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EXPERT COMMITTEE ON WATER FLUORIDATION

First Report

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WORLD HEALTH ORGANIZATION

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EXPERT COMMITTEE ON WATER FLUORIDATION

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EXPERT COMMITTEE ON WATER FLUORIDATION

First Report *

Water fluoridation as a public health measure to aid in the control of dental caries is receiving world-wide attention. Many government officials, public health administrators and others have asked for guidance in the form of an authoritative report presenting the subject in a way which will serve as a useful guide when water fluoridation projects are considered.

Fluoridation of water-supplies employs the fluoride ion as the active agent; a number (at least six) of simple and complex inorganic fluoride salts serve as sources. The element fluorine is not used as such; for this reason "fluoridation" rather than "fluorination" is the preferred term. Fluorides occur as a natural constituent of many water-supplies.

1. DENTAL ASPECTS

1.1 The problem of dental caries

Dental caries is one of the most prevalent and widespread diseases in the world. It is not restricted to any specific age, sex, or economic status, nor is it peculiar to any country or race. In countries where dental surveys have been carried out, it has been found that almost the entire population is affected by dental caries and its consequences. It has been found, too, that dental caries starts soon after the eruption of the deciduous teeth. Numerous studies have been made on the prevalence of caries among children in many countries, and it has been shown repeatedly that the average child reaching school age has many carious teeth. The consequences of the disease can be particularly serious both in childhood and adolescence. The carious lesions increase progressively in size, frequently leading to considerable suffering and eventual loss of teeth. The consequent reduction

* The Executive Board, at its twenty-first session, adopted the following resolution:
The Executive Board

1. NOTES the first report of the Expert Committee on Water Fluoridation;
2. THANKS the members of the Committee for their work; and
3. AUTHORIZES publication of the report.

(Resolution EB21.R6, *Off. Rec. Wld Hlth Org.*, 1958, 83, 7)

of function may affect nutrition in the growing child. Impaired mastication is the direct cause of digestive disorders, and secondary infection from a septic mouth may have far-reaching effects on general health. Not least among the unfortunate consequences of the loss of teeth caused by dental caries are traumatic occlusion, which can induce severe parodontal disease, and the serious psychological and social effect of facial disfigurement.

Throughout the world, dental decay represents an economic drain upon both health services and individuals. It would be extremely difficult to assess the amount of effort spent over many years in various countries to attempt to relieve this disease.

1.2 Treatment

Early detection and treatment of dental caries is effective in controlling the disease and its results. Even in those countries with the highest ratio of dentists to population, however, no more than one-third of the needs of the people in this respect are being met.

In many countries which together represent a large proportion of the world's population, the dentist/population ratio is extremely low. It is inconceivable, therefore, that the control of dental caries by treatment methods alone can be accomplished on a world-wide basis in the foreseeable future.

1.3 Prevention

As in the case of any disease, the ideal solution of the problem of dental caries is prevention. Efforts to prevent dental caries have taken many forms, ranging from oral hygiene to stringent dietary control. Specifically, these methods include reducing the consumption of sticky fermentable carbohydrates, brushing the teeth at regular time-intervals or immediately after meals, mouth-rinsing, using therapeutic dentifrices, and providing dietary supplements such as vitamins and minerals. The relative value of each method will not be assessed here. Whilst some of these methods are effective on an individual basis, their application on a public-health or population-wide basis, however, has on the whole been disappointing, since no one of them fulfils the requirement of being widely acceptable and practicable in application. The potential value of fluorides is, therefore, of special interest.

1.4 Fluorides and dental health

Historically, it is of interest that the empirical use of fluorides for the prevention of dental caries can be traced back to the last quarter of the nineteenth century. The origin of today's concept of fluoridation as a preventive measure, however, is directly attributable to observations made

in connexion with another dental disease, mottled enamel.^{7, 46, 49, 54} In 1931, fluorine in the drinking-water was identified as the cause of mottled enamel.⁴⁹ Prior work by McKay, concerned with a description of the disease and the location of endemic areas, had led to the conclusion that the causative factor was in the drinking-water.³⁵ Dean's subsequent studies, in which classical epidemiological techniques were employed, clearly defined the direct and quantitative relationship between the prevalence and severity of mottling and the concentration of fluoride in the drinking-water.⁹ With concentrations of 8 parts of fluoride in a million parts of water (8 p.p.m.), or more, the teeth of almost the entire population are brown-stained and pitted. As the concentration decreases, however, mottling becomes progressively less severe, so that at a level of about 1.5 p.p.m. it is of a mild to very mild degree.

The very mild mottling of teeth found in communities where the fluoride is in the range 1-1.5 p.p.m. is of no cosmetic significance and can be detected only by careful dental examination as a slight white flecking of the enamel. This observation led to the adoption in the United States of America of 1.5 p.p.m. fluoride as a minimum threshold of mottling for inter-State drinking-water standards.

The term "mottled enamel" is used loosely to describe any defect or discolouration of the enamel caused by ingestion of excessive amounts of fluoride during tooth development. Imperfections of enamel development occur frequently and may be caused by a wide variety of factors. Examples of causes are prolonged fever, vitamin deficiency and other faults in metabolism, and mechanical trauma. The non-fluoride imperfections are fairly common and usually are more damaging from the cosmetic standpoint than the slight flecking of enamel which is occasionally seen in children residing in communities using water containing about 1 p.p.m. fluoride. In diagnosis, special care is required not to interpret white spots as being specifically pathognomonic of fluoride mottling.^{4, 5, 8, 17, 26, 51, 60}

In reporting the studies on mottled enamel, an impression that the condition was accompanied by a relatively low prevalence of dental caries was noted. This impression stimulated further studies on fluorides in drinking-water as a factor in dental health.

