ENVIRONMENTAL FLUORIDE

BY

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NRC Publication No. 12,226

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FOREWORD

This monograph had its origin as a Task Force Report begun in late 1968 for NRC-Canada's Biology Division. When, in 1970, NRC-Canada formed an Associate Committee and Secretariat concerned with "Scientific Criteria for Environmental Quality", the original Task Force Report was updated and enlarged. The present monograph includes coverage of the scientific literature that came to the authors' attention prior to January 1, 1971.

Throughout, the intention has been to prepare a concise survey and bibliography pertaining to fluoride in man's environment, with emphasis on the major components that contribute to man's food-chains. An attempt has been made to distinguish between naturally occurring "baseline" fluoride levels and those arising from man's activities. An attempt has also been made to discuss the environmental interrelations that contribute to the "total impact" of environmental fluoride. Wherever possible, apparent deficiencies in the scientific knowledge have been pointed out.

During the preparation of this monograph, it was never the intention to present a comprehensive listing of every research report concerning fluoride, but rather to present a selected bibliography documenting the environmental interrelations being discussed. We have, however, attempted to refer to several review articles that have particular environmental relevance and these, along with the bibliographies contained in cited references, will enable the reader to locate additional sources of information.

It is hoped to prepare future Supplements to this monograph, so as to survey the scientific literature that has come to our attention since January 1, 1971.

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Sincere appreciation is expressed for the co-operation extended by the following researchers and organizations:

1. Dr. Peter Brewer,
   Woods Hole Oceanographic Inst.,
   Woods Hole, Mass., U.S.A.
2. Dr. C.C. Gordon,
   Department of Botany,
   University of Montana,
   Missoula, Montana, U.S.A.
3. Dr. J.S. Hart,
   Division of Biology,
   National Research Council of Canada,
   Ottawa, Canada.
4. Dr. Lennart Krook,
   Dept. of Pathology,
   State Veterinary College,
   Cornell University,
   Ithaca, N.Y., U.S.A.
5. Dr. David C. MacLean,
   Boyce Thompson Inst. for Plant Research,
   Yonkers, N.Y., U.S.A.
6. Dr. Gene W. Miller,
   Huxley College of Environmental Studies,
   Western Washington State College,
   Bellingham, Wash., U.S.A.
7. Dr. C. Ray Thompson,
   Statewide Air Pollution Research Center,
   University of California,
   Riverside, Calif., U.S.A.
8. Dr. Richard E. Warner,
   Dept. of Biology,
   Memorial University,
   St. John's, Newfoundland, Canada.
9. Dr. A.C. Wiese,
   College of Agriculture,
   University of Idaho,
   Moscow, Idaho, U.S.A.
10. The members of the International Society
    for Fluoride Research.

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FLUORIDE IN MAN'S NATURAL ENVIRONMENT

Fluoride is present in trace amounts in soils and rocks, but is more prevalent in active or once-active volcanic regions[1]. Fluoride gases and fluoride-bearing ash are released by active volcanoes[1], and waterborne fluoride is emitted by geysers[2], while some ground waters can also contain significant amounts of fluoride[1]. Normally, only a small amount of fluoride is available to the general environment because it is present in relatively insoluble minerals, e.g., fluorspar, cryolite, fluoroapatite[1]. The following summary illustrates the extent of fluoride distribution in man's non-industrial environment; because man's food-chain includes seafood, some information about the marine environment is also included.

Soil: The fluoride naturally present in various types of soil has been reported to range from 76 ppm in sandy soil to 2640 ppm in heavy clay[3]. The increase in fluoride content of soils is usually accompanied by an increase in the $CaCO_3$ concentration which mitigates against fluoride availability, so that over 90% of the fluoride exists in a bound (i.e. relatively unreactive) form.

Water: In North America, most naturally-fluoridated waters are "hard" waters which can contain up to 27 ppm fluoride[2], but also contain appreciable amounts of calcium and magnesium[4]. In India, the reverse pattern is seen, and the natural fluoride-bearing waters tend to be "softer" than relatively fluoride-free waters[5].

Air: According to a 1960 report[2], the concentration of fluoride ion in the air of residential and/or rural U.S. communities ranges between 0.04 and 1.20 parts-per-billion (i.e. ppb); this is equivalent to a range of approximately 0.03 to 0.90 μg F/m^3 (*Note: 1 ppb of HF is equivalent to 0.75* μg F/m^3)[Ref.6]. A more recent survey[7] of rural and urban "business-commercial, not industrial" regions of the U.S. detected a range of < 0.05 to 1.89 μg/m^3 of "total water-soluble fluoride" in ambient air. However, only 8% of the urban samples and 0.2% of rural samples contained more than 0.1 μg F/m^3 in these non-industrial locations, and the preponderance of the readings indicated a water-soluble fluoride concentration of less than 0.05 μg/m^3 in ambient air.

Vegetation: The fluoride content of vegetation is influenced by the nature of the soil, and the fluoride content of soil, water, and air. Normally, vegetation will contain (dry weight basis) as little as 1 ppm fluoride, although this can be as high as 11 ppm[8] or even 19 ppm[9]. Generally, fluoride contents of 10 ppm or less are considered "normal" concentrations of fluoride within vegetation[10,11,12]. Among the staple food products, only tea leaves contain relatively large amounts of fluoride, i.e., up to 400 ppm on a dry weight basis, with popular North American brands averaging about 60 ppm[8], while British brands appear to contain three times more. (*Note: The British consumer appears to imbibe about 0.4 mg F with each cup of tea*)[13]. Also of

interest is the fact that some species of toxic plants, indigenous to Africa, Australia and Brazil, can synthesize fluoroacetate which mammalian species can convert to fluorocitrate, with consequent inhibition of the Krebs Cycle pathway[9].

Terrestrial Mammals: The only mammalian tissues that tend to accumulate relatively high levels of fluoride are skeletal tissues[1]. Bone has a strong affinity for fluoride, which accumulates in the mineral phase by isoionic substitution of F^- for OH^-, thus converting hydroxyapatite to fluoroapatite[4,14]. In a relatively fluoride-free environment, whole bones rarely accumulate more than 1,000 ppm F (dry fat-free basis)[14]. In contrast, soft tissues rarely contain more than 5 ppm fluoride, although kidney can accumulate 20 ppm or more[1].

Wildlife: Little information has been found that relates to uptake of fluoride by wildlife under normal conditions. The one report found states that femur fluoride levels in rodents are normally in the range 140 to 300 ppm[15].

Ocean Water: Ocean water contains between 0.77 and 1.40 ppm (i.e., mg/L) of *total* fluoride[16]. Recent studies[17,18] show that approximately 50% of the total seawater fluoride is bound as the double-ion MgF^+. No such association occurs with seawater calcium[18]. Thus, the unbound ionic fluoride (i.e., F^-) concentration in seawater appears to range between about 0.4 and 0.7 ppm.

Seafood: Salt-water fish, living as they do in a fluoridated environment, can contain appreciable amounts of fluoride. Whole mackerel have been reported[8] to contain 27 ppm on a fresh weight basis (i.e. 84 ppm on a dry weight basis). Fish Protein Concentrate (i.e., FPC) prepared from whole dogfish can contain 761 ppm fluoride, but only 24 ppm when prepared from cod fillets, and direct analysis of various fish tissues has shown that most of the fluoride is present in the bones[19].

Man's Entire Food-chain: Available data are conflicting, as regards man's ingestion of fluoride under "natural" conditions. A United States survey[2] indicates that, disregarding fluoride intake from drinking water, the daily intake of fluoride in "fluoride free" areas will be between 0.34 and 0.80 mg per day. A more recent Czechoslovakian survey[20] reports that daily ingestion of fluoride amounts to 1.0 mg per day, of which 0.8 mg is ingested with food. However, local factors can influence intake of fluoride, as indicated by a Canadian survey[21] which shows that the traditional diet of Newfoundland (high in bone meal and tea) can contribute 2.74 mg of fluoride per day in areas where the drinking-water is fluoride-free. Similarly, the traditional diet of Viet Nam contributed 1.78 mg F/day, exclusive of drinking water[22]. Thus, it can be surmised that, under conditions whereby abnormally elevated concentrations of fluoride are not present in the land-air-water components of the environment, total daily intake of fluoride by man rarely exceeds 1 mg, even though it can approach 2 to 3 mg in some traditional diets.

FLUORIDE POLLUTION

INDUSTRIAL SOURCES

During the past 100 years, man has been responsible for steadily increasing the distribution and availability of fluoride in his environment. As noted at the 1966 symposium at Montreal:

> "any process that involves new materials taken from the earth's crust and subjected to heating at high temperatures will liberate fluorides"[23]

Some examples of this are found in low-grade coal, which can contain up to 550 ppm fluoride[24], and the use of fluoride-bearing clays or silicates in the manufacture of bricks, tiles, pottery, and glass[25-29]. However, much higher levels of fluoride are found in raw materials used extensively in various other industrial processes. Cryolite (3 $NaF.AlF_3$) contains about 54% F and is chiefly used in the electrolytic production of aluminum, although it is also employed in the manufacture of enamels, opaque glass, and insecticides[30]. The production of 20 tons of aluminum requires the use of 1 ton of cryolite[11]. Fluorspar (CaF_2), another fluoride-rich industrial ingredient contains about 48% F. During World War II, the world production of fluorspar increased from about 400,000 to 950,000 long tons (excluding USSR production), and remained at a high level during subsequent years[30]. During the years 1944-50, about 50% of the fluorspar used in the U.S.A. was for steel production, with 30% used in the production of hydrofluoric acid, and 10% in glass fabrication; lesser amounts were used in the smelting of iron, lead, antimony, silver, and in the production of enamels for metal-ware coating[30]. Fluorspar or other fluorine compounds are also used in the production of copper[31,32], nickel[31], zinc[33], and molybdenum[34]. For steel production, fluorspar is added at the rate of 5 to 8 pounds per ton in open-hearth processes and 14 to 40 pounds per ton in electric steel-smelting[30].

Another fluoride-rich ingredient is Florida phosphate rock (or similar types) which contains about 4.0% F, 30% to 90% of which can be evolved during thermal and/or chemical processing during the production of phosphate fertilizer and various other products[31,35]. The phosphate fertilizer industry has a particular problem in emission control, because the acidulated phosphate rock is stored in unsealed sheds ("dens") where it is allowed to "cure" for 30 to 60 days; so far, efforts to control gaseous fluoride emanations from these "dens" have met with limited or no success[35]. Fluoric emanations also occur from gypsum pond "lagoons" where aqueous fluoride effluents are treated in an attempt to precipitate the fluoride, but where a combination of high acidity and high fluoride levels can cause emission (i.e., 26 pounds/day) of gaseous fluoride[36]. Breaks in the dyke wall of such lagoons can cause fluoride contamination of the surrounding soil and vegetation[37]. Phosphate rock is also used in the production of elemental phosphorus, an operation that also gives rise to fluoric effluents[38]. All aforementioned processes require high-heat treatment (and/or acidification) and this entails volatilization of fluoride in gaseous and/or particulate form[23]. Another development dates to 1941, when some sectors of the petroleum industry began to use hydrofluoric acid as a catalyst in the alkylation of high-test gasoline[25,26,39]. No specific data are available on this topic, beyond the estimate that one such alkylating plant was using between 500 and 750 tons of HF per year, according to a 1945 report[26]. Hydrogen fluoride is used to isolate uranium-238 (as the hexafluoride salt)[40,42], and elemental fluorine is used as a rocket-propellant[41,42].

