
5	23.5	95	16.2	74.2	12.5	4.8	265

* O S = Bone surface covered with osteoid
  C F = Calcification front
  R L = Bone surface with resorption lacunae
  P R = periosteocytic resorption area

Fluoride in drinking water: The fluoride content in the drinking wa-
ter obtained from the wells ranged from 24 to 26 ppm. The mean intake of
fluoride from water alone by each patient was 39 to 65 mg a day; in view of
the fact that the same water had been used for processing and cooking all
food, the total daily fluoride intake must have been even greater (Table 2).

TABLE 2

Dietary Intake Per Day (Mean Values)

Patient No.	Age (Yrs) and Sex	Calcium (mg)	Phosphorus (mg)	Vitamin D (I. U.)	Fluoride (mg)
1	58 M	580	1800	90	48
2	12 M	630	1550	65	65
3	22 M	620	1700	110	52
4	42 M	810	1680	90	45
5	17 M	585	1960	75	39

Discussion

All 5 patients were male and symptomatic. Their ages ranged from

35 to 60 years and the duration of symptoms from 7 to 11 years. Clinical findings were similar to those reported previously by us (5). They included mottled discoloration of teeth, stiffness and rigidity of the spine, restricted and painful joint and spinal movements, backache and inability to close fists. The diet of all patients was adequate in calcium, phosphorus and vitamin D.

The laboratory investigations (Tables 3 and 4) showed extremely high levels of the plasma alkaline phosphatase, elevated levels of plasma IPTH, in-

TABLE 3

Laboratory Investigations

Patient No.	PLASMA					
	*Ca (mg%)	Phosphorus (mg%)	Alk. Phosphatase (K.A.U.)	Urea (mg%)	CO_2 (mEq/lit)	IPTH (pg/ml)
1	9.6	4.3	85	18	24	1350
2	11.2	3.0	60	16	25	2800
3	11.0	3.4	64	23	26	1300
4	10.6	3.5	48	27	24	1250
5	9.7	4.5	26	26	25	1225

*Corrected to Specific Gravity of Plasma

TABLE 4

Laboratory Investigations Continued

Patient No.	Creatinine Clearance ml/min per 1.73 m²	Phosphate Clearance	Tubular Reabsorption of Phosphate (%)	Urine Calcium (mg/day)	Urine Fluoride (mg/day)	Hydroxy Proline (mg/day)	Faecal Fat (g/day)
1	120	25	70	75	4.2	123	1.8
2	140	36	64	85	4.8	120	3.2
3	118	30	68	70	3.2	126	3.8
4	123	35	65	80	4.2	115	2.7
5	126	25	82	65	3.2	95	4.5

creased phosphates and decreased tubular reabsorption of phosphate suggestive of hyperfunction of the parathyroid glands. Each patient showed excessive excretion of urinary fluoride and a low urinary calcium. The chemical analysis of the iliac bone revealed excess of calcium and fluoride (Table 1).

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None of the patients had renal disease or malabsorption.

Skeletal radiographs were indicative of a combination of fluorosis and hyperparathyroidism. They included a generalized increase of bone density, calcification of the interosseous membrane, subperiosteal resorption of phalanges (Fig. 1 and 2) and coarse cystic trabeculations. Dental X-rays revealed resorption of the alveolar bone around the roots of the teeth with erosion or loss of lamina dura in all 5 cases.

The histological bone changes suggestive of hyperparathyroidism i. e. osteoclastic erosion of the bone trabeculae and an increased periosteocytic surface resorption area were observed in each patient (Table 1, Fig. 3).

It is of note that our case 2 (Table 3) had a suspiciously high plasma calcium and low plasma phosphorus indicating that this patient was about to develop tertiary hyperparathyroidism in the sense described by Davies et al. (6). Subsequently in this patient parathyroid hyperplasia was established during surgery when an adenoma of the right upper parathyroid gland weighing 3.8 g was removed (Fig. 4). Presumably, this was a possible case of tertiary hy-

Fig. 4

Parathyroid Adenoma
Composed of Masses of Chief Cells.
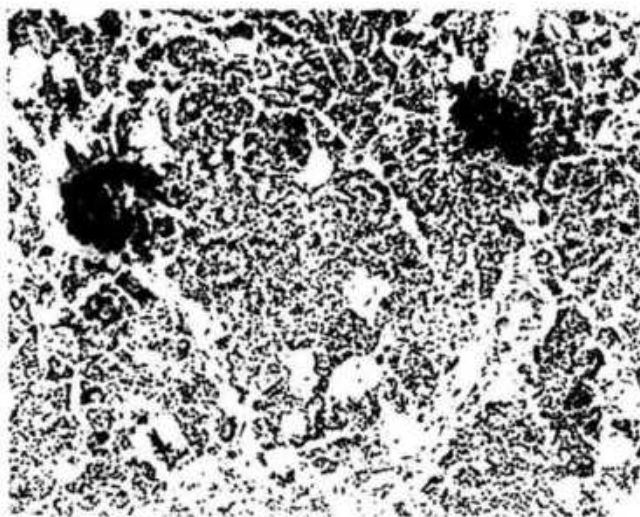
Other three glands showed secondary hyperplasia (x 100).

perparathyroidism in which the adenoma arose following the long standing hyperplasia as a result of excessive fluoride intake.

Reports in the literature on parathyroid hyperfunction in human ske-

letal fluorosis are sparse. Faccini (7) reported compensatory hyperplasia of
the parathyroid glands in experimental fluorosis. Bernstein and Cohen (8) con-
firmed parathyroid hyperplasia at surgery in three of their osteoporotic pa-
tients to whom fluoride had been administered for six months to one year.
Teotia and Teotia (9) reported secondary hyperparathyroidism and elevated
IPTH levels in patients with endemic skeletal fluorosis.

In a thorough experimental study, Faccini and Care (10) observed ov-
eractivity of the parathyroid glands in a fluorotic sheep which was demonstrat-
ed by an electron-microscopic study of the parathyroid glands and by concomi-
tant immunoassay of the amount of circulating parathyroid hormone. The
latter was as much as five times higher than resting and control levels. The
serum calcium remained within normal limits.