1.5 Dental caries and fluoride

Wide variations in the naturally occurring fluoride content in communal drinking-waters in many countries of the world provided exceptional opportunities for studying and determining the relation between the prevalence of dental caries and fluoride concentration. Notable among these countries is the United States of America, where more than 3 million people live in communities where the natural fluoride concentration of the drinking-water is 1.0 p.p.m. or greater. It was there that Dean and his

co-workers conducted carefully designed epidemiological studies in 21 cities.^{11, 13} In this series of comprehensive investigations, 7257 children aged from 12 to 14 years were examined. The 21 cities are located in a narrow geographical area where the mean annual temperature is approximately 50°F (10°C). All clinical examinations were made by two dentists who examined an equal number of children in each city. Rigid criteria were employed to ensure that the children studied had been continuous residents and regular users of the city water-supply.

These studies demonstrated that there was an inverse relationship between the fluoride level in the water and the incidence of caries.^{11, 12, 38, 39, 57} With low levels, the caries was severe, but with about 1 p.p.m. fluoride children had only one-third as much caries as had those of the same age in areas where there was very little fluoride in the water. With levels of more than 1 p.p.m. fluoride there was very little further reduction in caries.

The pattern of the initial series of investigations has been followed by a long and increasing list of independent investigators in other parts of the USA and in many countries of the world. These countries include Argentina, Canada, England and Wales, Greece, Hungary, India, Kenya, Norway, Sweden, Switzerland, Turkey, Union of South Africa, and USSR.¹⁰ With a remarkable degree of uniformity, the different observers reported the fact that there is an inverse relationship between the prevalence of dental caries and the fluoride concentration in drinking-water up to approximately 1 p.p.m. This fact was important. Maximum dental caries benefits were associated with a concentration of fluoride which is below the minimum threshold established for mottling of the teeth or dental fluorosis.

The public health significance of the striking difference in caries prevalence among children in fluoride and fluoride-free areas was further enhanced by a study of adult populations which demonstrated that the effect of fluoride continues into adult life without any appreciable diminution with age.⁴³ Groups of adults aged 20-44 years were examined in an area where the water contained 2.5 p.p.m. fluoride and compared with similar groups in a fluoride-free area. It was found that in each group studied, and up to 44 years of age, caries experience in the fluoride area was only about one-third as much as in the non-fluoride area.

As a logical sequence to all the knowledge which had been gained, it was decided in the USA in 1944 to add fluorides to some water-supplies as a means of preventing dental caries.

1.6 Introduction of fluoridation

The potential significance of the dental effects of fluorides in drinking-water stimulated broad interest in the physiological effects.

Fluorine in a combined state in nature is found almost everywhere

throughout the world, and is a constituent of certain minerals found in rock and soil. There is a substantial volume of literature reporting the world-wide geographical distribution of fluorides contained in domestic water-supplies where a fluorine/dental-carries relationship has been found. Fluoride is also found in teeth and bones and in many of the foods which are commonly eaten.

Studies concerned with ingestion, metabolism, and excretion of fluorides were undertaken not only in human subjects, but also in laboratory animals. Details of the scope and results of these studies will be discussed more fully in section 2. It is significant, however, that studies on controlled fluoridation of community water-supplies were not undertaken until the safety of the procedure had been assured beyond any reasonable doubt. Margins of safety had been estimated against the well-known toxicological effects of fluorine. It had been established, too, that the use of drinking-water containing several times the optimum fluoride concentration does not affect skeletal development or height and weight; that most of the fluoride ingested is eliminated; that fluoride has an affinity for calcified tissues and especially for teeth; that the first signs of having used drinking-waters containing fluoride during the period of tooth formation are found in the teeth; and that the rate of bone fractures among young adult males is no higher for those using fluoridated drinking-water than for others.

The controlled fluoridation of community drinking-water supplies was started in 1945, at Grand Rapids, Mich., USA,³ and shortly afterwards at Newburgh, N.Y., USA,⁴ and Brantford, Ontario, Canada.^{27, 28} In each case, fluorides were added to the water to bring the concentration up to 1.0-1.2 p.p.m., and for each fluoridation city a control area was selected. These studies were planned to extend over a period of 10 years, so that the deciduous dentition and most of the permanent dentition would be subjected to fluoride during the whole period of development and calcification, and would be exposed for some years to caries-attack. In addition, these studies were designed to determine, by actual performance, the feasibility of adding fluorides to water, the reliability and accuracy of the machinery, and the per capita cost. The studies were carefully planned and controlled, and the effect on general health was watched. One study (Newburgh) included an extensive paediatric research programme.

Detailed dental examinations were carried out on children between 4 and 15 years of age before fluoridation started and were repeated each year. Dental caries experience in the fluoridation areas was compared with that in the control areas, and also with caries experience among similar groups of children in Aurora, Ill., a natural fluoride area with 1.2 p.p.m. fluoride in the water.³ This was done to determine whether the added fluoride was as effective in reducing dental caries as fluoride which occurred naturally.

These studies have now been in progress for 12 years and the results have been published. Other studies have been set up in the intervening years and are showing comparable results.

1.7 Results of fluoridation

Reports of the results after 10 years of controlled fluoridation in three cities, two in the USA and one in Canada, show a remarkable uniformity.^{3, 4, 27, 28} The prevalence of dental caries in the permanent teeth of continuously resident children who had used the fluoridated drinking-water throughout life was decreased by some 60%, comparison being made either with the findings among their counterparts prior to fluoridation, or with the findings among children in the control cities selected for the separate studies. Dental caries prevalence in the deciduous or primary dentition was similarly reduced; the reduction ranged from 50% to 60%. The results obtained in the three studies confirmed the hypothesis that the use of drinking-water with 1 p.p.m. fluoride produces identical dental and general effects whether the fluoride occurs naturally or is added by mechanical means.