Fluoride-emitting industries are confronted by a dilemma. They can discharge the fluoride compounds into the surrounding air and water, thereby risking litigation arising from fluoride-induced damage. Or, they can attempt to recover the fluoride wastes and be faced with a formidable disposal problem. One steel operation returns its fluoride wastes back to the earth in "burial plots" similar to those used to dispose of radioactive wastes[42]. Other industries convert the fluoride to hydrofluoric or hydrofluosilic acids, or their sodium salts, which can then be marketed for other industrial purposes or sold as additives for the fluoridation of water supplies[43]. This can be financially attractive. In 1964, 25% fluosilic acid produced at 3 to 5 dollars per ton was selling for 45 dollars per ton[44]; by 1966, the city of Toronto was using 30 tons of hydrofluosilic acid per week for water fluoridation[43]. However, this market does not appear to have solved the disposal problem, because the firm supplying the hydrofluosilic acid (as a by-product of its phosphate fertilizer operation) was later the subject of a Royal Commission inquiry that revealed that the company's fluoric emissions had increased markedly since 1964[45].

The installation of water scrubbers, chemisorption equipment, and/or spray towers can reduce emission of gaseous fluorides; release of particulate fluorides can be reduced by electrostatic or mechanical precipitation, scrubbers, or bag filtration[11,46,47]. (*Note: The advantage of chemisorption in aluminum production is that it allows "recycling" of the trapped F to the pot*[47]). However, a very high degree of efficiency is required to deal effectively with fluoride effluents: with average emission rates greater than 1 lb. of gaseous HF per hour, control equipment should have an efficiency of 99% or better; in comparison, the control of "H_2SO_4 mist" effluents only requires this degree of efficiency when the average emission rate attains 30,000 lb. per hour[46]. And, to quote from the 1966 Montreal Conference,

> "prolonged exposure to ambient air concentrations of less than 1 part per thousand million parts of air by volume may create a hazard .... In this respect, fluorides are more than 100 times more toxic than sulfur dioxide"[23].

AIR POLLUTION:

In early 1967, it was announced that panelists at a meeting of the American Association for the Advancement of Science had listed fluoride as the third most serious air pollutant in a group headed by sulfur dioxide, and followed by ozone, fluorides, chlorine, and ethylene[48]. Airborne fluoride can be of two types, gaseous and particulate, each of which can contain components differing in solubility[6,49]. The magnitude of the problem can be appreciated upon realizing that, during 1961, an estimated 25,000 tons of fluorine was released into the atmosphere of England and Wales from coal-burning *alone*[45]. A similar amount was estimated to escape as gaseous fluoride from American superphosphate factories during the year 1933[50], but this estimate had risen to 70,000 tons of airborne fluoric effluent[31] for the year 1949. In 1966, it was reported that fluoride emission from a triple-superphosphate factory could range from 200 to 3500 lb. per day, and that the Florida Air Pollution Commission had set a maximum limit of 4,000 lb. (i.e., about 1,800 Kg) of gaseous and/or water-soluble fluorides per day as total emission in 2 counties[35].

As for aluminum operations, a Swiss report[11] records a gaseous emission of 0.56 Kg F and a dust emission of 4.5 Kg F per ton of aluminum processed; in Norway, the "total quantity of fluoride in the escaping gases" has been reported as approximately

20 Kg per ton of aluminum[51]. Aluminum factory emissions have also been reported as varying from 7 to 30 Kg gaseous fluoride per hour[52], and a total fluoride emission of from 10 to 1,000 Kg per day[53]. A Czechoslovakian survey[20] found that, close to an aluminum factory, the airborne fluoric distribution was 61% solid and 39% gaseous; further away, it was 15% solid and 85% gaseous. A U.S. report[47] states that from 1/3 to 2/3 of the total fluoride present in aluminum stack emission consists of particulate material.

In a steel plant, a fluoride emission of 4,600 μ g/m^3 was measured in waste gas from a blast-furnace, and a maximum value of 17,650 μ g/m^3 was recorded in an open-hearth stack; daily fluoride emission from this plant was estimated to be 39 pounds (i.e. approx. 18 Kg)[54]. In a zinc plant, the fluoride emission from waste-heat boilers was 15 pounds (i.e. approx. 7Kg) per day[54].

It has also been reported that, depending on the type of industrial operation, a factory-stack effluent can contain from 3.6 to 15,600 milligrams of fluoride "per liter", of which the gaseous phase may represent anywhere from 0.7 to 96.0%[49]. The compounds comprise an entire series of fluorides and silicofluorides, either as volatile acids or in salt-form, as well as emanations of cryolite, fluorspar, or whatever fluoride component is present in a particular molten flux[23,26].

Fluoride released as particulate matter tends to deposit as "fallout" in the general downwind vicinity of the fluoride-emitting factory. However, some emitted particulates are unstable, e.g., ammonium silicofluoride can react with acidic emissions to form hydrofluosilicic acid which can then react further to form silicon tetrafluoride and hydrofluoric acid; as a consequence, window panes in the area can be etched[29]. Roholm[55] has considered the etching of glass to be a reliable indicator of the presence of gaseous atmospheric fluoride. From the foregoing example, it is obvious that particulate fluoride effluents are not always stable and unreactive.

At a recent European symposium it was stated that dispersion of effluent gases does not solve the emission problem, i.e.,

> "The higher a chimney, the larger the area over which harmful gases are spread. Though this results in a lower concentration, the accumulation of pollutants goes on...."[56].

Corroboration of this statement can be found in a Norwegian study, which found that fluoride-induced injury to coniferous forests could occur at a distance of 32 Km from the emitting source and destruction of some species at a 10 to 13 Km distance[52]. At the European symposium, the construction of "air tight" production plants was also recommended; it was stated that fluoric gases from old aluminum factories, escaped "not through the chimneys, but through windows and doors"[56]. This is supported by the experience in a phosphate fertilizer factory in which the airborne concentration on the reaction floor of an unsealed "den" shed was 86 *milli*grams HF/m^3[Ref.45].

In Canada, fluoride emissions have been mentioned in connection with aluminum production (Kitimat, B.C.; also Arvida and Isle Maligne, P.Q.), phosphate fertilizer plants (Trail, B.C., and Medicine Hat, Alta.), and a large foundry in St. Catharines, Ont.[23]. There have also been studies of fluoric emanations from two other Ontario factories: a tile plant near Grimsby[27], and a phosphate fertilizer operation in Port Maitland[10,45].

At this point, it is pertinent to state that, in several surveys in which sulfur dioxide had been suspected as the primary air pollutant, fluoride was found to be the factor responsible for environmental blight[34,57]. (*Note: Reference 34 presents 3 surveys based on this type of "mistaken identity"*). In a 1952 report, it was stated that ..

> ".... the possible synergistic effects of subdamage concentrations of sulfur dioxide in admixture with gaseous fluorine compounds must be thoroughly investigated ..."[57].

A somewhat similar statement is again made in a 1968 presentation, i.e.,

> ".... it is not unreasonable to presume that, for instance, apple-trees may be more sensitive to SO_2 contamination if HF pollution is also present"[58].

This problem is very relevant: Industries that release fluoric effluents also use fossil fuels as an energy-source, thereby emitting significant quantities of sulfur dioxide. A recent USSR report[59] concludes that – where both pollutants are present in the same atmosphere – the concentration of SO_2 and HF should be expressed as a decimal fraction of the maximum permissible level for each pollutant; undesirable atmospheric conditions exist when the sum of these two fractions exceeds unity. However, studies are needed to evaluate this concept as regards long-term outdoor conditions.

Any discussion of fluoric air pollution must, of necessity, deal with airborne *concentrations* of fluoride. Such data is very rare. A 1960 report[2] of the HF concentration in the atmosphere of six U.S. cities showed average values ranging from 3 to 18 ppb (i.e., approx. 2 to 13 μg F/m^3), with high values on particular days of up to 80 ppb (60 μg F/m^3). However, in view of the much lower results obtained in the recent survey of U.S. "business-commercial, not industrial" regions[7], it is likely that the 1960 values were influenced by the proximity of industrial establishments. This is supported by data compiled in a 1967 Czechoslovakian survey[20] which recorded a maximum total airborne fluoride level of 1130 μg/m^3 in the vicinity of an aluminum factory.

Ideally, analysis of airborne fluoride should distinguish between highly reactive gaseous forms and particulate compounds that are either "inert" or unstable. A recent device[49] collects particulate matter on filters, and converts the gaseous fluorides to a less reactive chemical such as silicon tetrafluoride for subsequent analysis, with results expressed as units of fluoride per cubic meter of air. But, as recently as 1969, analytical difficulties had not yet been resolved concerning the *day to day* monitoring of atmospheric fluorides, i.e.,

> "No equipment is presently available which will reliably measure gaseous HF at the fractions of micrograms per cubic meter in air...But these are the levels which can cause major damage to crops"[60].

One of the monitoring devices still in use is a lime-treated paper or "limed candle" which absorbs gaseous fluorides while housed in protective shelters designed to permit adequate air circulation while minimizing contamination from particulate material. Results are expressed as μg (or mg) F/100 cm^2/month[27,45,53,61], and are presented as such. A 1970 review article has stated:

> "While investigators would like to relate the degree of injury to atmospheric or foliar fluoride concentrations, no one has yet managed to quantitatively correlate these factors in the field. Possible crop injury and losses can be evaluated only by field observations"[12].

However, Adams has shown[61] that a linear correlation (r = 0.946) exists between the uptake of fluoride on limed paper and the "cumulative time x airborne gaseous fluoride concentration", so that

(Hours of exposure x μ g F/m^3 in air) = 4.36 x (μ gF/dm^2 on limed paper).

Thus, for a one-month exposure period, it can be calculated that multiplying the "μ gF/dm^2/month" by the factor 0.006 provides an approximation ($\pm$ 10%) of the average gaseous airborne fluoride concentration, expressed in μ g/m^3. Adams has cautioned[61] that, at values above 200 to 250 μ gF/dm^2, the rate of fluoride uptake by limed paper decreases; thus, calculated airborne fluoride values above 1.2 to 1.5 μ g/m^3 would tend to *under*estimate the actual atmospheric concentrations. Nevertheless, the calculation provides a means of interpreting data obtained with limed-paper devices.

With this caclulation ("μ gF/dm^2/month" x 0.006), the limed-candle data obtained at "Station A" near an Ontario fertilizer factory[45] reflects an airborne fluoride level that averaged 0.48 μ g/m^3 in 1964, increased 45-fold to 21.8 μ g/m^3 in 1965, then decreased to 15.6 μ g/m^3 in 1966 and 8.0 μ g/m^3 in 1967. In terms of possible crop damage, the calculation can be used to assess field-survey data such as presented by Bovay in Switzerland[53], Adams *et al* in the State of Washington[62], and in two separate Ontario studies by Linzon[10] and Drowley *et al*[27]. (*Note: The effects of fluoride on vegetation is discussed later in this report. For now, it is sufficient to say that vegetation is considered to be most susceptible to fluoride during the growing season; also, a fluoride content of 35 ppm in dried vegetation is used to indicate that a state of fluoric air pollution exists, whether in the U.S., Canada, or Europe*). The recalculation of Bovay's data is illustrated in Appendix 1, while Appendix 2 presents data bearing on the other three surveys. These evaluations can be summarized as follows:

Appendix 1: The maximum permissible fluoride level in apricot leaves was attained when the average F concentration in ambient air was 0.38 μ g/m^3.