The mechanism leading to the hyperfunction of the parathyroid glands
in skeletal fluorosis is not clear. According to experiments by Havivi and Gug-
genheim (11), fluoride-containing bone from other species can resist resorption.
They found that fluorosed bone from mice had a reduced ^{45}Ca release, compared
with control bone,when the animals were given an injection of parathyroid ex-
tract for two weeks. Berry and Trillwood (12) and Proffit and Ackerman (13)
reported that a compensatory mechanism is mediated by the parathyroids when
the fluoride toxicity is not severe enough to cause a generalized cellular de-
pression. Thus it may be assumed that this development tends to overcome
the physical and chemical properties of bone apatite crystals.

Crystallographic studies by Zipkin et al. (14) have shown that the
apatite crystals in fluorotic bone are of a larger size than in normal bone.
This improvement in crystal texture is accompanied by the diminished solu-
bility and mobility of the bone salt. The fluoroapatite crystals, therefore,
are more stable and less reactive in surface exchange reactions since larg-
er crystals offer less surface area for a given weight of bone. It may there-
fore be assumed that these changes enhance the resistance of bone to the ac-
tions of the parathyroid hormone and may cause lowering of the plasma ion-
ized calcium, thus stimulating the compensatory activity of the parathyroids.

However, it seems unlikely that the reduced resorption of fluoride
bone alone is the exciting factor of parathyroid stimulation, particularly in
the light of certain animal experiments. Yates et al.(15) have demonstrated
evidence of parathyroid stimulation on a short-term basis using intraperiton-
eal lavage in rats. Faccini (7) performed immunoassay of parathyroid hormone
in sheep and demonstrated a significant increase in circulating hormone levels
only one week after initiating administration of fluoride. It is therefore pos-
sible that fluoride might induce secondary hyperparathyroidism by interference
with the equilibrium between bone and serum calcium, by accelerating crystal
growth or by producing a more rapid ion exchange.

Bibliography

1. Teotia, M., Teotia, S. P. S., and Kunwar, K. B.: Endemic Skeletal Flu-
    orosis. Arch. Dis. Children, 46:686, 1971.

2. Teotia, S. P. S. and Teotia, M.: Hyperactivity of the Parathyroid Glands
    in Endemic Osteofluorosis. Fluoride, 5:115, 1972.

3. Teotia, S. P. S. and Teotia, M.: Endemic Skeletal Fluorosis in Children.
    Evidence of Secondary Hyperparathyroidism. Clinical Aspects of Metabo-
    lic Bone Disease. Excerpta Medica, Amsterdam, 1972, p. 232.

4. Taves, D. R.: Determination of Submicromolar Concentrations of Flu-
    oride in Biological Samples. Talanta, 15:1015-1023, 1968.

5. Teotia, S. P. S., Kunwar, K. B. and Teotia, M.: Metabolic Studies on
    Skeletal Fluorosis with a New Approach to its Treatment (Preliminary
    Report). Fluoride, 2:142, 1969.

6. Davies, D. R., Dent, C. E., and Watson, L.: Tertiary Hyperparathy-
    roidism. Brit. Med. J., 2:395-399, 1968.

7. Faccini, J. M.: Fluoride and Bone (review). Cal. Tiss. Res., 3:1-16,
    1969.

8. Bernstein, D. and Cohen, P.: Use of Sodium Fluoride in the Treatment
    of Osteoporosis. J. Clin. Endocr., 27:197-210, 1967.

9. Teotia, S. P. S. and Teotia, M.: Secondary Hyperparathyroidism in Pa-
    tients with Endemic Skeletal Fluorosis. Brit. Med. J., 1:637-640, 1973.

10. Faccini, J. M. and Care, A. D.: The Effect of Sodium Fluoride on the
    Ultrastructure of the Parathyroid Glands on the Sheep. Nature (London)
    207:1399-1401, 1965.

11. Havivi, E. and Guggenheim, K.: The Effect of Copper and Fluoride on
    the Bone of Mice Treated with Parathyroid Hormone. J. Endocr. 36:
    357-361, 1966.

12. Berry, R. J. and Trillwood, W.: Sodium Fluoride and Cell Growth. Brit.
    Med. J., 2:1064, 1963.

13. Proffit, W. D., Ackerman, J. L.: Fluoride - Its Effect on Two Para-
    meters of Bone Growth in Organ Culture. Science, 145:932-934, 1964.

14. Zipkin, I., Schraer, R., Schraer, H., and Lee, W. A.: The Effect of
    Fluoride on the Citrate Content of the Bone of the Growing Rat. Arch.
    Oral. Biol., 8:119, 1963.

15. Yates, C., Doty, S., and Talmage, R. V.: Effects of Sodium Fluoride on Calcium Homeostases. Proc. Soc. Exp. Biol., 115:1103-1108, 1964.

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ENDOCRINE ASPECTS OF ENDEMIC FLUOROSIS

by

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SUMMARY: No significant alteration of function of the thyroid gland was observed in cases of fluorosis. Definite changes in the parathyroid status have been noted in a few patients. The mechanism is not precisely understood but it is related to the initial osteomalacia-like picture produced by fluoride ions in combination with calcium deficiencies. These changes constitute a compensatory homeostatic mechanism. These preliminary observations call for further elaboration.

Endemic hydrofluorosis is a state of chronic intoxication resulting from ingestion of excessive quantities of fluoride through drinking water. The disease manifests itself mainly as dental mottling and skeletal changes. Bones become rough, irregular, thick and heavy. It is associated with osteosclerosis, osteophytosis and calcification of ligaments, especially the interosseous membrane of forearms and legs.

In a disease with such a predominant involvement of the skeleton, some alteration in the structure and function of the parathyroid glands would be expected. Cannel (1), in describing the bone changes in fluorosis, pointed out that in many respects fluoride and parathormone exert a similar action on bone and that a final picture may be a combination of fluoro-

sis and hyperparathyroidism.

Of all the soft tissue organs, the thyroid gland contains most fluoride. Fluoride is a halogen and an antagonism is said to exist between iodine and fluorine for their affinity to thyroid. An increased incidence of goiter and hypothyroidism has been reported in some endemic areas (2). Changes in the structure and function of the thyroid gland have been described in experimental animals to which excessive doses of fluoride have been administered over long periods.

In view of these earlier observations, it was decided to study the function of the thyroid and parathyroid glands in cases of endemic fluorosis in a systematic and comprehensive manner.