Dental caries experience in the teeth of children born prior to fluoridation was also appreciably reduced. The extent of the reduction among these children, however, was inversely related to their age at the time fluoridation was started. Maximum benefits, equal to those observed in children of communities having naturally occurring and optimum concentrations of fluoride in the drinking-water, were found in children born after fluoridation began.

Observations on growth and development, calcification of bones, elimination of fluorine in the urine, dysplasia of the teeth, gingivitis, hearing, sight, and blood were made in one or more of the study projects, and particularly in the Newburgh project. Comparison of these observations with established norms, with counterparts prior to fluoridation, or with opposite numbers in control cities revealed no deleterious or beneficial effects other than those relating to dental caries experience.

1.8 Fluoridation projects

To date 32 million people in more than 1500 cities and towns in the USA are using mechanically fluoridated drinking-water.⁵³ Controlled fluoridation programmes are also in operation in one or more communities in the following countries: Australia (2), Belgium (1), Brazil (3), Canada (10), Chile (1), Colombia (1), El Salvador (1), Federal Republic of Germany (1), Great Britain (4), Japan (1), Malaya (1), Netherlands (1), New Zealand (1), Panama Canal Zone (2), Sweden (1), Venezuela (1). Approved plans for the first fluoridation projects in Norway and Switzerland

are in the process of being implemented. These facts on the current status of fluoridation programmes are included to reflect the world-wide extent of endorsements by responsible health officials and their advisory councils.

2. SAFETY OF WATER FLUORIDATION

2.1 General

When an element such as fluorine, that can be toxic in excessive amounts, is to be absorbed by large human population groups continuously for extended periods, it is of the utmost importance that the biological effects be thoroughly investigated. Many substances, when absorbed by living organisms in small doses, may be essential to life or may produce almost imperceptible functional or tissue changes, whereas large doses evoke severe signs of intoxication. As long as such manifestations remain reversible and do not impair in any way the normal physiological processes, they cannot be spoken of as toxic effects. Following the administration of large doses of fluorides, a characteristic pattern of response has been discovered; certain organs and tissues are involved preferentially. With smaller doses, special attention can be directed to these tissues, using methods selected to discover aberrations in structure or in the normal physiological functions. From this point of view, therefore, the effects of fluorine have been determined clinically and experimentally. For each of the systems and organs, the aim has been to fix quantitatively, for the different tissues, the highest doses which can be given without provoking signs of intoxication. The base-line for comparison in such observations has always been the optimal concentration for the prevention of dental caries.

This work has not been the monopoly of one science, but scientists from different disciplines, biologists, physiologists, toxicologists, chemists, veterinarians, pathologists, physicians, and dentists, in many countries of the world, have made important contributions by clinical observations and laboratory experimentation. The rich literature on the subject comprises nearly 3000 research publications in the last 20 years. Important findings have been confirmed in the laboratories of many countries. It is not implied that this research field is unique in freedom from controversy. Contradictory conclusions, however, have in some cases been based on tests under quite different experimental conditions, and in others ambiguous descriptions or illogical interpretations can be blamed.

In this section, those biological properties of inorganic fluorides that are reasonably well established are described in general terms to furnish evidence that the knowledge of the effects of fluorides is sufficiently extensive and detailed to guarantee adequately the safety of water fluoridation.

2.2 Fluoride effects on cells and bacteria

The fluoride ion, like the chloride ion, penetrates cells. Therein, when sufficiently high concentrations are established, fluoride inhibits certain enzymic reactions. A considerable number of metabolic reactions may be interfered with in varying degree; apparently, many enzymes have some susceptibility to fluoride, but the inhibiting concentrations *in vitro* range for different enzymes from over 10^{-2} to 5×10^{-6} M. The mechanisms of these inhibitions are in most cases unknown. In certain instances, enzymes inhibited at one concentration are stimulated by lower concentrations. Although a considerable number of enzyme systems have already been studied, as yet unknown or untested enzymes may be those critically sensitive to fluoride. Thus the principal toxic effects of fluorides cannot at present be attributed with certainty to one or a few enzyme systems, but the actual concentrations in the body are such that many fluoride effects must be enzyme mediated. No evidence of enzyme inhibition by fluoride is known in persons ingesting fluoridated water with concentrations optimal for dental health.

Enzymatic inhibition presumably accounts for the bacteriostatic effects of fluorides as well as for the interference with cell growth in tissue culture. Adding 1 p.p.m. fluoride to the water-supply has created no problem in industrial bacterial processes—for example, brewing. Interference with the growth of certain rickettsiae and viruses has been reported, but not at 1 p.p.m.

Because oral bacteria have long been held responsible for part of the caries process, it might have been expected to find a change in the oral flora in populations drinking water containing 1 p.p.m. fluoride. In general, no such change has been found, nor have alterations in the biochemical functions of the saliva been observed. Oral bacteria in media containing 1 p.p.m. fluoride *in vitro* have shown no reduction in acid production.