Appendix 2: (i) Damage to 25% of the surface of gladiolus leaves and 6% of Ponderosa Pine needles was observed at an airborne F level of 0.37 μ g/m^3. Therefore, the "no damage" condition lies somewhat lower
(ii) Damage to peach orchards occurred at 0.26 μ gF/m^3, but not at 0.19 or 0.14 μ g/m^3.
(iii) Although Linzon's data shows that "greater than normal" uptake of F by vegetation occurs at a "growing season" airborne fluoride level of 0.40 μ g/m^3, only one of the 1969 samples contained fluoride in excess of 35 ppm[10]. Thus, the maximum acceptable average airborne F level would seem to be below 0.40 μ g/m^3.

Overall: In terms of this evaluation, the average gaseous F level in ambient air should be below 0.4 μ g/m^3 and might have to be as low as 0.2 μ g/m^3, if damage to sensitive vegetation is to be avoided. (*Note: Apricot, gladiolus, Ponderosa Pine, and peach orchards are all considered very susceptible to fluoride-induced injury*[12]).

The high degree of agreement among the trends indicated by the four sets of data is of interest, especially considering that the fluoric effluents originated from 4 different types of industrial operation, i.e., aluminum[53], ferro-alloy and aluminum[57], a tile factory[27], and a phosphate fertilizer operation[10], all of which would be expected to emit

different proportions of particulate fluoride in their airborne effluents. Therefore, if airborne particulate fluoride can "contaminate" the limed-paper devices (as has been alleged[45]), it certainly did not introduce obvious disparities in the above comparison. One other fact emerged from the intercomparison: Whereas a shut-down of the tile factory[27] reduced the airborne fluoride concentration to 0.11 μ g/m^3, a closing-down of the phosphate fertilizer operation[10] brought airborne fluoride levels down to only 0.40-0.43 μ g/m^3. Here, it must not be forgotten that fluoric emanations from storage dens[35] and gypsum-pond lagoons[36] can still occur during a shut-down of a fertilizer plant *per se*. Also, it has been stated[63] that airbone fluoride concentrations lower than o.3 μ g/m^3 can damage sensitive plants if present continuously.

Some comparisons can be made: The Province of Alberta[64] proposes to allow an airborne fluoride level of 3.00 μ g/m^3 for a 24-hour period, whereas the State of Texas[65] allows 2.63 μ g/m^3 and Montana[65] permits 0.75 μ g/m^3 (calculated as F). For a one-month period, Texas[65] allows 0.75 μ gF/m^3, while Montana[65] permits 0.18 μ g/m^3 (i.e., 30 μ g/dm^2/28 days) and Ontario uses an index of 0.24 μ g/m^3 (i.e., 40 μ gF/dm^2/30 days)[66]. In this connection, it is relevant to state that, in 1970, it was reported[66] that a 30-day sampling had revealed an airborne fluoride level of greater than 1.8 μ g/m^3 (i.e., > 300 μ gF/dm^2/30 days) in the industrial area of Hamilton, Ontario.

At a recent European Symposium on air pollution, airborne fluoride was indicted, along with sulfur dioxide, as accounting for the destruction of 400,000 hectares of European forests[67]. Such factors as factory production-capacity and management, regional topography, and weather conditions were emphasized [51,53], particularly in terms of "stagnant air periods" during which atmospheric fluoride could attain unexpected levels. Roholm[55] has documented his reasons for concluding that at least one air pollution disaster was caused by industrial fluoride effluents. The possible role of fluoride has also been mentioned[68] in relation to other calamities in industrially-polluted localities.

POLLUTION OF RAIN:

At a 1969 Fluoride Symposium in Barcelona, the account of a survey[24] in coal-burning industrial regions of Germany revealed that rainwater could contain from 0.28 to 14.1 ppm F, i.e. representing increases of up to 88 times the fluoride levels found in control areas. About 98% of this rain-borne fluoride is in particulate form. The concentration is influenced by the extent of coal combustion, the direction of the prevailing wind, and proximity to the emitting source. Of particular significance was the fact that rainwater fluoride was directly correlated with the levels found in vegetation. A 1949 Tennessee study[31] had observed a range of 0.06 to 1.23 ppm F in rainwater and had associated this with extensive soft-coal burning and industrial effluents. A 1948 American survey of the Pittsburgh region[69] suggested an association between the fluoride content of vegetation and coal smoke, but had not suspected a possible role of rainwater. A significant solubility of particulate fluoride in rainwater has been assumed to contribute to fluoride accumulation in the sub-surface soil of industrial regions[3].

SOIL POLLUTION:

As noted in the opening section of this report, available data suggest that less than 10% of the fluoride naturally present in soils is water-soluble[3]. On the other hand, tests

in which various fluoride salts were added to soil and the soil then leached with water led to the conclusion that the *added* fluoride was not firmly bound even after two years[3]. This added fluoride was also available for uptake by plants[3,70], but the availability, as measured by leaching or by analysis of plants, was markedly dependent on the type of fluoride salt added. The following table presents data from the 5th leaching[3]:

Fluoride added mg/100g soil	F in leach water, mg/l.			
	NaF	KF	$Na_3Al\ F_6$	$K_3Al\ F_6$
10	1.3	0.67	1.1	1.3
20	2.4	1.8	2.9	3.1
60	22.7	9.8	16.0	25.4
120	67.6	22.7	68.4	114.4
180	74.4	44.6	93.2	185.9

The reasons for these differences remain unexplained. The higher availability of cryolite may indicate that more-complex fluoride salts are less readily retained by soil. Recent work on fluoride-containing fertilizers support such a concept. A series of Swiss studies[71,72] has shown that the availability of fertilizer-borne fluoride is enhanced by the presence of borate, and that much of this effect is due to the formation of hydrolyzable fluoroborate complex. Analysis of phosphate fertilizers[15] showed a range of 0.58 to 2.34% F, and it has recently been shown that such fertilizer-borne fluoride can cause marked elevations in the fluoride content of vegetation[15,73].

Little data is available on the amount of fluoride being added to the soil by industrial pollution, but a recent Czechoslovakian report[20] records a level of 7337 Kg/km^2 as compared to a value of 82 Kg/km^2 in a non-industrial area (*Note: 7337 Kg/km^2 corresponds to approx. 65 lb/acre).*

POLLUTION OF WATER:

To introduce this segment, it is appropriate to quote from a chapter of a 1962 text, subtitled "Water Pollution Potential of Air Pollution Control Devices";

> "Disposal of waste products from industrial operations is made by any of four general processes. Waste products are discharged for dilution and transport from their source into (1) the atmosphere, (2) a watercourse... (3) to open waste lagoons or storage areas, or (4) as in the case of high-level, long-lived radioactive fission products, to permanent storage in closed containers... The universal use of watercourses for disposal of wastes inevitably led to conflicts between this and other uses of water. Protection of water quality for higher uses than waste disposal places definite limitations upon the quantities of wastes that can be discharged into watercourses"[42].

The chapter then deals with a U.S. Atomic Energy Commisssion plant producing uranium and thorium metal where the disposal of liquid wastes was hampered by "low flow in the (adjacent) stream", and where "the problems of waste disposal....are many and varied. The biggest single problem is fluorides". Mention is also made of a triple superphosphate fertilizer plant where "the liquid from the scrubber is treated by chemical and physical means to reduce the concentration of fluoride to below 5 ppm

(i.e., 5 mg/1.) before it is discharged... This conforms with the stream pollution requirements of the State"[42]. Typical effluents from metallurgical electroplating operations apparently contain between 5 and 10 mg HF/liter[33].

The effects of waterborne fluoride on the ecology of aquatic life have not been studied extensively. However, it is known that the LC50 for rainbow trout varies inversely with water temperature, i.e., from a low of 2.3 mg/1 at 65°F to a high of 7.5 mg/1 at 45°F[74]; carp can apparently tolerate fluoride concentrations approx. 40 times higher[75]. Toxicity to fish decreases as the hardness of the water (i.e, Ca and Mg) increases[74-75].

It is also known that exposure of aquatic vegetation to 100 mgF/1 for 5 days increases its fluoride content 50-fold, whereas exposure to 20 mgF/1 for 14 days increases the fluoride content 38-fold[76]. However, no information has been found concerning exposure to lower levels of waterborne fluoride for longer times.

Problems have been encountered by an industrial installation producing elemental phosphorus, whereby 22,800 pounds of fluoride per day were discharged into Newfoundland's Long Harbour[38]. In commenting on this situation, it was stated that:

> "Fluosilicic acid did kill fish at the level this substance was believed to be present in the plant effluent, but we cannot experimentally disassociate the pH effect from any possible effect of fluoride .... The pertinent conclusion, for the moment, is that this effluent cannot be permitted..."[38].

The solution to this fluoride-disposal problem was the construction of a "retaining pond"[38].

A further quotation from the Newfoundland report is pertinent:

> "The fact that should be borne in mind is that water contains the air which fish breathe, and this can no more contain chlorine, cyanide or similar substances than can the air which mammals breathe. In the aquatic environment, the analogy is further complicated by the fact that many flora and fauna concentrate the poisonous substances. This may affect the aquatic form directly, or may affect the next organism in the food-chain".[38]

The problem of corrosion has sometimes been mentioned in connection with waterborne fluorides. A recent report[77] has dealt with corrosion of stainless steel; at 180°F, this can occur (in sensitized areas of the metal) with concentrations less than 1 ppm F^- in solution.

In most respects, water quality requirements for industries are consistent with those for public drinking water supplies, and — for fluoride — the U.S. Public Health Service has set "allowable limits" between 0.8 and 1.7 ppm, and "maximum permissible limits" between 1.4 and 2.4 ppm[42]. However, it has also been stated ...

> "There are no universally accepted standards for waste disposal from industrial operations. Each situation requires a special study involving the quantity and type of waste involved... In planning air pollution control where discharge of collected waste to streams is contemplated, the potential impact on downstream water users must be considered."[42]

FLUORIDE IN VEGETATION

UPTAKE, SYMPTOMOLOGY AND TOXICITY:

Much of the research on fluoride has focussed on damage to vegetation, because some species are extremely fluoride-sensitive and extensive damage may entail serious economic loss. However, the specific mechanism by which plant-life is adversely affected by fluorides has yet to be explained. It is known that, in industrially-contaminated regions, the fluoride content of vegetation can increase by a factor of 2 to 260-fold, particularly in leaf tissues[78,79]. In roses, the stems contained 1/10, and blooms 1/20 as much as leaf tissues[80]. In an industrial area of Germany, a high value of 2585 mg fluoride/kg dry wt. was observed in beech leaves and 1503 mg/kg in an unidentified clover[79]. In California, the yield from orange trees was reduced by 15 and 22% when 75 and 150 ppm fluoride had accumulated in the foliage[81]. In this and other species, the reduction in growth and yield was accompanied by a proliferation of weaker offshoots at the expense of the main stem, thus producing dwarfed plants[80] with decreased leaf area and leaf life, and impaired ability to support the fruit load, with consequent premature leaf and fruit drop[81].