Material and Methods

Twenty-five radiologically proven cases of skeletal fluorosis were selected for determination of their parathyroid functions. They were hospitalized in Rajendra Hospital, Patiala, where the following bio-chemical tests were done:

1. Serum calcium was estimated by the oxalate permanate procedure.

2. Serum inorganic phosphorus was estimated by the method of extraction with trichloroacetic acid by molyobdic acid procedure.

3. Serum alkaline phosphatase activity was determined by the modified method of King and Armstrong.

4. Phosphate clearance test.

5. Calcium deprivation test.

The radiological studies included a detailed analysis of skia-grams of the hands   and   additional X-rays of the spine and bones of the forearms in order to establish the diagnosis of fluorosis. Histo-pathological study of bone biopsy was done by routine methods.

A similar number of controls of similar age and sex were subjected to the above-mentioned investigations for the parathyroid function.

Twenty-six cases of proven skeletal fluorosis and a similar number of controls were investigated for their thyroid function . The following tests were done:

1. Protein bound iodine (PBI)
2. Basal Metabolic Rate (BMR)
3. Serum Cholestrol
4. E.C.G.

In addition, these patients were subjected to thorough clinical examination for any evidence of hypothyroidism.

Results

Parathyroid Functions

Out of the 25 cases studied, 21 were males and 4 were females; the control group contained 19 males and 6 females. The ages of the fluorotic patients varied between 27 and 70 years, the majority falling in the 50 to 60 age group.

Biochemical Changes

SERUM CALCIUM in the fluorotic patients ranged between 7.8 to 13.2 mg/100 ml, with a mean value of 10.2 mg% and S.D. of ± 0.9. In the controls the serum calcium varied between 8.7 to 11.0 mg%, with a mean value of 9.9 mg% and S.D. of ± 0.7.

SERUM INORGANIC PHOSPHORUS in fluorotic patients varied between 2.4 to 4 mg% with a mean value of 3.3 mg% and S.D. of ± 0.5. In the controls the serum inorganic phosphorus values varied between 2.6 and 4.3 mg%, with a mean of 3.4 mg% and S.D. of ± 0.5.

SERUM ALKALINE PHOSPHATASE in fluorotic patients varied between 5 to 26 King Armstrong units with a mean value of 13.3 K.A. units and a standard deviation of ± 5.4. In the controls, the serum alkaline phosphatase values varied between 5 to 14 units, with a mean value of 8.7 K.A. units and a S.D. of ± 2.7.

PHOSPHATE CLEARANCE VALUES in 25 fluorotic patients varied from 5.6 to 19.7 ml/minute with a mean value of 11.8 ml/minute and S.D. of ± 3.1. Phosphate clearance values in controls ranged from 3.2 to 23.10 ml/minute, with a mean value of 9.8 ml/minute and S.D. of ± 3.1 (Table 1).

CALCIUM DEPRIVATION TESTS were carried out on 25 fluorotic patients. Urinary calcium excretion in 24 cases was measured on patients with a diet normal in calcium content (about 1 gm). Subsequently the same patients were placed on a baseline diet containing about 100 mg calcium in 24 hours. On the 4th, 5th, and 6th day of low calcium intake, 24 hours urinary calcium measurements were done. Similar stu-

dies were made in control patients.

TABLE 1

Parathyroid Function Tests

No. of cases		Serum calcium mg %	Serum inorganic Phosphorus mg %	Serum Alkaline Phosphatase K.A. units	Phosphate clearance ml/minute
25	Range	7.8 to 13.2	2.5 to 4.5	5 to 26	3.2 to 23.1
	Mean	10.2	3.3	13.3	9.8
	S.D.	+ 0.9	+ 0.5	+ 5.4	+ 3.1
Controls					
25	Range	8.7 to 11.0	2.6 to 4.3	4 to 14	5.6 to 19.7
	Mean	9.9	3.4	8.7	11.8
	S.D.	+ 0.7	+ 0.5	+ 2.7	+ 3.5

The 24 hour urinary calcium excretion in fluorotic patients on a normal diet varied between 34.9 to 184.6 mg with a mean value of 100.9 mg and S.D. of $\pm$ 41.25. On the 4th day of low calcium diet, 24 hour urinary calcium excretion varied between 46.2 and 170.3 mg, with a mean value of 106.9 mg and S.D. of $\pm$ 35.19. On 5th day of the low calcium diet, the 24 hour urinary calcium excretion varied between 35.8 and 198.7 mg, with a mean value of 114.1 mg and S.D. of $\pm$ 42.16. On 6th day of low calcium diet, the 24 hour urinary calcium excretion varied between 30.9 to 324.2, with a mean value of 116.8 mg and S.D. of $\pm$ 71.48 mg (Table 2).

TABLE 2

Calcium Deprivation Studies

No. of cases		24 hour Urinary Calcium Excretion mg			
		On normal diet	On 4th day of deprivation	On 5th day	On 6th day
25	Range	34.9 to 184.6	46.2 to 170.3	35.8 to 198.7	30.9 to 324.2
	Mean	100.9	106.9	114.1	116.8
	S.D.	+ 41.25	+ 35.19	+ 42.16	+ 71.48
Controls					
25	Range	54.0 to 273.7	33.9 to 198.7	34.1 to 183.3	45.6 to 191.2
	Mean	135.6	113.8	106.5	104.7
	S.D.	+ 63.67	+ 40.94	+ 40.01	+ 35.52

In the control group, on a diet containing a normal amount of calcium, 24 hour urinary calcium excretion varied between 54 and 273.7 mg, with a mean value of 135.6 mg and S.D. of ± 63.67. On the 4th day of the low calcium diet, the 24 hour urinary calcium excretion ranged between 33.9 and 198.7 mg with a mean value of 113.8 mg and S.D. of ± 40.94. On the 5th day of the low calcium diet, the 24 hour urinary calcium excretion varied between 34.1 and 183.3 mg with a mean value of 106.5 mg and S.D. of ± 40.01. On the 6th day of low calcium diet, urinary calcium excretion varied from 45.6 to 191.2 mg with a mean value of 104.7 mg and S.D. of ± 35.52.

Radiological Changes

X-rays of hands (A.P. view) were obtained in 22 cases of radiologically proven skeletal fluorosis and were studied for any evidence of hyperparathyroidism.