2.3 Fluoride effects on the intact animal

2.3.1 Absorption

Soluble fluorides are rapidly absorbed from the gastro-intestinal tract.³⁰ A number of fluorine compounds are used to fluoridate water; each is to be considered as a source of F^- —only this ion is absorbed¹⁶—and no important differences exist in the absorption and subsequent distribution. Ingestion of fluorides together with solid food or with milk, and especially with large quantities of calcium salts, may decrease the absorption markedly, presumably because sparingly-soluble calcium salts are formed. Some of the fluoride in solid food undoubtedly is available and is absorbed; however,

this contribution is generally a minor fraction of the total absorbed daily. In any case, absorption is rarely, if ever, complete; 10-15% of the ingested fluoride usually is excreted in the faeces.^{34, 56}

2.3.2 *Distribution and excretion*

The published concentrations of fluoride in the blood vary greatly (no doubt reflecting the analytical difficulties). The most reliable estimates lie in the range of 0.01-0.2 p.p.m. Whether the drinking-water contains essentially no fluoride or as much as 1 p.p.m., the average concentrations in the blood remain in this narrow range of extremely low values. Blood F levels vary with the fluoride intake in a not clearly defined manner. After the ingestion of a large (even a toxic) dose of fluorides, however, the concentrations reach peak values in one half to one hour and thereafter decrease promptly, reaching the normal range in 24 hours or less.^{40, 47} The increment of blood fluoride from drinking fluoridated water is consequently slight and of short duration.

A large fraction of the absorbed fluoride is promptly excreted in the urine; the renal clearance is considerably greater for the fluoride ion than for chloride or for sodium ions.^{6, 30, 34} Of the retained fraction, almost all is taken up by the mineral crystals of the skeletal tissues. The uptake in bones and teeth is most rapid in young developing individuals. A gradual saturation of the skeleton takes place which, on a constant fluoride intake, is reflected in an increase in urinary excretion.

The soft tissues take up very small quantities of fluoride, comparable to but less than the concentrations in the blood. No storage occurs in soft tissue.^{20, 56} Two organs contain slightly higher concentrations than the others: the thyroid and the kidney. The thyroid has been described as "halogen blind", but the fluoride uptake is not at all comparable to the exceptional concentration of iodine by the thyroid. The thyroid F level rises and falls with the blood level. The kidneys as the excretory apparatus for fluoride understandably exhibit a transient high concentration during the few hours in which most of the excretion occurs following absorption.

A slightly higher concentration of fluoride has also been reported for the placenta, which is permeable at least in some degree to fluoride ions: the blood of the mother and the foetus have been reported to contain about the same concentrations of fluoride.²³

The concentration of fluoride in milk is generally given as about 0.2 p.p.m. for both human and cow's milk. Variations in milk F levels with widely varying fluoride intakes are remarkably small.²³

The fluoride content of saliva is low and does not vary significantly with the amount ingested.

2.3.3 *Metabolism of calcium, phosphorus and magnesium*

No effects whatsoever have been detected on the mineral metabolism, specifically of calcium, phosphorus and magnesium, when the drinking-water contains 1 p.p.m. fluoride. Blood serum contains normal concentrations of these elements even when fluoride intake is considerably elevated. Contrary to the frequently repeated opinion that toxic doses of fluoride reduce the ionic calcium concentration in blood, no marked changes occur in humans and animals and tetany is almost never seen in fatal poisonings. High doses of fluoride do not affect the deposition of radiocalcium and radio-phosphorus in the femurs and mandibles of experimental animals.

Both calcium and magnesium form complexes with fluorine so that certain antagonistic actions have been observed *in vitro* with selected relatively high concentrations (10^{-3} M Mg^{++} and 10^{-3} M F^{-}). *In vivo*, diets rich in calcium decrease fluoride absorption (and toxicity), but no similar relation with phosphorus exists.

2.3.4 *Age, development and growth*

An increasing body of evidence testifies to the absence of any effect on somatic and psychic growth of children in areas in which drinking-water contains optimal amounts of fluoride.²⁴ The normal development of the skeleton both morphologically and in mineral content (bone age and X-ray opacity) and the normal development, calcification, and eruption of teeth have been demonstrated in several studies. A delayed eruption of permanent premolars was described in children from a European area with optimal amounts of fluoride in the drinking-water. The explanation was found in the earlier eruption of the corresponding teeth in the low-fluoride control area following early extractions of carious deciduous molars.

In experimental animals, large daily doses of fluorides depress growth; however, no growth retardation has been observed when the diets contain 100 p.p.m. or less, in a large group of experiments including observations up to four years' duration.²⁵ Optimal doses of fluorides do not interfere with normal repair of bone fracture.

On a given daily intake of fluoride, younger individuals retain more fluoride in their skeletal systems than do older children or adults. Fluoride retention in the skeleton continues throughout life, even with a low intake.

2.4 Fluoride effects on organs

2.4.1 *Hard tissues*

The skeleton is the sole storage site of fluoride. This important fixation mechanism may account for as much as 1/5 to 1/2 of the day's intake in

young individuals or in short-term experiments ;^{33, 48} however, on long-continued administration, steady states are established in which smaller fractions of the fluorides are stored. The fixation mechanism is an exchange with the hydroxyl of the apatite mineral,³⁷ giving what may be called a mixed apatite which serves the same functions as hydroxyapatite. Stored fluoride is mobilized both by exchange with hydroxyl ions, a relatively rapid process, and by osteoblastic and osteoclastic remodelling, a process so slow that a year or more is required for half removal.^{25, 29, 44} The capacity of the skeleton to hold fluoride is impressive. If an individual drank water containing 1 p.p.m. fluoride during a lifetime of 70 years and all the fluoride were stored in the skeleton, less than a quarter of the hydroxyapatite would have to be converted to fluorapatite. Much higher fluoride levels in bone mineral have been observed in symptom-free animals given fluorides.