The absolute fluoride content is not necessarily a criterion of fluoride damage, because fluoride tolerance varies greatly between species and even between varieties of one species. This is illustrated in Appendix 3, which lists the comparative susceptibility of some plant species, and from which it can be seen that some fluoride-sensitive species are unaffected by SO_2. Appendix 4 gives similar data for trees, and also for gladiolus and roses, showing that different varieties differ markedly in their resistance to fluoride. These data indicate that the fluoride-induced damage is not related to the number of stomata, nor to leaf area, color, or organic composition of the vegetation. In general, however, it can be said that the most susceptible plants accumulate much less fluoride (whether under "normal" or polluted conditions) than do the more resistant types. This can be illustrated by the fact that gladiolus may become necrotic when they have accumulated 20 ppm or foliar fluoride (dry weight basis), whereas cotton plants appear healthy even after accumulating 4,000 ppm[6]. The same trend is usually seen among varieties of one species[85].

Three factors have been implicated to explain the difference in fluoride-sensitivity[6].

1) The location of the fluoride i.e., surface or interior;
2) The degree of interchange between the interior and exterior of a leaf;
3) The translocation of fluoride to leaf tips and margins. Apparently, the fluoride-sensitive plants absorb and transport fluoride at a relatively greater rate then do the more resistant types, and can concentrate it in those peripheral areas where damage is first seen. (*Note: It is possible that fluoride-induced injury occurs when a plant possesses the ability to translocate fluoride quickly to localized sites, where it accumulates faster than it can be excreted (i.e. exhalation) and/or faster than plant's particular "defense mechanism" can counter interference with vital intracellular processes).*

The fluoride-induced damage observed in plants is of two types: Chlorosis and necrosis. Chlorosis appears at much lower exposure-dosages than necrosis, and can take the form of chlorotic flecks at the tips and upper margins of the leaf[85]. More extensive bleaching (progressing from yellow to brown) of the chlorophyll begins in the same area and extends downward from the tip, especially along the margin of

older leaves. As the dosage of fluorides increases, the chlorotic band along the margin broadens and lengthens with the intensity of chlorosis remaining greatest at the tip. With sustained or increased exposure to fluoride, wilting, marginal tissue collapse, changes in color, loss or older leaves, and reduced yields are seen as the damged areas tend to become necrotic[12,86,87]. The symptoms are severe tip, marginal, and intercostal necrosis, as well as cupping and other distortions.

The positional location and appearance of the chlorosis caused by fluoride distinguishes it from chlorosis caused by some other factors, including sulfur dioxide[82], and this is also true of necrotic symptoms[88]. However, deficiencies of calcium, magnesium, potassium or water can produce symptoms similar to fluorotic damage and also cause the plant to be more susceptible to fluoride-induced damage[12,89].

Studies with the very sensitive gladiolus species have shown that continuous exposure to levels of airborne volatile HF below 0.5 ppb (or even below 0.1 ppb[12]) are sufficient to induce tip burn, whereas higher levels (1 to 3 ppb) induce necrosis[90]. Overall results indicate that airborne H_2SiF_6 is more active than HF in inducing damage[85]. Although NaF sprays also induce F damage[81], they do not seem to have as severe an effect as does sustained exposure to gaseous fluoride[91]. Most of the intake from air is believed to involve gaseous fluoride by means of gas-exchange through the stomata, after which the fluoride can eventually penetrate into the cytoplasm[6].

The study of fluoride-induced damage in plants is complicated by the fact that the plant can take up fluoride from the air and also through the root system. Plants can increase their fluoride content 20-fold through uptake from the root system after additions of a solution of sodium fluoride or of particulate cryolite dust to the soil surface[85]. Fluoride uptake can also occur from the use of fluoride-containing fertilizers[15,71-3].

Only about 40% of the fluoride associated with plant leaves appears to be present on the surface[6] and can be removed by washing with dilute acid, Alconox or EDTA[6,87]. Some of this surface fluoride appears to move from the interior of the leaf, and surface fluoride can be present even on leaves of plants that have received fluoride exclusively from the soil.

Fluoride migrates to the tips of narrow leaves, and to the leaf margins of broad-leaved species, where it accumulates[6,82]. This pattern of distribution coincides with the areas where extensive chlorosis (and/or necrosis) is first seen. It is felt that injury not only depends on the amount of fluoride absorbed by the plant but also on the rate of translocation and accumulation at a particular location[6]. Studies of the effects of intermittent fumigations have revealed that post-fumigation fluoride loss can occur from leaves[90,92].

It has been demonstrated[58] that fluoride-sensitive indicator plants can serve as a useful index of possible crop damage arising from air pollution.

MODE OF ACTION:

Most investigations on the possible mode of action of fluoride in plants have assumed that there is interference either with one of the major physiological functions (e.g., photosynthesis or respiration), or with a metabolic pathway (glycolysis or the pentose-phosphate cycle[6,92]). Growth-promoting hormones such as β-indoleacetic acid

promote uptake of fluoride[53]. Cytogenetic studies[93] have shown that HF fumigation is capable of inducing paracentric inversions, with the possibility of obtaining abnormal phenotypes in the progeny of treated plants. Cytogenetic deficiencies, duplications, and translocations are thought to be due to fluoride inhibition of enzymatic systems responsible for DNA replication. It has also been shown[94] that fluoride induces changes in RNA structure, characterized by a lowered relative content of cytosine and an increased guanine to cytosine ratio and it has recently been shown that fluoride stimulates RNA-ase activity[95]. Since such processes take place within the cytoplasm, it appears likely that only intracellular fluoride can induce a toxic effect. Histological examinations of the effects of fluoride on conifer needles have established that phloem cells are the first to be injured, and parenchyma cells are most sensitive[12]; moreover, the active phloem cells die prior to older ones, and hypertrophy occurs throughout the parenchyma and in epithelial cells, causing occlusion of the resin canals; however, mesophyll cells beneath the stomata do not collapse (as in SO_2 fumigation)[15]. These observations help to distinguish fluoride-induced necrosis from that caused by SO_2 and other agents[12,15].

Fluoride inhibits a number of enzymes that are active in plant metabolism, including phytase[96], acid phosphatase and ATP-ase[92], succinic dehydrogenase and enolase[92,97] and phosphoglucomutase[94,97]. However, with the singular exception of succinic dehydrogenase[97], no relation between these enzyme inhibitions and fluoride induced injury to plants has yet been established. Several observations indicate that exposure to airborne or waterborne inorganic fluoride can result in interference with normal Krebs cycle function in vegetation. Constant 18-month exposure of trees to fluoride-bearing solution-cultures resulted in large increases in the citrus acid content of oranges, with concomitant loss of weight, taste, and yield[98]. An increased citrate and malate content in tomato and bean leaves has also been observed after a 72-hour fumigation with HF (12.4 ppb), although the citrate level fell markedly during the subsequent fumigation period[92]. Also, an increase in total organic acids has been observed in leaves with fluoride-induced chlorosis and necrosis, with malic acid increasing more markedly than citric acid[99]; this was accompanied by a decrease in sucrose concentration, but an increase in reducing sugars and total amino acids, notably asparagine.

ORGANIC FLUORIDES:

It has been known for over 25 years that a plant indigenous to Africa, *Dichapetalum cymosum*, accumulates fluoroacetate[9,82,92]; and more recently, other plant species growing in Africa, Brazil, and Australia have been shown to accumulate this compound[9]. Fluoroacetate is apparently non-toxic to these plants, and it has been suggested that some plants can utilize it by cleaving the carbon-fluoride bond with consequent evolution of CO_2[9]. However, mammals can convert fluoroacetate to fluorocitrate[92], which is a potent inhibitor of aconitase[100,101] and can thus lead to the accumulation of citrate.

In 1968, it was observed that both fluoroacetate and fluorocitrate accumulated in soybean fumigated with HF[102], and in forage crops collected near a phosphate fertilizer plant, an area high in atmospheric fluoride[103]. The identification was made by paper chromatography and infrared spectrum analysis. It was also found that the organic fluoride extracted from soybean was 550 times more toxic than inorganic fluoride, on the basis of aconitase inhibition[102]. In follow-up studies[104], fluoroacetate and fluorocit-

rate were identified (by gas chromatography) in wheatgrass grown near a phosphate fertilizer factory, but were not detected in greenhouse-cultivated wheatgrass grown in the absence of significant fluoride. Yet another study[105] has shown that lettuce possesses the ability to convert fluoroacetate to fluorocitrate, a process that was accompanied by an 87% increase in citrate content.

Thus, it appears that some forms of edible vegetation have the capacity to produce fluoroacetate and fluorocitrate, and that this capacity may be stimulated by exposure to environmental levels of inorganic fluoride. How *many* species of edible vegetation possess this ability, and *what* environmental conditions trigger such accumulations, are questions that have yet to be answered. Furthermore, the toxicological significance of these findings awaits thorough investigation. Fluorocitrate (and fluoroacetate by *in vivo* conversion to fluorocitrate) is known to be extremely toxic to mammals, and it appears probable that the presence of such organofluorides will markedly alter the pattern of "toxicity-symptomology" accruing from ingestion of fluoride-polluted forage plants and of edible vegetation consumed by humans.

MAXIMUM PERMISSIBLE LIMITS FOR FLUORIDE IN VEGETATION:

Studies with dairy cattle have indicated that the maximum permissible level for ingested fluoride should be between 30 and 50 ppm on a "total dry feed" basis[1,106]. Such estimates include the presence of particulate fluorides which, although they may not contribute to crop damage, become metabolically available upon ingestion[106,107].

The Texas limit in forage is 40 ppm F, "averaged over 12 consecutive months"[65]. Montana[15,65] and Alberta[64] have set limits of 35 ppm F in forage. Bovay[53] has reported that the State of California has set a maximum level of 35 ppm in the tips of (dried) gladiolus leaves; this would appear to be excessive, because gladiolus leaves tend to accumulate less fluoride than leaves of many other species[86] and can become necrotic when they have accumulated 20 ppm F (dry weight basis)[6].

A recent report[108] has emphasized the fact that analysis of fluoride in vegetation is difficult, and that both inter- and intra-laboratory results can show wide variations. For this reason (and until such time as the situation, hopefully, improves), it would seem desirable to rely on definite trends based on data from several sources, rather than on a single value reported from a particular laboratory.

As for organic fluorides, no data are available concerning the limits of fluorocitrate in vegetation; presumably, such a limit would be next to "nil" in vegetation destined for ingestion.

THE EFFECTS OF FLUORIDE ON ANIMALS.

SOURCES:

Livestock and wildlife can be exposed to toxic amounts of fluoride even under natural conditions[1]. However, this almost invariably occurs through consumption of naturally fluoridated water. Thus, for sheep raised in endemic areas, the daily fluoride intake can be estimated by the equation (see data given on P. 316 of Ref. 1):

$$\text{mg F per day} = 2.4\,(\text{ppm F in water}) + 2.0$$

It has been reported that, in these endemic areas, waterborne fluoride is 40 times more toxic to sheep than fluoride ingested as fluoroapatite, and 2 to 5 times more toxic than normal dietary fluoride[1].

Industrially-contaminated areas present a quite different situation. In these ...

> "... animals develop symptoms of poisoning after feeding on the exposed vegetation. Fluorides represent a special hazard to animals because vegetation exposed to prolonged atmospheric concentrations of only a few parts per thousand million parts of air by volume (i.e., ppb), or lower, may accumulate sufficiently toxic amounts to cause fluorosis in animals ingesting this forage".[23]

And, at a recent European Symposium, it was stated:

> "The most important problem concerning damage to animals by air pollution is, no doubt, the poisoning of domestic animals caused by fluorine in smoke, gas, or dust from various industries."[51]

However, as will be seen in subsequent sections, the use of fluoride-containing mineral supplements and insecticides can also contribute to ill-effects in animals.