In skiagrams of hands, subperiosteal erosions, which are said to be characteristic of hyperparathyroidism were observed in 10 cases (45.4%) (Fig. 1), a coarse trabecular pattern was present in 11 cases (50% (Fig. 2). Cystic changes in carpal and metacarpal bones were present in 4 cases (18.2%) (Fig. 3), erosions of the terminal tufts was present in one case and evidence of new bone formation was observed in 5 cases (22.7%). Calcifications of interosseous membrane which constitute a diagnostic index of skeletal fluorosis were present in all 22 cases (Fig. 2).

Histopathological Evidence

Histopathological study on bone biopsy was carried out in 23 cases. Bone biopsies were obtained from tibia, iliac crest, rib and vertebral body during cervical decompression. The compact bone showed complete loss and disordered orientation of the lameller pattern. The Haversian system was enlarged and poorly formed with changes in lacunae and canaliculi. In some cases, a peculiar type of pigmentation could be seen scattered irregularly in the sections. In spongy bones, areas of osteoid tissue were found among the well formed trebeculae. Areas of osteoid tissue extended into muscular attachments sometimes showing ossification of non-osseous tissues under the influence of fluoride. The bone trabeculae were very dense at places and contained considerable amounts of calcium. Areas around the vascular spaces stained deeply with eosin.

Thyroid Function

On examination, the thyroid gland of the 26 patients was morphologically normal. There was no evidence of localized or generalized swelling of the gland. Nor was there evidence of hypothyroidism in the form of subjective symptoms or objective signs.

TABLE 3

Radiological Changes

Name	Age & Sex	Subperios-teal erosion	Coarse pattern	Cystic ap-pearance	Erosion of terminal tufts	New bone formatio
N. D.	55 F	+	+	+	−	−
H. S.	45 M	−	−	−	−	−
H. S.	50 M	−	+	−	−	−
C. S.	50 M	−	−	−	−	+
B. S.	45 M	+	+	−	−	−
B. S.	60 M	+	+	+	−	−
M. S.	80 M	+	+	−	+	+
B. L.	55 M	+	+	+	−	+
B. S.	62 M	+	+	+	−	+
J. S.	35 M	−	−	−	−	+
A. S.	57 M	+	+	−	−	−
G. S.	45 M	−	−	−	−	−
G. S.	50 M	+	−	−	−	−
R. S.	55 M	−	−	−	−	−
P. S.	58 M	−	+	−	−	−
H. S.	68 M	+	−	−	−	−
C. S.	55 M	−	+	−	−	−
M. L.	60 M	−	+	−	−	−
S. S.	50 M	−	−	−	−	−
H. S.	60 M	−	−	−	−	−
P. S.	60 M	−	−	−	−	−
H. S.	52 M	+	−	−	−	−
Total:		10	11	4	1	5

SERUM CHOLESTEROL in fluorotic patients varied between 100 to 165 mg%, with a mean value of 134.5 mg% and a S.D. of ± 20.3. These values were within normal range and were confirmed in the control groups in which the values ranged between 112 to 172 mg%, with a mean value of 142.2 mg% and S.D. of ± 16.5.

PROTEIN BOUND IODINE values in fluorotic patients varied between 2.8 to 7.2 μg% with a mean value of 4.7 mg% and S.D. of ± 1.48. P.B.I. was less than 4 microgram percent in eleven cases. This is the

Fig. 1

Skigram of Forearm Bones;
A Coarse Trabecular Pattern of the Radius
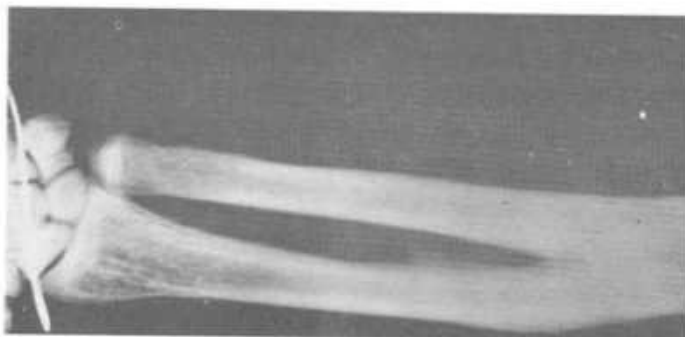
Calcification of interosseous membrane

Fig. 2

X-Ray of Hands in Fluorosis

Cystic changes in the metacarpal bones

lowest normal value as worked out in 25 healthy controls and is the ac-
cepted figure of other laboratories. P. B. I. in healthy controls varied
between 4 and 7.8 micrograms percent with a mean value of 5.4 micro-
grams percent and S. D. of $\pm$ 1.1.

Fig. 3

X-Ray of Hands in Fluorosis

Subperiosteal bone resorption and destruction of terminal phalanx
of left index finger.   Evidence of new bone formation.

BASAL METABOLIC RATE was found to range between -18 and
+6%, well within the normal accepted range. In the control group, these
values varied between -15 and +12% (Table 4).

TABLE 4

Thyroid Parameters

No. of cases		Serum choles-terol in mg%	P.B.I. microgram percent	B.M.R. in %
26	Range	100 to 165	2.8 to 7.2	-18 to + 6
	Mean	134.5	4.7	-
	S.D.	± 20.3	± 1.48	-
Controls				
26	Range	112 to 172	4 to 7.8	-15 to + 12
	Mean	142.2	5.4	-
	S.D.	± 16.5	± 1	-

The ELECTROCARDIOGRAM was normal in all cases except in
one in which there was evidence of left ventricular hypertrophy due to an
associated ischemic heart disease.

Discussion

Parathyroid Function: Cannel (1), in describing the bone changes of fluorosis, pointed out that in many respects fluorosis and hyperparathyroidism exert a similar action on bones and that the final picture may be a combination of fluorosis and hyperparathyroidism.

The assessment of parathyroid function is possible either by the study of

i.   Biochemical changes

ii.   Characteristic radiological lesions

iii.   Bone resorption and other histopathological changes

iv.   Radio-Immunoassay of parathormone

v.   Hydroxyproline in the urine

In this study, we had no facilities for estimation of I. P. T. H. (immunreactive parathormone) and hydroxyproline. We employed the first three parameters for the assessment of parathyroid function namely serum calcium, serum inorganic phosphorus, phosphate clearance and calcium deprivation studies. None of these methods revealed any significant alteration in the patients with skeletal fluorosis as compared to the normal controls.