There are limits to the capacity of the skeleton to store fluoride without detectable structural changes. When large daily doses are ingested for extended periods, three clinical conditions may be defined, in order of decreasing dose: crippling fluorosis, asymptomatic osteosclerosis, and mottled enamel.

2.4.1.1 *Crippling fluorosis.* In rare instances of excessive industrial exposures to fluorides (both man and animals) or where natural waters contain very high fluoride concentrations, particularly when consumed by undernourished or malnourished population groups, the disease known as crippling fluorosis may appear. Fluoride intakes of 20-80 mg per day, or more, for periods up to 10 to 20 years are required.⁴² The disease is characterized by severe osteosclerosis, fresh areas of osteoporosis, exostoses, and calcification of certain ligaments, especially the broad ligaments of the spine (producing "poker back") and of the pelvis. Motion of the joints is so restricted that simple daily duties can no longer be performed.

2.4.1.2 *Asymptomatic osteosclerosis.* Adult humans ingesting (or gaining by other routes) lesser amounts of fluoride, but still enough so that the daily urinary excretion exceeds 5 mg/l, will, after periods of 5 to 10 years, develop an asymptomatic increase in the X-ray opacity of certain bones, called osteosclerosis. The changes frequently seen first in the sacral vertebrae ultimately may involve other bones, for example, long bones, pelvis, etc. No functional abnormalities accompany these radiographic changes. A drinking-water content of 8 p.p.m. fluoride (e.g., Bartlett, Texas) constitutes approximately the borderline for osteosclerosis development; 14 of the 113 persons examined there exhibited such bony changes. In the large group of animal studies where X-ray examinations were made, osteosclerosis failed to develop even in periods up to 4 years when the diets contained as much as 50 p.p.m. fluoride.²⁵

2.4.1.3 *Mottled enamel.* The well-known chronic dental fluorosis (mottled enamel) appears when drinking-water supplies contain 2 p.p.m. or more and when these waters are ingested during the first 8 years of life.

Mottled enamel is a sign of disturbed enamel formation. Moderately severe mottling is characterized by unsightly discolouration, and severe mottling by pitting and irregularities of the enamel surface. The prevalence and severity of mottling increases with increasing concentrations of fluoride in drinking-water.⁹ Usually only permanent teeth are affected, but mottling of deciduous teeth is found in areas of exceptionally high water concentrations of fluorides. Teeth cannot become mottled after eruption. Severe chemical trauma from very high fluoride doses disturbing normal development may affect both enamel and dentine.

Due recognition has not been given to the fact that children consuming water containing 1-1.5 p.p.m. fluoride have well-formed teeth with shallow grooves and well-rounded cusps. These teeth are aesthetically superior and more resistant to caries than the teeth of children consuming waters containing no fluorides or very small amounts. The mechanism of this beneficial action is not known. A reasonable hypothesis may be constructed from the following facts: (a) fluorides reduce the solubility of tooth mineral; (b) fluorides in sufficient concentration inhibit bacterial metabolism; and (c) relatively high concentrations of fluoride may be found in the most external layer of the enamel, thus providing conditions for a decreased solubility of the surface enamel and possibly an increased fluoride ion concentration locally in the immediate surface fluid layer.

2.4.2 *Kidney*

In animals given large doses of fluorides for short periods, histological studies show that the kidney is more susceptible to structural injury than any other organ. Well-defined microscopical changes have been described with diets containing 200 p.p.m.⁴¹ Gross changes and functional changes are reported in relatively short-time studies when the drinking-water contained 50 p.p.m. Histologically, a characteristic pattern of injury and necrosis of the columnar epithelial cells (according to the fluoride dose) has been described.

The frank injury to the kidney caused by large doses of fluoride has raised the question of the effect of fluoridated drinking-water on persons suffering from kidney disease. No evidence has been forthcoming that fluoridated water worsens concurrent kidney disease. The urinary fluoride excretion of children and of elderly people suffering from kidney disease is within normal range.

In severe kidney failure a lessened urinary excretion of fluoride has been observed. Any reduction in the normal rapid removal of fluoride

by the urine would inevitably increase the fraction of the fluoride deposited in the skeleton, and thus reduce the urinary fluoride content. In terminal nephritis the patient may succumb to uraemic poisoning and renal failure, but the fluoride retention will never be life-endangering.

2.4.3 *Thyroid gland*

The possible connexion between fluoride and the thyroid gland is of special interest in those countries where endemic goitre exists,¹⁴ and the study of this aspect of the problem perhaps grew from the ability of fluorine to displace iodine in certain chemical reactions. Although this simple concept was shown conclusively not to apply to the iodination reactions in thyroid metabolism—at least for less than 50 p.p.m. fluoride in the daily ration—fresh interest in the fluoride-thyroid relation arose from the discovery of the properties of fluorine derivatives of thyroxine. Difluorothyroxine reduced the intensity of the Basedow syndrome. The anti-Basedow effect, however, could not be attributed to fluorine, but to the fluorinated organic molecule.

Other facts seemed superficially to indicate an antagonism between fluorine and iodine: regions which are rich in fluorine may be poor in iodine; cows receiving a diet rich in fluorine accumulated fluorides in the thyroid gland; the resorption of fluorine in the kidneys reduced the resorption of iodine; rat thyroid tissue contained a relatively higher amount of fluorine than was found in the other soft tissues. On the other hand, a whole series of observations directed to this specific point showed that, with concentrations of fluoride optimal for the prevention of caries, there are no functional disturbances or organic lesions of the thyroid. It was proved experimentally that a daily dose of 1-2 mg of fluorine did not have a harmful effect on the thyroid. The accumulation of iodine in the thyroid was not affected by chronic fluoride poisoning and the passage of iodine through the acinous and then the colloid sections of the thyroid, as well as the distribution of thyroid hormone in the blood plasma, were not changed. In Switzerland, with its endemic goitre, the relation between fluorine and thyroid function particularly attracted the attention of medical investigators: clinical examinations of children receiving sodium fluoride tablets (1 mg of fluoride per day) for about two years failed to reveal any clinical or functional change in their thyroids. In a locality where the water contains naturally 1.4 p.p.m. fluorine, goitre has been effectively overcome by iodized sodium chloride (5 mg of potassium iodide per kg of kitchen salt) despite the fluorine in the water.