UPTAKE:

A recent German study has shown that, in an industrially-contaminated area, forage supplied more than 90% of the fluoride ingested by fluorotic cattle[(Fig.3, Ref. 109)].

The intake of fluoride from air is relatively slight, while that from mineral supplements and water also tends to be low, unless the animals have access to highly-fluoridated forms of these. Grazing on pastures located near a fluoride-emitting factory can result in a 50 to 100-fold increase over normally-ingested fluoride (i.e., 0.16 mg/kg), while barn-feeding in the same contaminated area causes an increment of 5 to 10-fold[109].

The toxicity of fluoride depends on the type of fluoride ingested and how much of it is absorbed into the bloodstream. In steers, inorganic fluoride is more available from commercial 'soft phosphate' than from NaF or CaF_2, in the approximate ratio 3:2:1, respectively[110]. Whereas phosphate enhances fluoride absorption from the digestive tract, physiological concentrations of calcium and magnesium reduce absorptivity[111], presumably by formation of insoluble fluoride compounds in the digestive tract. Fluoride availability is lowest when ingested as insoluble compounds such as fluoroapatite[106].

Once absorbed into the bloodstream, inorganic fluoride has two main pathways, i.e., excretion in urine, and deposition in bone[1]. In all animal species studied, fluoride ingestion can cause urinary fluoride levels to rise quickly to 3 to 4 times the normal level, and it is possible to subsequently attain an upper limit of 70 to 80 ppm (in

cattle)[1]. Although urinary fluoride can be used as an index of fluoride exposure, the interpretation of results can be made difficult by certain forms of renal disease, ingestion of chelating agents (which accelerate removal of bone fluoride), and previous fluoride intake.

Among body tissues, inorganic fluoride is primarily incorporated into the mineral constituent of bone by means of a F for OH substitution in the apatitic calcium phosphate. This occurs rapidly, at first, but then proceeds more slowly in species where bone undergoes cortical remodelling[14]. The most rapid uptake of fluoride occurs at the bone surfaces, particularly in extensively vascularized cancellous type of bone[14,112]. With time, the process of bone remodelling results in more extensive incorporation of fluoride in the sub-surface regions of bone, although this is a much slower process than the initial surface-exchange[14]. Thus, fluoride levels can vary in different bones and in parts of the same bone[113], depending on factors such as dosage, type of diet, time, type of bone, and the metabolic status of an individual subject[4,14,112].

In adult animals not unduly exposed to fluoride, the fluoride concentrations in whole bones rarely exceed 1,000 ppm (dry, fat-free basis)[14]. No abnormalities are detected in bones containing up to 2,500 ppm fluoride (See Appendix 5), but microscopic alterations are seen with higher levels up to 5,000 ppm. Gross roentgenographic abnormalities are demonstrable at bone fluoride levels above 5,000 ppm, and become very pronounced at levels above 8,000 ppm. The 'saturation point' of fluoride in bone has been reported to be 15,000 to 20,000 ppm; the higher of these values is probably the more correct. In contrast, most soft tissues rarely contain more than 5 ppm fluoride, although kidney can accumulate 20 ppm or more[4].

The gradual incorporation of fluoride into bone, and the attendant conversion of hydroxyapatite to fluoroapatite, produces a bone mineral of reduced solubility and reactivity[4]. In a recent review[112], evidence has been presented to show that this overstimulates the parathyroid gland, which compensates by producing more of the hormone responsible for bone resorption. It has also been shown that fluoride can stimulate over-production of uncalcified osteoid that, in the absence of sufficient calcium, can remain uncalcifiable[114]. An entire spectrum of bone abnormalities can be induced by fluoride accumulation (See Appendix 5). In this connection, Johnson[14] has stated:

> "the increased osteoclastic and osteoblastic activity were not the direct result of the fluoride, but were secondary to the changes in the biological properties of the normal bone, following its excessive fluoridation... The rapidity with which these changes appeared determined whether precocious remodelling, porosis, sclerosis, hyperostosis, or osteomalacia was the predominant manifestation at any stage.... Very high levels of fluoride resulted in severe osteomalacia".

EFFECTS:

In cattle, the clinical signs of skeletal fluorosis can take time to appear[115], and are usually first seen as lameness or stiffness which can develop in one leg after another, and is thought to be caused by calcification of tendons and the periarticular structures[28]. In more acute stages, fluorosis can involve spontaneous fracture of the pedal bone, metatarsal, 3rd phalanx, and/or ribs, which eventually immobilizes the animal[28,109]. Fluoride can also induce dental disfigurement[105], and if this is severe, it can result in teeth which crumble and wear excessively, until the associated pain makes it

difficult for the animal to maintain an adequate food intake (see p.197 of Ref. 45). In afflicted animals, body weight decreases to the point of cachexia. Milk production is sometimes decreased in cattle, and so is wool production in sheep[1]; also, mortality of the newborn is due to the impoverished condition of the mother rather than to a failure of the reproductive process itself. The clinical signs of fluorosis apparently differ little between livestock species, although cattle and sheep seem to be more susceptible than swine and horses, while poultry appears least easily affected[1,106].

As indicated previously, not only contaminated vegetation but fluoride-containing mineral supplements and fluoridated water have also been responsible for the appearance of the fluorosis syndrome. A recent Swedish study[116] has investigated fluorosis in cattle in a non-industrial region, in which the drinking-water contained 0.9 to 4.0 ppm fluoride and where a mineral supplement was used which contained a top level of 1,000 ppm of fluoride. Stiff movements, emaciation, dental changes, and infertility were seen, but no disturbance in milk production. The bones contained a relatively low level of only 2,000 to 2,900 ppm of fluoride, and the skeletal lesion was osteoporosis, agreeing with Johnson's classification[14] in which osteoporosis is the earliest bone abnormality induced by fluoride. Kidney lesions were also observed[116], with atrophy of the tubules and fibrosis.

Laboratory animals can also develop fluorosis, and dietary pellets containing 130 to 400 ppm fluoride have been responsible for guinea-pig fatalities[117]. A quotation from one of the reports reveals the attitude that is needed when confronted with such "idiopathic" situations:

> "A diagnosis of chronic fluorine intoxication can be achieved only when the complexity of the disease is realized and the pathogenesis, symptomology and lesions are properly correlated, interpreted, and evaluated."[117]

The chronology of symptoms were loss of weight, reduced food intake, reduced mobility, excess salivation, polydipsia, apparent difficulty in swallowing, leading to dyspnea, convulsions, coma, and eventual death. Dental changes included abnormal overgrowth combined with excessive wearing down of overly soft teeth with malocclusion and enamel hypoplasia[117]. The dental pattern resembled that seen in High P-Low Ca rickets and in hypovitaminosis C. Other findings included an increased number of stillborn young, anemia, and kidney tubule dilatation with cortical interstitial fibrosis. Bone ash contained 3,940 – 6,700 ppm fluoride (i.e., 40 times greater than normal), and the bones were brittle and showed increased resorption but no other macroscopic change. Vitamin C had a beneficial effect, and the syndrome was considered to be "a borderline chronic fluorosis accompanied by the dependent changes of subacute hypovitaminosis-C". It was also suggested that "the guinea-pig might be expected to be particularly susceptible to low-level fluoride intoxication by virture of ... the inability of this animal to synthesize Vitamin C"[117]. Similarities between fluorosis and scurvy have been reported by several other investigators[cf 118].

Anemia, impairment of blood sugar regulation, and other blood derangements have been reported in rabbits exposed to low levels of waterborne fluoride[119]. Whereas lower dosages up to 0.05 mg/kg per day had no discernible effect, a level of 0.066 mg/kg significantly reduced the hemoglobin, erythrocyte, reticulocyte, and sugar concentrations by 14 to 38%. Higher dosages of 0.10 to 0.80 mg/kg per day induced regeneratory anemia, hypoglycemia, interfered with prompt regulation of blood sugar, and

caused a reduction in weight-gain. Thus, fluoride can induce various metabolic changes without extensive skeletal involvement. Some of these effects may be species-related.

Unfortunately, information relating to fluoride effects on wildlife is extremely sparse. Bees are known to be extremely sensitive to fluoride and the complete extinction of bee colonies has been reported in studies of fluoride-polluted regions[20,45]. Also, rodents can accumulate extremely high levels of fluoride in their bones, from ingestion of fluoride-containing dust which coats vegetation in some fluoride-polluted localities[107].

It must be pointed out that the preponderance of studies on fluoride toxicity has been concerned with inorganic fluoride. Two reviews on fluoroacetate pharmacology[100,101] have dealt exclusively with lethal toxicity, and indicate that the main effects are on the nervous system (i.e., nausea, hallucinogenic behavior, twitching of facial and other muscles, epileptiform convulsions, progressive weakness, respiratory impairment, then ventricular fibrillation and death). It appears that plants can accumulate levels of organic fluorides that might be toxic to animals. It is also known that fluoroacetamide is widely used as an insecticide, and that it can be converted to highly-toxic fluorocitrate by animals[120]. Field studies[102-104] have recently shown that animals grazing on fluoride-polluted pastures had higher blood citrate levels than found in controls.

THE EFFECTS OF FLUORIDE ON MAN

SOURCES AND DOSES:

For the past several decades, man has been exposed to an increasing distribution of fluoride in his environment (See Appendix 6). As industrialization becomes even more widespread, the distribution of fluoride will no doubt become more extensive. This should be of most concern in heavily-industrialized areas, but the total fluoride intake of residents in non-industrial areas has also been increasing because:

1) Many metropolitan centres have a fluoridated water supply;
2) Metropolitan populations have access to foods grown in fluoride-polluted areas and foods and beverages processed or prepared with fluoridated water, or seafood concentrates rich in fluoride.
3) Man is exposed to fluoride-containing aerosols, pharmaceuticals, and/or cosmetics.
4) There is a possibility that high-octane gasolines manufactured by HF catalysis may contain sufficient fluoride to contribute to pollution in centres where the automobile population is high, and where busy airports are nearby.

As said earlier in this report, most common foods contain only 0.1 – 0.3 ppm of fluoride[8]. However, it has been shown[121] that the use of fluoridated water (1.0 ppm F) in the processing of foods and beverages will increase their fluoride content to 0.4 – 1.0 ppm, with an average 3½-fold increase. It was estimated[121] that adults residing in a fluoridated community would ingest between 2 and 5 mg (or more) fluoride per day from foods and beverages, and this estimate was subsequently corroborated when another laboratory reported a range of 3.57 to 5.37 mg per day (Table 1 of Ref. 122). Nevertheless, studies designed to monitor the *total amount* of fluoride ingested by humans are almost non-existent; instead, it has become the practice to merely measure the concentration of fluoride in the water-supply, even though this provides no information about the *total* daily intake of fluoride. The only comprehensive study found in the scientific literature is that of Krepkogorsky[22], who studied North Vietnamese populations and estimated that the maximum total fluoride intake by adults should not exceed 3.2 mg per day. It has been reported that the traditional diet of Newfoundland adults contributes 2.74 mg of fluoride per day in areas where the drinking-water is fluoride-free[21]. But, generally, the North American situation is impossible to assess, because of the lack of information pertaining to the fluoride content of foodstuffs supplied by today's large-scale food distributors. Data on individual variation in adult consumption of fluoridated water (and beverages) is also scanty. One small-scale survey[121] has found that some indoor workers (not doing heavy manual labor) will consume only one liter of fluoridated beverages per day, while some of their similarly-employed colleagues regularly consume as much as three liters. It was also pointed out that

> "Laborers exposed to outdoor summer conditions would undoubtedly ingest still more as would individuals subject to chronic polydipsia".[121]

One balance study[123] of ten people with total fluoride intakes ranging from 3.5 to 22.3 mg fluoride per day indicated net retention of -0.8 to +8.6 mg per day. However, the exact significance of the observed fluoride balances is difficult to assess, because it was stated that

> "There is no doubt that these subjects...(whose) intake of fluoride...had been high for long periods of time, had accumulated 'abnormal' quantities of fluoride in their tissues".[123]

Thus, the observed balances could have been influenced by the extent and duration of prior exposure to fluoride and the resulting degree of skeletal saturation. Uptake of fluoride by the skeleton tends to proceed more slowly as saturation is approached[1,14], and this would result in greater excretion of fluoride, provided that kidney function is unimpaired.