A small but statistically significant rise in serum alkaline phosphatase was detected in the patients with skeletal fluorosis. Serum alkaline phosphatase values varied from 5 to 26 K. A. units with a mean value of 13.3 ± 5.4 K. A. units. However, Teotia et al (3) have reported much higher alkaline phosphatase values (up to 98 K. A. units) in patients with juvenile fluorosis.

Classically, radiological changes of osteosclerosis, osteophytosis and, calcification of ligaments and interosseous membrane, have been described in cases of endemic fluorosis. The most pronounced changes are seen in the vertebral column, particularly in the cervical region.

Teotia et al (4) have described some additional radiological changes including subperiosteal resorption of phalanges, distention of proximal and distal ends of long bones, widened metaphysis with rarification and irregular erosions, resorption of bones, erosions of lamina dura, rickets, osteomalacia and nutritional osteoporosis.

Coarse trabecular pattern, subperiosteal resorption in the phalanges and cystic changes have been found in a significant number of cases of the present series, suggesting that some skeletal changes resembling those of hyperparathyroidism do take place in cases of fluorosis.

Teotia et al (4) have studied serum immunreactive parathyroid hormone (IPTH) in 5 patients with endemic skeletal fluorosis and found consistently high levels of IPTH in these cases. The IPTH levels correlated positively with the quantitative observation in mineralized and non-mineralized bone, with levels of serum alkaline phosphatase, with urinary excretion of total hydroxyproline (THP) and with radiological findings. However no direct correlation between IPTH levels and serum calcium and urinary calcium levels was observed. It was concluded that the hyperactivity of the parathyroid gland in skeletal fluorosis in the presence of decreased solubility of the bone mineral (fluoroapatite) represents a compensatory attempt to maintain a normal equilibrium of extracellular, ionized calcium.

Jowsey et al (5) in experimental work on kittens demonstrated that decreased density of the spinal column and some changes in the trabecular pattern occurred at the end of long bones when cats were kept on a low calcium intake for 10 weeks. By radiological, microradiographic studies and tetracycline labelling, they have demonstrated that a low calcium diet will produce osteoporosis in the adult cat. They also have shown that the parathyroid glands increased in size with increased vascularity, suggesting hyperplasia, which perhaps may be directly related to the increase in the resorption process of the bones.

Few reports from different regions of India show the difference in the clinical picture of fluorosis: Krishnamachari and Krishanaswamy (6) have shown a high incidence of genu valgum in a much younger age group. Our own research team in their study in Rajasthan (to be published) also observed an increased incidence of changes indicative of rickets and osteomalacia in patients with fluorosis. These differences in the clinical picture in different regions of India are probably related to the variation in the calcium intake in the diet. In Punjab, where the dietary intake of calcium averages about 1 gm, osteomalacia and rickets are not encountered in cases of fluorosis. However, in Andhra Pradesh and Rajasthan, a low calcium intake coupled with intake of fluoride produces changes of rickets and osteomalacia. These observations have been corroborated by the experimental work of Jowsey et al (7).

The increased parathyroid activity in this disease, in our opinion, is related to the initial osteomalacia-like picture and is a compensatory homeostatic mechanism.

The data on histopathology of bones in humans is very meagre. Workers from outside India have reported various changes, predominantly

in experimental animals. These include increased osteoid tissue (8, 9, 10), irregular mineral deposition (11, 10), altered properties of bone matrix (8, 10, 11), a brown discoloration of mineralized bone (11), globular bodies in bone and vascular spaces (8, 10, 11), changes in the number of bone cells (8, 10, 12) and cytological abnormalities (11, 12). Data on histopathological studies in cases of endemic fluorosis is, however, very sparse (13, 14, 15) and conflicting.

The changes in compact and spongy bone, observed in the present series, on histopathological examination have already been described; they broadly conform to those described in experimental animals.

Thyroid Function

The relationship between fluoride intoxication and thyroid function is highly debatable. Muhler and Hine (16) believed that the thyroid gland was more sensitive to the effect of fluorides than all other soft tissue organs. Changes in the structure and function of thyroid have been described in experimental animals to which excessive doses of fluoride have been administered over long periods. Association of fluoro-toxicosis and endemic goiter has been reported from different countries (2). However, Singh et al.(14) and Siddiqui (17) did not notice any undue incidence of goiter in endemic areas. Leone et al.(18) also did not observe any difference in goiter incidence while comparing the morbidity rate of high fluoride and low fluoride areas.

In the current study, serum cholesterol, B.M.R. and E.C.B. have been within normal range. P.B.I. was decreased in some cases but we found no evidence of goiter or clinical hypothyroidism in these individuals.

Bibliography

1. Cannel, W. A.: Medical and Dental Aspects of General Fluoridation. H. K. Lewis and Co. Ltd., London, 1960.

2. Wilson, D. C.: Fluorine in Etiology of Endemic Goiter. Lancet, 1:211, 1941.

3. Teotia, M., Teotia, S. P. S., and Kanwar, K.: Endemic Skeletal Fluorosis. Arch. of Diseases in Childhood. 46:686, 1971.

4. Teotia, S. P. S. and Teotia, M.: Secondary Hyperparathyroidism in Patients with Endemic Skeletal Fluorosis. British Med. Journ., 1:637, 1973.

5. Jowsey, J. and Gershon-Cohen, J.: Effect of Dietary Calcium Levels on Production and Reversal of Experimental Osteoporosis in Cats. Proc. Soc. Exp. Bio. and Med., 116:437, 1964.

6. Krishnamachari, K. A. V. R. and Krishnaswamy, K.: Genu Valgum and Osteoporosis in an Area of Endemic Fluorosis. Lancet, 2:877, 1973.

7. Jowsey, J., Riggs, B. L., Kelly, P. J., and Hoffman, D. L.: Effect of Combined Therapy with Sodium Fluoride, Vitamin D and Calcium in Osteoporosis. Amer. J. Med., 53:43, 1972.

8. Belanger, L. F.: Rachitimetric Effect of Fluoride Feeding on Skeletal Tissues of Growing Pigs. Am. J. Path., 34:25, 1958.