From the results of a large group of experiments on animals, it was concluded that no alteration in thyroid structure or function occurs when daily ingestion levels are less than 50 p.p.m. in the diet.

2.4.4 *Skin and related structures*

The toxic effects of very large doses of fluorides on skin, hair, and nails attracted attention to the possibility of such changes when water is fluoridated. Systematic examinations of children in the Newburgh study showed entirely normal epithelial structures.

From several sources have come reports indicating that the soft tissues of the mouth and the dental supporting structures are in no way affected by drinking-water containing 1 p.p.m. fluoride. Neither the gums nor the underlying alveolar bone and parodontal membrane present any morphological or functional changes when compared with those of people living in areas with essentially no fluoride in the drinking-water.

2.5 Health studies

The most convincing evidence of the safety of water fluoridation comes from the numerous population groups (3 million in the USA, 0.5 million in England) who have drunk naturally fluoridated water containing 1 p.p.m. or more during their lifetimes. In these groups water drinking has been, of course, uncontrolled, and there have been well and ill babies as well as healthy young adults and frail elderly people. Medical practitioners and specialists in these areas have never detected and defined a systematic aberration in health of any kind related to the fluoride consumed (except mottled enamel in endemic areas). Large-scale epidemiological tests are lacking. The long-range detailed paediatric study of the Newburgh-Kingston children, including observations on growth, blood count, X-ray of bones, etc., offers convincing evidence of the normal health of children drinking 1 p.p.m. in their water.^{24, 32, 45} The Bartlett-Cameron survey, a 10-year longitudinal study of 168 individuals, demonstrated no adverse health effects with even 8 p.p.m. in the drinking-water, although tooth mottling and a low incidence of osteosclerosis were found.³¹ Mortality and morbidity rates are comparable for fluoridated and non-fluoridated population groups: the mortalities from five leading causes of death—heart disease, cancer, cerebral accidents, nephritis and liver cirrhosis—were the same in 32 pairs of American cities, one of each pair receiving fluoridated water, the other not.¹⁹

Studies so far have failed to establish any relation between fluoride and arthritic changes (arthropathies) in bone.⁵⁰

No confirmed cases of allergy to fluoride have been described in population groups drinking controlled or naturally fluoridated water.¹

All these findings fit together in a consonant whole that constitutes a great guarantee of safety—a body of evidence without precedence in public health procedures.

3. ENGINEERING ASPECTS

The addition of fluorides to public water-supplies has proved to be similar to other routine mechanical procedures widely employed in water-works practice. This fact has been demonstrated during a 12-year period and in over 1500 communities. Suitable types of equipment have been developed for feeding fluorides either as solids or as solutions, being generally comparable to feeders for other waterworks chemicals. Depending mainly on the scale of operations, either volumetric or gravimetric feeders have been found satisfactory. The detailed operating procedures are familiar to, or can be readily grasped by, experienced water treatment personnel. The application of fluorides has proved practicable in different types of plants with different degrees of complexity of treatment. The fluoride compounds commonly used include sodium fluoride, sodium silicofluoride, magnesium silicofluoride, ammonium silicofluoride, and hydrofluosilicic acid. Promising work has been done with calcium fluoride, using an alum dissolver—a process which may further reduce the present reasonable cost.

In the application of fluorides to a public water-supply, there are a number of safeguards that should be applied for the protection of the public and the operators of the treatment plant. The exact nature of these safeguards depends on the local characteristics of each individual plant, the type of fluorine compound selected for use, and the nature of supervision that can be exercised. Since there is a wide variation in individual situations, and since research and development can be expected to offer new methods of application and control, it is not practicable to describe exact methods, controls, materials, or techniques. It is possible, however, to establish minimum criteria as a basis for engineering design, plant operation, and control.

The dosage to be applied is related to the optimum concentration of fluorine for the prevention of dental caries. It depends upon the amount of fluorine present in the water-supply prior to treatment and on the climate. The figure for fluorine dosage in drinking-water should be established after careful study by appropriate health officials. The specified dosage is the fluoride content of water as delivered to consumers.

The precision of fluoride application should be carefully controlled. Chemical feeding equipment should be designed to adjust the amount of the fluoride to the rate of water flow at the point of application, and to maintain a variation of not more than 0.1 mg/l above or below the established dosage. The design of feed equipment should provide for positive protection against overdosage of fluoride in case of malfunctioning of the feed mechanism. Examples of specific hazards would be siphonage

of fluoride solution through a defective discharge valve into a water line under negative pressure, or the continuation of fluoride application after the flow of water has been reduced or stopped. Most cases of failure of equipment are likely to result in under-treatment, and this should be carefully guarded against if the principal purpose of fluoridation is to be fulfilled.