In a more recent[122] balance-study of fully ambulatory hospital patients with no previous history of high fluoride exposure, the fluoride retention appeared to be a linear function of total fluoride intake (which varied between 4 and 14 mg), i.e.,

mg F retained = 0.396 x (mg F ingested)

In humans, this remains true whether fluoride is ingested as a component of Fish Protein Concentrate or as sodium fluoride[122,124]

As for other sources of dietary fluoride, it has been reported[73] that the escalating use of fluoride-containing fertilizers has increased the fluoride intake from Japanese foods from 4.38 mg per day in 1958 to 11.13 mg per day in 1965.

ANALYSIS AND DIAGNOSIS

Methods for the determination of total fluoride in biological tissues involve preliminary defatting and ashing of the material, after which the fluoride is isolated (by steam-distillation or diffusion) then estimated colorimetrically[121,125-130]. These various steps are necessary to avoid sources of interference, but are time consuming and have probably mitigated against the use of fluoride analyses in diagnostic studies. In this regard, it is also important to remember that, just as different portions of plants[72], or even of individual leaves[79] vary in fluoride content, so do different parts of an individual skeletal system. Appendix 7 shows that the more extensively-vascularized and reactive cancellous (i.e., spongiosa) type of bone can accumulate 2 to 10 times more fluoride than can cortical bone. Because of its reactivity, cancellous bone is probably the most sensitive "skeletal barometer" for use in monitoring fluoride uptake, especially considering that (in humans) iliac crest biopsies are relatively simple to perform.

Analysis of urine may provide information relevant to current fluoride exposure, although the result can be influenced by prior exposure[127], chemotherapy[131], or state of kidney function[132]. Moreover, urine fluoride levels provide no information whatsoever concerning accumulation of fluoride in body tissues, with the possible exception of blood[133].

Taves has recently shown[134] that there are two forms of fluoride in human blood serum; i.e., of the total 0.14 ppm (4.6 μ M), normally found, only 0.02 ppm (0.7 μ M) is present as free fluoride ion, while the remainder is protein-bound. Taves has developed a diffusion procedure and micro-colorimetric method to enable direct estimation of the low concentration of ionic fluoride in serum[128,135]. Serum ionic fluoride levels are a very sensitive index of fluoride accumulation in humans[132], and have been termed "a rational method of assessing fluoride effects"[136]. Not much is yet known about the "protein-bound" fluoride which normally accounts for about 85% of the total fluoride in human serum; however, it has been suggested that this bound

fluoride consists of covalently-bonded organic fluoride[137]. (*NOTE: Information on analysis of organic fluorides can be found in references 101, 103, and 138*).

The degree of dental fluorosis (mottling) has been used as an index of fluoride exposure in humans, but it is important to note that dental mottling only occurs if fluoride is ingested during the period of tooth formation, i.e., pre-eruption. Dental mottling thus provides no indication whatsoever of fluoride exposure that commenced after eruption of the permanent dentition.

TOXIC EFFECTS:

Because of the difficulty of the analysis (as far as is known, no Canadian hospital or medical laboratory routinely conducts diagnostic fluoride analyses), and considering the variability of the effects of chronic low-dose fluoride ingestion, it is difficult to document the effects of fluoride on man in Canada. Undesirable side-effects (i.e. dermatological, gastro-intestinal, and neurological symptoms) were seen in one percent of a group of children and pregnant women ingesting 1.0 – 1.2 mg. fluoride per day in tablet-form[139]. The same symptoms have since been observed in people who had adverse reactions after using fluoride-containing toothpaste[140]. (*Note: studies with rats have shown that fluoride is well absorbed and retained from either fluoride-containing dentifrice*[141] *or multiple-vitamin preparations*[142]). A Czechoslovakian survey[20] of children residing in an industrially-polluted region found a decreased hemoglobin and increased erythrocyte level associated with a 2 to 3-fold elevation in the fluoride content of teeth, fingernails, hair, and urine. The children's daily intake of fluoride was estimated to be 2.15 mg. per day, of which 1.40 mg. was obtained from food, 0.55 mg. from air, and 0.20 mg. from deep-well drinking water[20]. In another survey of children inhabiting an industrially-polluted area[143], dental fluorosis was most severe in those with Vitamin C deficiency, as was a tendency to hemorrhage with signs of vascular fragility. A survey[144] of workers exposed to fluoride in an aluminum factory revealed a 21 to 35% increase in total cholesterol, as compared to non-exposed control subjects; the increase was 52 to 56% when expressed on the basis of protein-bound cholesterol. Thus, there is evidence to indicate that intake of fluoride can induce metabolic changes of a non-skeletal nature in man as well as in animals.

With regard to fluoride-induced bone changes[1,106], it must not be forgotten that an entire spectrum of abnormalities can be seen, the most severe being osteomalacia[14,55]. The variable spectrum of skeletal abnormalities has been observed in chronic alcoholics who ingested wines containing between 8 and 73 ppm of fluoride (added as an antiferment)[145]. In these rare cases, alcohol was felt to be a predisposing factor, with the attendant status of malnutrition probably contributing to the severity of the fluorosis[146]. It has been established[147] that some individuals habitually ingest more than 6 liters of beer per day for more than 20 years. Analysis of beer processed with fluoridated water has shown[121] that it contains 0.7 ppm F. Thus, it is possible to ingest 4 mg. of fluoride per day from beer *alone*, in addition to dietary (and other) sources ... and to sustain this for 20 years or more.

Local factors can influence the extent of fluorosis. It has recently been found that, in India, less skeletal fluorosis occurs in villages where the drinking-water contains more calcium and magnesium[148], probably because these ions constitute a protective mechanism not available in extremely soft waters[4]. It has long been known that calcium supplements protect against fluorosis[50], and this is borne out by current observations[149].

Such an interrelation of factors must be borne in mind when considering the human being.

Johnson has described fluoride-induced bone abnormalties[14], which range all the way from osteoporosis, to osteosclerosis, hyperostosis, osteophytosis, and the most severe fluorotic manifestation, osteomalacia (See Appendix 5). Although osteosclerosis has been more commonly observed[1,131,148,150], osteomalacia results when high-fluoride therapy is used with inadequate concomitant calcium supplementation[149], and also occurs in people on long-term hemodialysis with fluoridated water[151]. In the latter study, it was shown that the absence of kidney function in the patients caused abnormally-high retention of fluoride in serum and bone. Studies have been done on humans ingesting between 4 and 14 mg. fluoride per day, and have shown that about 90% of the ingested dose is absorbed[122,152]. However, whereas individuals with normal kidney function can excrete from 54 to 61% of the ingested fluoride *via* urine (Table 2 of Ref. 122), those with kidney dysfunction can excrete only 17 to 22% (Table 17, Ref. 152). Thus, persons with impaired kidney function had only 1/3 the ability to void absorbed fluoride. It is therefore not surprising to find that another report arrived at this conclusion:

> "The highest (bone) fluoride levels were observed in older adults showing the end-stage kidney of bilateral pyelonephritis and (or) polycystic disease".[153]

Such findings again emphasize the vital importance of the kidney as a means of excreting absorbed fluoride. However, epidemiological surveys of populations ingesting naturally-fluoridated water have not included such subjects, e.g.,

> "Those with chronic illness and diseases known to affect bone structure were excluded. Thus, there were none with primary or metastatic bone cancer, long-standing cancer of other organs, or renal or parathyroid disease."[154]

Faccini has recently stressed that ...

> "... any stabilizing effect fluoride may have on the skeleton will eventually be counterbalanced by a compensatory increase in parathyroid function".[112]

Thus, not only kidney function, but also parathyroid gland function, is seen to be a crucial factor in a human being's ability to tolerate a lifetime of exposure to fluoride. An adequate dietary supply of calcium and magnesium is also indicated, and animal experiments have revealed the importance of Vitamin C. It is important to remember that fluoride can induce many types of derangements, and that these are not necessarily skeletal.

In 1933, De Eds had concluded that:

> "Further scientific investigation on the physiological effects of fluorine, especially under conditions of continued administration or intake, is desirable".[50]

Early in 1969, these words by Faccini appeared:

> "In the last 35 years, over 16,000 papers have been published on the biological effects of fluoride ... the majority of the investigations have concentrated on demonstrating the innocuous nature of low levels of fluoride; while such work is essential before adopting aritificial fluoridation of water-supplies, it has furnished little positive information on the action of fluoride. At the other extreme, many investigators have followed the effects of very toxic doses of fluorides".[112]

In between the extremes described by Faccini, there has been very little done, especially in the realm of "borderline" or sub-clinical toxicity. And yet, it is precisely in this area that knowledge of most importance to Man could be brought to light. To this day, many investigators still think of fluorosis exclusively in terms of osteosclerosis, whether crippling[148] or non-crippling[131]. This attitude is no longer valid because osteosclerosis is only one of many skeletal abnormalities that can be induced by fluoride[14,55,145]. Other symptoms include anemia and other blood derangements, as well as skin, eye, gastro-intestinal, and neurological symptoms[20,50,55,139,140,143].

ORGANOFLUORIDES:

There are several possible sources from which humans can be exposed to significant intakes of highly-toxic organic fluorides. For instance, ingestion of fluorocitrate and fluoroacetate synthesized by food plants exposed to fluoric air-pollution can be expected to induce chronic toxicity symptoms quite different from those associated with inorganic fluoride[100,101]. Fluorocitrate poisoning involving alterations in Krebs Cycle metabolites, blood sugar irregularities, convulsive seizures, and respiratory failure, can also result from ingestion of vegetation contaminated by fluoroacetamide insecticides[120].

Fluoroalkane gas propellants (e.g. Freon) used in aerosol dispensers for cosmetic or household purposes can induce fatal bradyarrhythmias, especially in asthmatics[155]. High-heat pyrolysis of polytetrafluoroethylene (i.e., Teflon) plastic liberates carbonyl fluoride whose toxic effects are partly attributable to metabolically-induced release of inorganic fluoride and concomitant inhibition of succinic dehydrogenase[156]. Fumes produced by heating Teflon cooking-pans to temperatures slightly over 500°C have caused death in small pet birds within 20 to 30 minutes[157]. Post-mortem examination of the birds revealed symptoms of acute lung oedema, heart muscle degeneration, and liver dystrophy; in contrast, small mammals were unaffected by the same experimental conditions[157].

Fluoride-containing drugs can also cause adverse reactions in man. The appetite-depressant, fenfluramine, has induced some unusual side-effects of the psycho-mimetic type[158]. In man, fenfluramine has been shown to be rapidly absorbed into the tissues, then slowly released, with 66 to 93% of its urinary metabolites excreted as m-trifluoromethylhippuric acid[159]. Animal studies have shown that the toxicity of fenfluramine is greatly increased by simultaneous intake of amphetamine[160].