9. Morquriedge, K. and Finn, S. B.: Effect of Fluorine on Activity of Vitamin D in Rachitic Rats. Journ. Nutrition, 20:75, 1940.

10. Roholm, K.: Fluorine Intoxication. A Clinical Hygienic Study with a Review of Literature and Some Experimental Investigations. H. K. Lewis and Co. Ltd., London, 1937.

11. Johnson, L. C.: Histogenesis and Mechanism in the Development of Osteo-fluorosis. Fluorine Chemistry, Vol. 4, Academic Press, New York, 1965.

12. Weatherell, J. A. and Weidmann, S. M.: Skeletal Changes of Chronic Experimental Fluorosis. J. Path. Bact., 78:233, 1959.

13. Reddy, O. B., Mallickharyunarao, C., and Sharda, D.: Endemic Fluorosis. Journ. Ind. Med. Ass., 53:275, 1969.

14. Singh, A., Jolly, S. S., Bansal, B. C., and Mathur, O. C.: Endemic Fluorosis. Medicine, 42:229, 1963.

15. Srikantia, S. G. and Siddiqui, A. H.: Metabolic Studies in Endemic Fluorosis. Clin. Sc., 28:477, 1965.

16. Muhler, J. C. and Hine, H. K.: Fluorine and Dental Health. Indiana University Press, Bloomington, 1959.

17. Siddiqui, A. H.: Fluorosis in Nalgonda Dist. Hyderabad-Deccan. Brit. Med. Journ., 11:1408, 1955.

18. Leone, M. C., Shimkin, M. B., Arnold, F. A., Jr., Stevenson, C. A., Zimmerman, C. R., Geiser, B. B., and Lieberman, J. E.: Medical Aspects of Excessive Fluoride in Water Supply. Pub. Health. Rep., 69: 925, 1954.

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FLUORIDE IN THE ENVIRONMENT

by

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SUMMARY: Data on the fluoride content of a variety of environmental agents are presented. Included are tobacco, detergents and other cleaning materials, certain kinds of dusts (wood, steel, fiberglass, asbestos), pollen grains and fertilizers. These agents vary widely in their fluoride content. The possible bearing of these findings on total fluoride intake in humans is discussed.

Numerous assays for fluoride have been made on organs, urine and blood of humans and animals, on water, air, vegetation, on forage for domestic animals and on food for humans. However, relatively little information exists concerning the fluoride content of materials in our environment with which we have daily contact. Whereas these items are undoubtedly less significant with respect to their effect on human health than fluoride in food and water they may conceivably, under certain conditions, contribute materially to a person's total fluoride burden.

In the following we shall present preliminary data on determinations of fluoride in various agents which, through inhalation or ingestion, are liable to enter the human body. They concern mainly items to which one is exposed occupationally such as in the building, farming, food processing trades or they may be natural constituents of airborne inhalants. Our data are limited to a few agents only. Supplementary data will be presented at a later date.

In assessing the significance of these values in terms of human health, several factors must be taken into account: Are these agents ingested or inhaled? Are they in gaseous, liquid, or solid form? If particulates, what is their size? Are they in inorganic or organic form? Where in the body are they being deposited? With what other elements is fluoride associated in the human body which might either reinforce or inhibit its action?

Fluoride contained in steel dust, for instance, is not likely to induce symptoms in humans. Metal particles, because of their heavy weight, are not readily dispersed in the air and, therefore, do not reach the lungs in large magnitudes. On the other hand, fluoride might conceivably influence the production of the so-called "red lung" which is primarily caused by airborne iron oxide. Similarly, the presence of fluoride in asbestos might be a factor in the action of the so-called asbestos or ferruginous bodies on the lungs. They are

TABLE 1

Fluoride Content of Various Items in ppm

Building Materials

Asbestos samples
	A	579
	B	239
	C	225
	D	70
	E	122

Dust in a tool factory	361.7
Dust within 10 meters of a construction site of a new home	13.1
Dust outside a fiberglass factor	40.4
Fiberglass	1250, 1258
Fly ash	241

Cleaning Fluids

Oxydol	0.4
Ajax soap	0.8
Soil cleaner	1.2
Blue Cheer	1.8
Snowy dry bleach	2.1
Ajax cleanser	7.0
Washing Powder (German)	
Ariel	1.1
Fewa	9.8
Omo	19.0
Fakt	63.4
Spülmittel Dixi	0.8

Tobacco

Cigarette - Ernte (Germany)	17.0
Erntekrone Zigareen (Germany)	19.2
Grossglockner (Austria)	21.7
Falk cigarette (Austria)	22.1
HB cigarette (Germany)	24.2
Roth Händle (Germany)	26.8
Cigarettes (U.S. brands)	25

Fertilizers

Schwefelsaures Ammoniak	0.003
Stallmist (Fresh manure)	0.003
Kalkammonsalpeter	0.01
Kainit	0.01-0.02
Thomasphosphat	0.01-0.14
Kalidungesalz 40%	0.02-0.03
Branntkalk	0.05-0.19
Mergel	0.06-0.27
Dolomitkalk	0.22
Kalkstickstoff	0.58
Huttenkalk	3.9-10.2
Superphosphat	14.6-25.7
Rhenaniaphosphat	15.0-27.7
Hyperphos	31.0-36.4
Rohphosphate	33.4-41.1

Miscellaneous

Pollen	
June Grass	2.4
Timothy	3.03
Short ragweed	3.62
Wood	
Walnut	1.1
Linden	1.4
Cedar	2.3
Pine	2.9
Ash	3.3
Sycamore	3.5
Willow	3.6
Mahogany	4.7
Oak	5.0
Elm	12.6
Salt	
From Detroit streets	.42
Morton salt	.42

encountered in the lungs for many years after exposure to asbestos-containing materials of the kind used in roofing and insulating. They induce cancer of the lungs and intestinal tract and mesothelioma, a malignant tumor in the pleura.

Relatively large amounts of fluoride are found in fiberglass. It is not impossible that its presence could be a factor in the irritating action of this agent on the mucous lining of the upper respiratory tract.

In pollen grains, fluoride is present in minute amounts, approximately 3 ppm. In view of the size of the pollen grain, which is in the range of 20 to 60 microns (1), not much pollen is likely to reach the lower air ways and the alveolar bed. However, no studies are available to indicate whether or not even minute amounts of fluoride contribute to the marked, well established antigenicity of pollen grains. Pollen is retained in the nasal mucous membranes (2). It migrates toward the nasal cartilage, where it disintegrates slowly as the result of the action of macrophages and other cellular elements. Even minimal amounts of fluorides might thus adversely affect the mucous membranes of the nasal passages and of the sinuses.