Control of fluoridation should be maintained through frequent and regular inspection, sampling and analysis, and careful training and supervision of operating personnel. Adequate records are essential, e.g., it is imperative to compare the amount of chemical used and the total amount of water treated. Sampling should extend not only to points in the treatment plant, but to representative outlets in the distribution system.^{18, 52} The number of samples and the frequency of collection should be related to the amount of water treated, in order to ensure that the samples examined are representative of the water treated or consumed. The fluoride analytical method used for laboratory examination should be as reliable and precise as possible. The WHO Study Group on International Standards of Drinking Water Quality has recommended the method described in *Standard Methods for the Examination of Water, Sewage, and Industrial Wastes*.² Precautions should be taken to protect operators against the toxic hazards related to the handling of the fluoride compounds.^{15, 36, 55, 61} Protective measures include such items as the use of dustless compounds when possible; protective masks, gloves and clothing; exhaust fans and hoods; and enclosed chutes, hoppers, or conveyors.

Design of the plant and selection of equipment should be put in the hands of a competent and experienced engineer. Laboratory control should be carried out under the supervision of a qualified water chemist. All operating personnel should be thoroughly trained in their duties, both for their own protection and to ensure reliable operation.

The selection of method and the fluoride compound to be applied will usually be decided on the basis of cost. Rapid changes are taking place, based on experience and research, and it is desirable to provide not only for the immediate situation, but for possible changes in methods to improve reliability and economy. It is necessary, also, to consider the availability and cost of equipment and materials in each locality, as these factors are extremely variable among different countries and areas.

4. ALTERNATIVE METHODS

With present technical development, fluoridation of drinking-water is limited to regions served by waterworks where adequate control of the dosage is technically and economically possible. This means that large population groups, varying in size with the development and urban-

ization of the different countries, cannot obtain prophylactic fluoride doses through the drinking-water.

Local applications of fluoride compounds may in part provide a substitute for fluoridated drinking-water where the latter is not available. This method was originally based on the finding of higher enamel fluoride content in regions with high concentrations of fluoride in the water, and on the fact that the enamel apatite has a strong affinity for fluoride ions. Topical treatment with fluoride solutions after cleaning and drying of the enamel surfaces has been found to reduce the caries incidence to a varying extent for periods of several years. The cost in professional working time is, however, relatively high and limits its application as a large-scale public health measure. The results with mouthwashes and dentifrices containing fluoride have in most cases been negative, but studies of these methods are continuing.

Local fluoride application cannot therefore replace drinking-water fluoridation. On the other hand, one of these forms of application does not exclude the simultaneous use of the other, provided that the local application is not complicated by swallowing of fluoride quantities which may lead to over-dosage.

Various vehicles have been proposed for the systemic administration of fluoride in regions where water fluoridation cannot be applied. The most important of these vehicles seem to be milk, table salt, and fluoride tablets which are now all being tested.^{21, 22, 58, 59} Milk might be a possible alternative vehicle in countries with a universal milk consumption by the children, while salt might be possible for regions with a low or irregular milk consumption.

At present, the value of milk and salt for fluoride administration cannot be compared with that of drinking-water, since the evidence in favour of the first two vehicles is incomplete; in particular, there is a total lack of clinical evidence of their effectiveness. On the other hand, tablets have been shown to have some positive effect, although the experiments with tablets have been performed for a much shorter time and on a much smaller scale than drinking-water fluoridation.

Continued research on these fluoridation methods should be encouraged. If their effectiveness, practicability, and safety of application can be satisfactorily demonstrated, they may become very valuable in regions where water fluoridation is impossible.

5. SUMMARY

1. Dental caries is one of the most prevalent and widespread diseases.
2. There is no hope of controlling the disease by present treatment methods alone.

3. Among the numerous preventive methods, the fluoridation of drinking-water supplies is the most promising.

4. The effectiveness, safety, and practicability of fluoridation as a caries-preventive measure has been established.

5. 1 p.p.m. fluoride has been shown to give maximum benefits : first, by epidemiological studies where fluoride occurs naturally in the water, and, secondly, where fluoride has been added at optimum concentrations through mechanical means.

6. Hundreds of controlled fluoridation programmes are now in operation in many countries. Some have been in progress for the past 12 years, so that conclusions are based on experience. No other public health procedure, during the initial stages of its application, has had such a background in time or extent.

7. The biological effects of fluorides have been described in nearly 3000 clinical and experimental reports in the past 20 years. This literature is not only extensive but of broad scope.

8. Fluorides penetrate cells and in sufficiently high concentrations inhibit certain enzymes, but no evidence of enzymal inhibition has been found in persons drinking fluoridated water containing concentrations of fluoride optimal for dental health.

9. Most of the fluoride absorbed into the system is rapidly excreted, principally in the urine ; the rest is deposited in the minerals of the bones and teeth.

10. When large doses or excessive amounts of fluorides are ingested for protracted periods (many years), the skeletal system exhibits structural changes. The clinical manifestations are classed as (a) crippling fluorosis (20-80 mg of fluoride or more per day for 10 to 20 years ; calcification changes in bone together with calcification of ligaments) ; (b) asymptomatic osteosclerosis (more than 5 mg/l of urine excreted daily for 5 to 10 years ; hypercalcification in one or more bones without disability) ; and (c) mottled enamel (drinking-water containing 2 to 8 p.p.m. fluoride or more during the first 8 years of life ; interference with enamel formation, stained or in severe cases irregular enamel surfaces). Adequate factors of safety guarantee the absence of these changes when water containing 1 p.p.m. fluoride is drunk.

11. Toxic doses of fluorides (50 times that used in controlled water fluoridation) injure the kidneys. There is no evidence of kidney injury or of any effect on concurrent kidney disease in the populations drinking fluoridated water where fluoride concentrations range up to 5 p.p.m.