Fluorinated anesthetics have been another source of concern. Fatalities have occurred in humans after anesthesia with methoxyflurane, a metabolically unstable compound that can result in extremely high levels of inorganic (plus at least 2 forms of organic) fluoride in blood and urine[161]. Obese patients may be most susceptibe to methoxyflurane toxicity, apparently because of the extremely high solubility of methoxyflurane in fatty tissues[162], from which it is gradually released as metabolites[161]. Aside from inorganic fluoride, 2 organofluoride metabolites of methoxyflurane have been identified in man, i.e. dichloroacetic acid and methoxyfluoroacetic acid[163]. The symptoms of methoxyflurane toxicity include fever, chills, and jaundice with hepatocellular necrosis and fatty change, and "... are similar to those described in association with halothane"[162]. However, the main metabolite following halothane anesthesia in man appears to be trifluoroacetic acid, with very little conversion to inorganic fluoride[164]; but, in small mammals, trifluoroethanol has also been identified as a break-

down product of halothane, and has been shown to be over 10 times more toxic than trifluoroacetic acid[165]. Animal studies with yet another metabolically-unstable anesthetic, fluroxene, have shown that trifluoroethanol glucoronide is the major metabolite, while trifluoroacetic acid was identified as a minor breakdown product[166]. These observations confirm the suggestion that "... different mechanisms exist for the biotransformation of halothane and that of fluroxene in man"[167], and extend it to include methoxyflurane. More knowledge about the toxicity of the various breakdown-products is urgently needed, along with consideration of possible synergistic effects. Meanwhile, extracorporeal hemodialysis has served as a means of partial detoxification[168], and peritoneal lavage might be useful in cases where hemodialysis facilities are not available.

CONCLUSIONS:

Modern-day man is probably exposed to more environmental fluoride than was heretofore suspected, and consideration must be given to the total ingestion from various sources as well as the types of fluoride present in air, foods, beverages, and other commodities. An effort should also be made to study the symptomology of chronic fluorine intoxication, especially the early non-skeletal manifestations of arthritic-like symptoms that may be complicated by metabolic and/or nutritional inadequacies. Finally, it must be emphasized again that dental fluorosis (i.e. mottling) will *only* be seen in subjects who have been exposed to fluoride during the time when the enamel of the permanent teeth is being formed, and its absence cannot be assumed to indicate freedom from other fluoride-induced effects including effects of organofluorides and their metabolites.

In Appendix 6, a flow-sheet is presented to illustrate the contemporary "fluoride sequence" as it affects the present-day ecology and, in particular, man.

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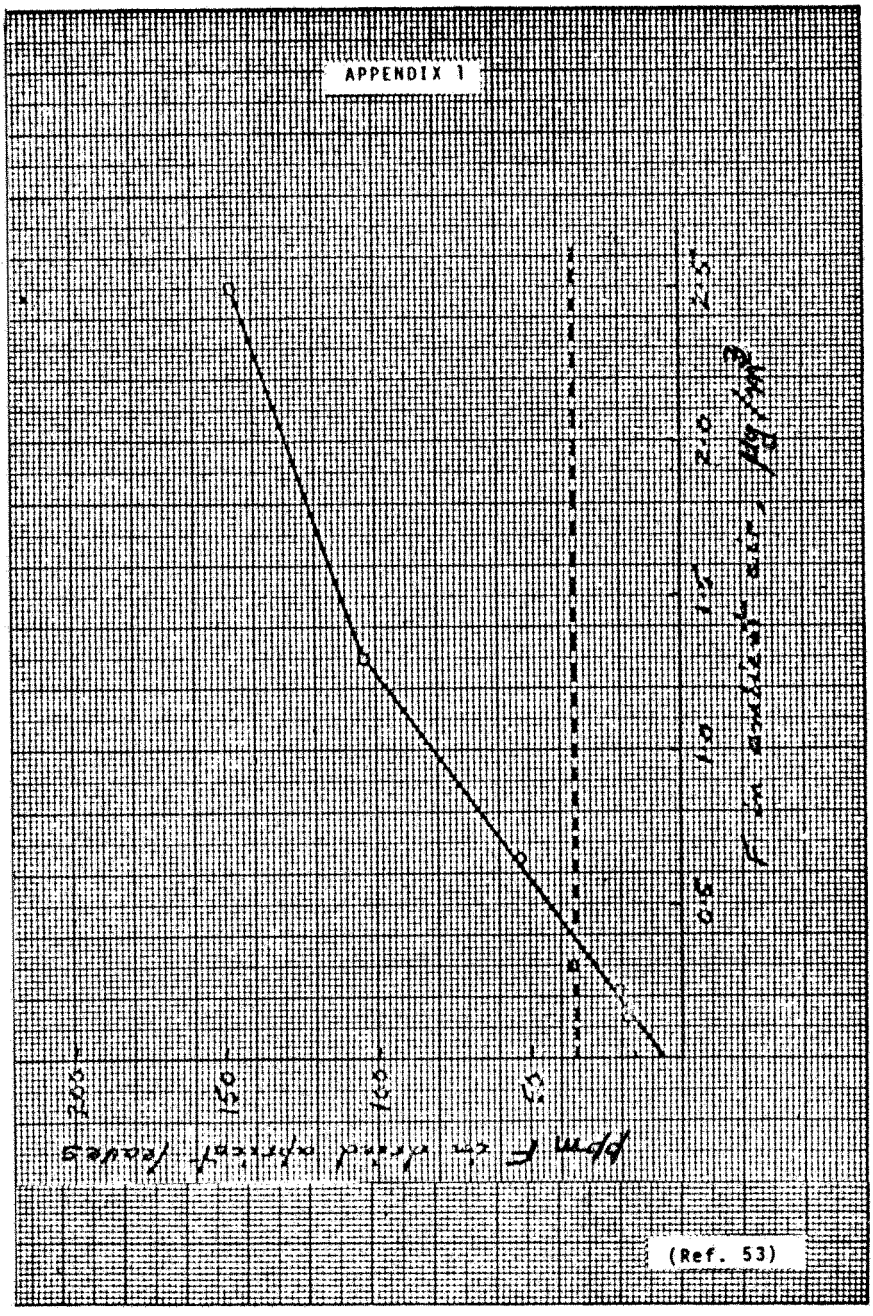

APPENDIX 1
(Ref. 53)

APPENDIX 2

RESULTS OF CONVERSION OF DATA OBTAINED WITH LIMED-PAPER MONITORING, TO YIELD AN ESTIMATE OF THE AIRBORNE F CONCENTRATION.

Author	Year	Estimated Average Airborne Gaseous F $\mu g/m^3$	Damage to vegetation during the growing season
i)			
Adams et al.[62]	1956	1.77 (July-Aug.)	33% of surface of gladiolus leaves.
"	"	" "	67% of surface of Ponderosa Pine Needles
"	"	0.58 "	26% of surface of gladiolus leaves
"	"	" "	18% of surface of Ponderosa Pine Needles
"	"	0.37 "	25% of surface of gladiolus leaves
"	"	" "	6% of surface of Ponderosa Pine Needles
ii)			
Drowley et al.[27]	1960-61	0.26 (16 months)	Moderate damage to peach orchards
"	"	0.19 (")	No " " " " "
"	"	0.14 (")	No " " " " "
iii)			
Linzon[10]	1965	4.73 (yearly)	Extensive damage to vegetation
"	1966	3.11 "	" " " "
"	1967	1.57 "	" " " "
"	1968	0.93 "	See Below
"	1969	0.71 "	" "
"	1968	0.43 (May-Sept.)*	75% of suspected vegetation had >10 ppm F
"	1969	0.40 "	28% " " " "

* The source of emission was not in production during the growing season. However, airborne F emanations are to be expected from gypsum-pond lagoons[36], and storage dens[35].

APPENDIX 3

COMPARATIVE SUSCEPTIBILITY OF PLANT SPECIES EXPOSED FOUR TO EIGHT HOURS TO APPROXIMATELY 500 P.P.B. SO_2 AND 50 P.P.B. OF HF GASES AND THE STOMATAL COUNTS ON THE UPPER AND LOWER SURFACES OF LEAVES. THE SPECIES ARE ARRANGED ACCORDING TO DECREASING SENSITIVITY TO HF GAS

Species	Susceptibility to gases*		No. of stomata per sq. mm. in epidermis	
	HF	SO_2	Upper	Lower
Jerusalem cherry, *Solanum Pseudo-Capsicum* L.	XXXX	o	73	374
Gladiolus vars., *Gladiolus* sp.	XXXX	X	187	189
Tulip, *Tulipa* sp.	XXXX	o	58	36
Maize, milo, *Sorghum* sp.	XXX	o	66	187
Ixora, *Ixora* sp.	XXX	o	o	326
Corn vars., field, *Zea mays* L.	XXX	o	55	70
Apricot, Moorpark, *Prunus* sp.	XXX	X	o	235
Prune, Italian, *Prunus* sp.	XXX	XXX	o	240
Buckwheat, *Fagopyrum esculentum* Moench.	XX	XXX	45	145
Smartweed, perennial, *Polygonum* sp.	XX	XX	23	99
Grape, wild, *Vitis labrusca* L.	XX	XX	—	—
Corn vars., sweet, *Zea mays* L.	XX	o	46	94
Sweet potato, *Ipomoea batatas* Lam.	XX	XXX	26	26
Iris, *Iris* sp. var. Great Lakes	XX	X	43	45
Apple, *Malus* sp.	XX	X	o	219
Rose, *Rosa* sp.	X	XX	o	96
Lamb's-quarters, *Chenopodium album* L.	X	XX	115	189
Dock, curly, *Rumex* sp.	X	XXX	23	104
Stevia, *Piqueria trinervia* Cav.	o	o	10	90
Cotton, *Gossypium hirsutum* L.	o	X	53	134
Tobacco, Turkish, *Nicotiana tabacum* L.	o	XXX	83	137
Taxus, *Taxus* sp.	o	XX	o	106
Bean, *Vicia* sp.	o	XX	47	178
Chicory, escarole, *Cichorium* sp.	o	XXXX	42	81
Dandelion, *Taraxacum officinale* Weber	o	XXX	121	165
Spanish needles, *Bidens* sp.	o	XXX	79	360
Nightshade, *Solanum nigrum* L.	o	XXX	—	—
Celery, *Apium graveolens* L.	o	XXX	101	158
Tomato, *Lycopersicon esculentum* Mill.	o	XXX	32	112
Pumpkin, *Cucurbita pepo* L.	o	XXX	—	—
Cucumber, *Cucurbita sativus* L.	o	XXX	—	—
Pigweed, *Amaranthus retroflexus* L.	o	XXX	—	—
Alfalfa, *Medicago sativa* L.	o	XXXX	113	124
Clover, sweet, *Melilotus* sp.	o	XXX	420	208
Coleus, *Coleus blumei* Benth.	o	XXX	64	188
Geranium, *Pelargonium* sp.	o	XXXX	33	175
Buttonbush, *Cephalanthus* sp.	o	XXXX	o	242
Eggplant, *Solanum melongena* L.	o	XXXX	—	—
Galinsoga, *Galinsoga parviflora* Cav.	o	XX	1	55

* o = no markings; X = slight markings; XX to XXXX = moderate to pronounced markings.