Fluoride in detergents will reach certain food products when such containers as tanks, milk bottles and dishes are not sufficiently rinsed. It is thus liable to account for increased fluoride levels in certain food items.

With respect to cigarettes, since 1000 gm of tobacco contains approximately 25 milligrams of fluoride and since one cigarette weighs approximately one gram, a person who smokes fifty cigarettes per day would inhale approximately 0.8 mg fluoride (only about 80% of the cigarette is consumed and not all the smoke is inhaled). On the basis of 30 liters of air inhaled per minute a worker would inhale during his 8 hour work day considerably more than that inhaled from smoking 50 cigarettes a day. The 8 hour maximum allowable concentration (MAC) value is 0.5 mg/m^3 in Russia, 2 mg/m^3 in Germany, and 2.5 mg/m^3 in the U.S.A. It is generally recognized that most occupational diseases are aggravated by smoking and even relatively minute amounts of tobacco smoke may, under certain conditions, contribute to respiratory illness (3).

The above-outlined points emphasize the need for further research on the health effects of fluoride in numerous, thus far unexplored, areas.

Bibliography

1. Waldbott, G. L.: Health Effects of Environmental Pollutants. C. V. Mosby Company, St. Louis, 1973, p. 185.

2. Stromme, O.: Studies on the Histopathology of Pollinosis, Thronsen and Company, Oslo, Norway, 1952.

3. Naeye, R. L., Mahon, J. K., and Dellinger, W. S.: Effects of Smoking on Lung Structure of Appalachian Coal Miners. Arch. Environ. Health, 22:190-193, 1971.

STUDIES ABOUT FLUORIDE EMISSIONS
FROM BROWN COAL-ELECTRICAL POWER PLANTS

by

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Dresden, G. D. R.

This study was initiated as the result of observations that there has
been increasing mortality of bees near power plants which were burning brown
coal. Fluorides are considered to be a major cause of death of bees in indus-
trial areas. In the D. D. R. (East Germany), no data on the fluoride content
of fossil fuel is available. The authors analyzed 68 samples of brown coal ob-
tained from mines in the D. D. R., three being situated west of the Elbe river
and three on the east side. The study covered a period of ten mining days.
The distillation method of Willard and Winter and the colormetric determina-
tions according to Megregian were employed.

In the layers of the mines the fluoride content ranged between 2 and
178 ppm (water-free) in ashed coal between 14 and 1440 ppm. East of the Elbe
river, the values ranged between 6 and 50 grams per ton and west of it be-
tween 2 and 178 grams per ton (water-free). Wide variations were noted be-
tween the individual mines as well as between the layers in an individual mine.

In order to determine whether the fluoride remains in the ash as an in-
organic compound when heated to 900 to 1200° C or escapes as a gaseous com-
pound, coal was burned for two hours at a temperature between 450 and 1000°
C. Even at 450° C, between 2% and 84% emanated; at 1000° C, this percentage
ranged between 78 and 100%. In the power plants, especially in antiquated fa-
cilities, considerable amounts of dust escape which contains hydrogen sulfide,
manganese, boron, aluminum and arsenic. The acidity of the coal ash is a
major factor in the release of atmospheric fluoride. In the samples of coal
mined west of the Elbe river, the pH ranged between 11.8 and 12.5; and in
those derived from east of the river, between 9 and 10.8. In the mines, not
only coal itself but the accompanying layers of sand or clay contained consi-
derable fluoride.

The authors comment on the difference in the degree of dispersion
between gaseous and particulate fluorides. They estimate that emitted flu-
oride gas travels between 1 to 2 km in contrast to dust containing particu-
late fluoride which has a wider expansion radius depending on the topography
of the area, the height of the chimneys, particle size and many other factors.
In the past, emission of fluoride from power plants has received little atten-
tion and damage to the environment near such plants is usually attributed
mainly to SO_2.

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DIETARY FLUORIDE IN DIFFERENT AREAS IN THE UNITED STATES

by

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In the past, fluoride intake has been found to approximate 3 to 4 mg/day in the Chicago area about 2 mg of which was derived from the diet. The authors analyzed hospital diets obtained from 16 different U.S. cities for their fluoride content which ranged from 2400 to 2600 kcal. The diets were packed in plastic containers as separate individual meals (breakfast, lunch and supper) and shipped in dry ice to the laboratory for analysis. The composition of each individual meal was recorded and each food item was weighed. The Singer and Armstrong method of analysis was utilized.

Results: The fluoride levels of the diets varied by as much as a factor of 2. In Corvalis, Oregon, for instance, the dietary fluoride amounted to 3.44 mg/day as compared with 1.73 mg in the Martinez, California, diet. The same variations were noted in diets from the same state.

In the 12 fluoridated cities the fluoride levels of drinking water also varied by a factor of 2 with a low of 0.53 mg/liter in Durham, North Carolina compared to 1.27 mg/liter in Cleveland, Ohio. In non-fluoridated areas the dietary fluoride amounted to approximately 1.0 mg/day. In different fluoridated areas the dietary fluoride varied greatly but these differences did not correlate with the fluoride content of water. Nor was there any correlation of dietary fluoride in cities where the water was not fluoridated. In Iron Mountain, Michigan, for instance, with 0.08 ppm of fluoride in water the dietary fluoride content was as high as in some areas with 1 ppm fluoridated water. In non-fluoridated areas, the dietary fluoride was more uniform (approximately 1.0 mg per day) than in fluoridated ones where the values ranged from 1.7 mg to 3.4 mg per day. These differences may be due to the fact that diets consist largely of processed food canned in areas where the level of fluoride in water differed from that in the locality from which the diets were obtained. Other factors involved in the variability of fluoride content of food is the locality in which the foods are grown; fertilization or spraying of the food; the type of food processing; whether the food is prepared with fluoridated or non-fluoridated water or whether the edible portion of the food is leaf, root, or fruit. It was concluded that in fluoridated areas, dietary fluoride content exclusive of drinking water amounts to 1.7 to 3.4 mg per day as contrasted with 1.0 mg/day in non-fluoridated areas.

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INTERFERENCE OF FAT AND FLUORIDE
ON GASTRIC EMPTYING OF RATS

by

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High fat diets enhance the toxicity of excessive dietary fluoride as indicated by the depression of growth in rats and by increased retention of fluoride in femura, heart and kidneys. The authors examined the relationship between dietary fat and fluoride by observing its growth-depressing action, by studying the in vivo oxidation of ^{14}C-labeled fat substrates (^{14}C-tripalmitin and ^{14}C-palmitate) in test meals and by monitoring the passage of such meals through the gastrointestinal tract.

METHOD: Five to 25.5 percent of fat (35% of the nutrients) was added to the diet of female rats. The animals were placed in individual glass metabolism chambers through which air was continuously drawn into a CO_2 trapping solution in order to measure the CO_2 produced by oxidation of fat. For the gastric emptying studies, the animals were fed the specified test meal by stomach tube and their stomachs were isolated after killing the animals at specified intervals. The stomach contents were extracted with 100 ml chlorophorm/methanol (1:1). For the radioactivity measurements, a liquid scintillation spectrometer was used.

RESULTS: Whereas the control rats gained 76% within 49 days, the fat-fluoride group showed an average gain of only 20% in weight.

The oxidation of ^{14}C - tripalmetin was strikingly delayed in the animals receiving the fat meal compared with that of the control animals. A lesser degree of delay occurred with ^{14}C - palmitic acid.

Stomach emptying studies: In the animals receiving 0.65 gm ^{14}C - tripalmitic labeled corn oil plus 1 mg of fluoride, 80% of the radioactivity remained in their stomachs after three hours compared with 24% in the controls. At 5 hours, 73% of the radioactivity was still present in the stomach of the fluoride animals but only 6% in the non-fluoride controls. When corn oil supplement was increased to 1.7 gm, similar results were obtained. When more water was added to the test meal and the fluoride concentration reduced from >50 mM (950 ppm) to <25 mM, the disappearance of ^{14}C - palmitic from the stomach was not as striking as when less water was included in the test meal.

The weight of the stomach contents also showed a difference in the two groups of animals. It averaged (stomach plus content) 3.9 g in the controls and 5.4 g in the fluoride-treated animals after 3 hours, and 2.3 g and

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5. 2 g respectively after 5 hours.

The authors point out that the fluoride levels under consideration are far in excess of those ordinarily consumed by man. Fluoride had less effect on the passage of ^{14}C labeled fat when non-fat constituents were added and the size of the test meal increased. The authors conclude that the action of fluoride on the emptying of the stomach could be a major factor responsible for the increased toxicity of fluorides to rats when dietary fat is increased.

* * * * *

URINARY FLUORIDE LEVELS IN
POLYTETRAFLUOROETHYLENE FABRICATOR

by

P. L. Polakoff, K. A. Busch, and M. T. Okawa
Cincinnati, Ohio

Fluorocarbonpolytetrafluoroethylene (PTFE) (teflon, halon, fluon) was introduced for commercial use in 1941. It has had a tremendous increase in production in recent years. Total production figures of fluorocarbons of which PTFE assumes a significant percentage rose from 14, 000 tons in 1965 to 610, 111 tons in 1961. Lubricity, chemical inertness, plasticity, and low toxicity are the properties which make it useful.

In 1951, a short-lived influenza-like illness was described in workers in close proximity to PTFE at sintering temperatures of approximately 350° C. The disease called polymer fever clears spontaneously within 24 hours. It is characterized by chills, pains in muscles and joints, nausea, tightness in the chest and fever. It is similar to the well-known metal fume fever which was described in 1831. According to recent studies, the pyrolysis products of PTFE at temperatures below 275° C constitute no hazard. At 300° to 360° C, tetrafluoroethylene, hydrogen fluoride and silicon fluoride and an incompletely characterized waxy supplement have been isolated. Above 380° C,

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small amounts of toxic gases, namely hexafluoropropylene and octafluoroisobutylene have been found. At 400° C, pyrolysis yields perfluoroisobutylene and carbonyl fluoride. In animals, fatal doses of individual pyrolysis products cause pulmonary edema.

The authors carried out a twofold, medical and environmental evaluation in a small factory manufacturing PTFE where 130 persons are employed. PTFE dust, derived from general molding and machining of the product, was collected in the factory and analyzed for fluoride. The medical evaluation comprised a questionnaire which was answered by 77 of the 130 employees. Seventy percent of these individuals had been employed on the job for more than 5 years, sixty percent of the workers had been smoking while on the job.

Air concentrations of PTFE in the factory ranged from 0 to 5.48 mg per m^3. Of the 77 individuals, 86% had experienced polymer fume fever some time in the past, 14% had had more than 3 episodes of the disease in the preceding 12 months. One third of the workers had been absent from work because of presumed polymer fume fever. Since only 10% of these had consulted a physician for the disease some of the workers might have mistaken other diseases with similar symptoms such as influenza for polymer fume fever.

Seventy-seven urine samples showed concentrations of 0.098 to 2.19 ppm fluoride. These specimens were spot samples and were pooled. They were not obtained from 24 hour collections. The local water supply contained 0.19 ppm fluoride. Fluoride intake through food was not determined. Patients with a history of one or more episodes of PTFE fume fever had a significantly higher average concentration of fluoride in the urine than what is considered "normal". However, no significant increase in urinary fluoride was noted in workers with exposure to PTFE of less than 1 year. This fact was attributed to improved, recently installed, ventilation facilities in the plant.

The authors stated that the carboxylate end group of PTFE, when heated to the fabrication temperature, decomposes and releases carbon dioxide and a vinyl bond in the polymer chain. The vinyl bond can react and form acid fluoride COF which, when hydrolyzed, forms carboxylate end group. Through repetition of this series of reactions a build-up of volatile components CO_2, COF_2, and HF is formed which is metabolized in the human body and leads to excretion of free fluoride ion in the urine. Such reactions only occur when the plastic is heated above 300° C. PTFE is, otherwise, considered to be inert.

* * * * *

CORRECTIONS

In the July, 1974 issue: On page 149, the last line on the page, Table 1 should be Table 2. On page 150, in lines 8 and 10, "he" should be replaced by "she" and "his" by "her" respectively.

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