(Ref. 82)

FLOWER COLOR, LEAF AREA, C_6/C_1 RATIOS, AND NECROSIS ON DIFFERENT VARIETIES OF GLADIOLUS

Variety	Color[a]	C_6/C_1 ratio[a]	Area[a] (in^2)	Leaf necrosis[a]
Abu Hassen	1[b]	0.59	5.5	16%
Adrena	4	.71	9.7	43
Beneres	4	.63	10.2	16
Black opal	3	.64	9.4	41
Bridal orchid	2	.75	11.9	15
Dieppe	3	.82	9.3	32
Elmer's rose	4	.70	11.8	35
Florence Nightingale	6	.81	8.1	40
Gold	5	.82	6.2	37
Green light	6	.84	8.0	65
Jo Wagenaar	3	.58	10.4	10
Julia Mae	4	.62	11.3	14
King David	1	.67	10.8	11
Lavender lace	2	.64	6.9	32
Leif Ericson	5	.51	10.4	27
Manchu	6	.63	10.1	43
Mid America	3	.79	8.8	16
Mother Fisher	6	.80	11.1	32
Orange gold	7	.68	8.2	46
Peter Pan	7	.76	5.0	83
Poinsettia	3	.73	8.4	25
Prof. Goudriaan	6	.72	9.6	36
Purple Burma	1	.65	10.1	29
Red charm	3	.65	9.4	16
Red cherry	3	.76	11.1	10
Redowa	1	.56	8.6	4
Rose charm	4	.54	7.1	18
Sans Souci	3	.70	9.9	24
Snow baby	6	.61	5.9	15
Snow princess	6	.63	6.8	34
Spic and span	4	.80	7.4	30
Spotlight	5	.70	8.9	16
Summer queen	4	.66	5.6	43
Trail's end	4	.69	6.9	42
Uhu	1	.69	9.4	28
Violet charm	2	0.72	7.8	31

[a] Color, leaf area, and leaf necrosis are data of HENDRIX and HALL (1958).
[b] Color key: 1, purple; 2, lavender; 3, red; 4, pink; 5, yellow; 6, white; 7, orange.
[a] Means of two to five determinations.

(Ref. 83)

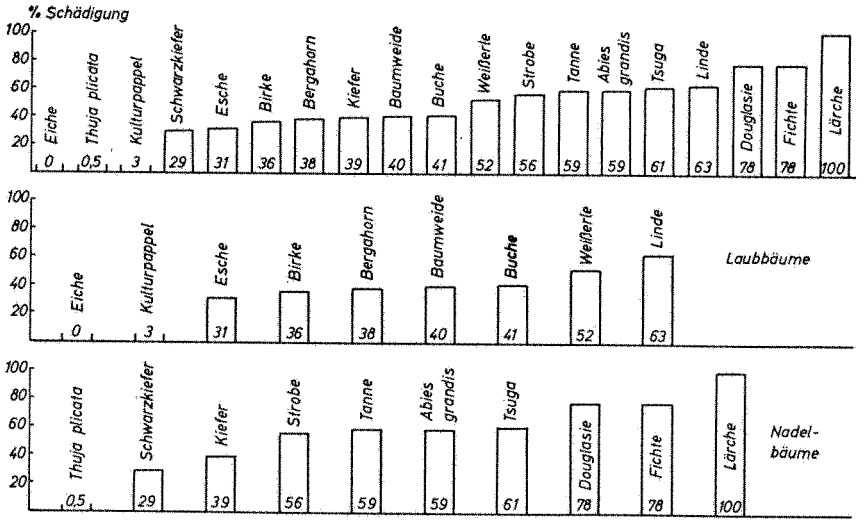
APPENDIX 4

Visible injury to and fluoride accumulation in rose foliage exposed to approximately 2 ppb HF for 6 months. Necrosis and chlorosis were rated as follows: 0= none, 1 = slight, 2 = moderate, 3 = severe.

Rose variety	Necrosis	Chlorosis	F content
Bravo	1.75*	1.00	223*
Buccaneer	0.50	2.50**	142*
Charlotte Armstrong	1.75**	0.75	125*
Dean Collins	1.00*	0.25	130
Forty Niner	1.00*	1.00*	311*
Lowell Thomas	1.50*	1.50*	153
Tiffany	0.75	2.25**	128
Circus	1.00*	1.50*	235
Crimson Rosette	1.00*	0.75	176
Frolic	1.75*	0.50	323
Goldilocks	0.75	2.25**	149
Jiminy Cricket	2.00**	2.50**	235
Lilibet	1.75**	0.75	180
Summer Snow	1.25*	1.25*	280

*Significantly different from control at the .05 level.
**Significantly different from control at the .01 level.

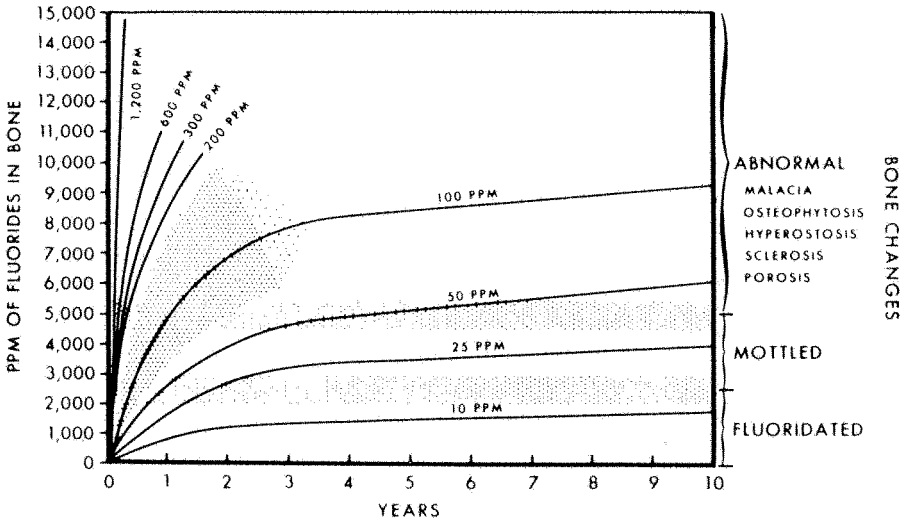
(Ref. 80)



Schädigungs-Reihenfolge = Resistenz-Reihe von 19 untersuchten Baumarten bei zehntägiger Begasung mit 0,075 mg F/m³. Bei den Nadelbaumarten wurde die Schädigung der einjährigen Nadeln bewertet

(Ref. 84)

APPENDIX 5

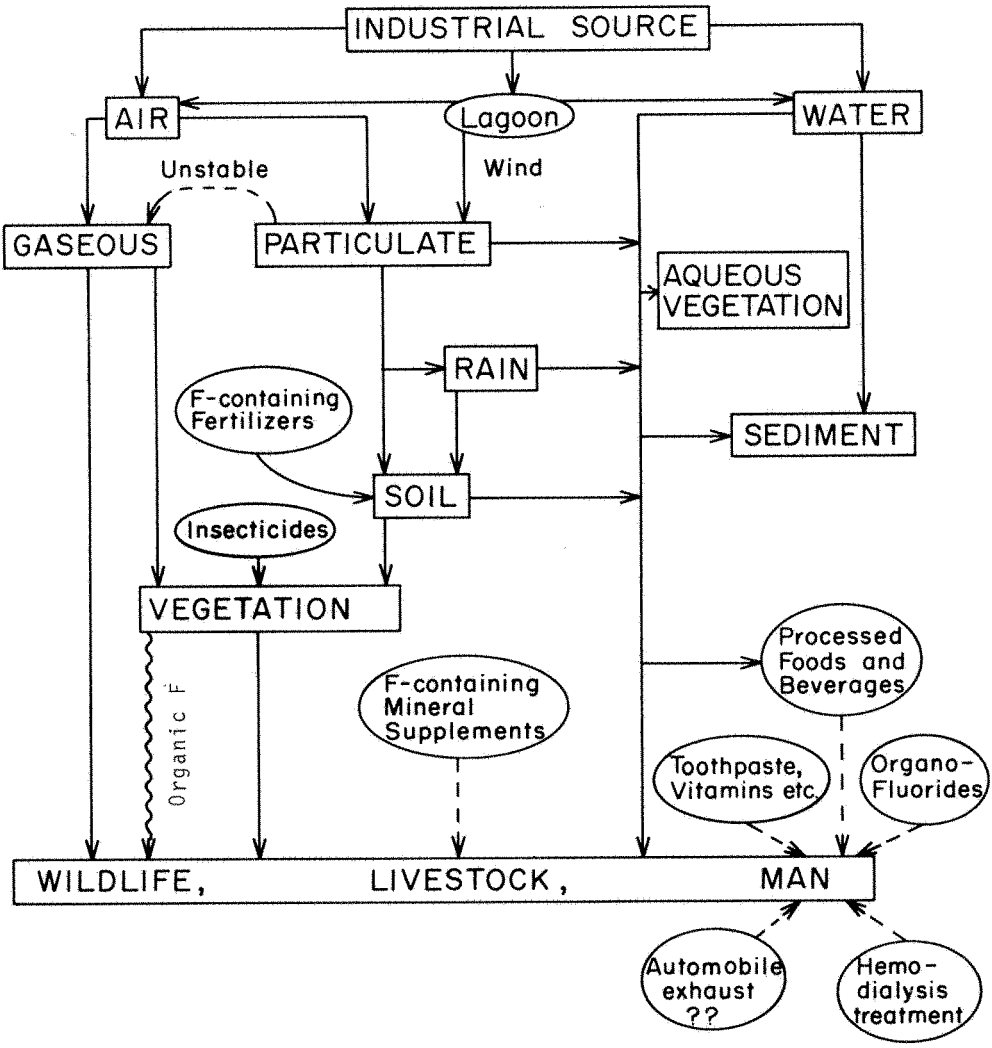


The graph shows approximate amount of fluoride in bone as a function of time on different fluoride intakes. The horizontal bands show the boundaries between fluoridated, mottled, and abnormal bone fluoride levels. The curves are based upon averages from metacarpal and metatarsal data. The curve for 100 ppm includes the wide range of values during the first 3 years. Cattle (and human) bones constantly remodel throughout life; therefore, the curves do not level off but continue to rise slowly (in contrast to the flat plateau for rats which do not have cortical remodeling).

(Ref. 14)

APPENDIX 6

THE MAN-MADE FLUORIDE CHAIN



APPENDIX 7

(From Soriano, M., Revista Clinica Espanola 97: 375; 1965. Table III).[113]

Patient Identification	Name of Bone	Type of Bone	% F in ash
4	Coxal	Spongiosa	1.180
"	Femur	"	1.190
"	Tibia	"	1.120
"	Femur	Cortical	0.381
"	Tibia	"	0.450
5	Coxal	Spongiosa	0.977
"	"	"	0.850
"	Femur	"	0.809
"	Rib	"	0.732
"	Femur	Cortical	0.091
12	Coxal	Spongiosa	1.090
"	Tibia	Cortical	0.552

This publication is a review of selected environmentally-relevant scientific literature aimed at identifying sources, pathways, and effects of fluorides. It was prepared prior to the formation of the National Research Council's Associate Committee on Scientific Criteria for Environmental Quality by two scientists within the Division of Biology, NRC. It is directed toward the compilation of scientific knowledge and as such has been approved by the Division of Biology; it is not a "Criteria Document" nor does it deal with legal standards for fluoride.