12. No relation between thyroid dysfunction and naturally fluoridated water has been established. In animal studies, daily doses in excess of 50 p.p.m. in the diet produced structural and functional changes in the

thyroid. In humans, drinking-water containing 1-5 p.p.m. fluoride is without demonstrable effect on the thyroid.

13. Growth and development, somatic and psychic, are normal in children drinking water containing 1 p.p.m. fluoride.

14. The formation of teeth and even their resistance to caries and their appearance are improved when water containing optimal concentrations of fluoride is consumed.

15. Over 3 million people in the USA, over half a million in England, and large population groups in other countries have, during their lifetime, consumed water containing 1 p.p.m. fluoride or more. Mortality and morbidity rates for five leading causes of death are comparable for cities in the USA with fluoride and non-fluoride public water-supplies. No relation between fluoride and arthritic changes in bone has been found, nor have confirmed cases of allergy to water containing 1 p.p.m. fluoride been described.

16. The addition of fluorides to public water-supplies has proved to be similar to other routine mechanical procedures widely employed in waterworks practice. Suitable equipment has been developed, reliable analytical procedures are available, and appropriate safeguards have been established.

17. No other vehicles or techniques for the prophylactic application of fluorides can at present replace the fluoridation of drinking-water as a public health measure. Where water fluoridation cannot be used, research into other vehicles and improved methods of local fluoride application should, however, be encouraged.

6. CONCLUSIONS

1. Drinking-water containing about 1 p.p.m. fluoride has a marked caries-preventive action. Maximum benefits are conferred if such water is consumed throughout life.

2. There is no evidence that water containing this concentration of fluoride impairs the general health.

3. Controlled fluoridation of drinking-water is a practicable and effective public health measure.

REFERENCES

1. Abelson, J. H. (1948) A case of hypersensitivity to sodium fluoride in a dentist. *Fortn. Rev. Chicago dent. Soc.*, **16**, 6
2. American Public Health Association (1955) *Standard methods for the examination of water, sewage, and industrial wastes*, 10th ed., New York, N.Y.
3. Arnold, F. A., jr, et al. (1956) Effect of fluoridated public water supplies on dental caries prevalence. *Publ. Hlth Rep. (Wash.)*, **71**, 652
4. Ast, D. B. et al. (1956) Newburgh-Kingston caries-fluorine study. XIV. Combined clinical and roentgenographic dental findings after ten years of fluoride experience. *J. Amer. dent. Ass.*, **52**, 314
5. Bone and Tooth Society, London (1955) [Report on Symposium on Fluorosis presented at the Institute of Orthopaedics, London, 20 January 1955]. *Brit. dent. J.*, **98**, 177
6. Chen, P. S., jr, et al. (1956) Renal clearance of fluoride. *Proc. Soc. exp. Biol. (N.Y.)*, **92**, 879
7. Churchill, H. V. (1931) Occurrence of fluorides in some waters of the United States. *Industr. Engng Chem.*, **23**, 996
8. Davies, G. N. (1957) An independent assessment of the results of the Newburgh-Kingston fluoridation study. *N.Z. dent. J.*, **53**, 17
9. Dean, H. T. (1942) *The investigation of physiological effects by the epidemiological method*. In: Moulton, F. R., ed., *Fluorine and dental health*, Washington, D.C., p. 23 (Publication of the American Association for the Advancement of Science No. 19)
10. Dean, H. T. (1954) Fluorine in the control of dental caries: some aspects of the epidemiology of the fluorine-dental caries relationship. *Int. dent. J.*, **4**, 311
11. Dean, H. T., Arnold, F. A., jr, & Elvove, E. (1942) Domestic water and dental caries. V. Additional studies of the relation of fluoride domestic waters to dental caries experience in 4,425 white children, aged 12 to 14 years, of 13 cities in 4 States. *Publ. Hlth Rep. (Wash.)*, **57**, 1155
12. Dean, H. T. et al. (1941) Domestic water and dental caries. I. A dental caries study, including *L. acidophilus* estimations, of a population severely affected by mottled enamel and which for the past 12 years has used a fluoride-free water. *Publ. Hlth Rep. (Wash.)*, **56**, 365
13. Dean, H. T. et al. (1941) Domestic water and dental caries. II. A study of 2,832 white children, aged 12-14 years, of 8 suburban Chicago communities, including *Lactobacillus acidophilus* studies of 1,761 children. *Publ. Hlth Rep. (Wash.)*, **56**, 761
14. Demole, V. (1951) Iode, fluor, thyroïde chez les écoliers en Suisse. *Bull. schweiz. Akad. med. Wiss.*, **7**, 430
15. Dust control procedures in the fluoridation of public water supplies in New York State. *Monthly Rev. Div. industr. Hyg. N.Y.*, 1953, **32**, 21, 27
16. Feldman, I., Morken, D. & Hodge, H. C. (1957) The state of fluoride in drinking water. *J. dent. Res.*, **36**, 192
17. Forrest, J. R. (1956) Caries incidence and enamel defects in areas with different levels of fluoride in the drinking water. *Brit. dent. J.*, **100**, 195
18. Gidley, H. K. & Millar, J. H. (1955) West Virginia fluoridation control tests. *J. Amer. Wat. Wks Ass.*, **47**, 257

19. Hagan, T. L., Pasternack, M. & Scholz, G. C. (1954) Waterborne fluorides and mortality. *Publ. Hlth Rep. (Wash.)*, **69**, 450
20. Hein, J. W. et al. (1956) Distribution in the soft tissue of the rat of radioactive fluoride administered as sodium fluoride. *Nature (Lond.)*, **178**, 1295
21. Held, A.-J. & Piguët, F. (1954) Prophylaxie de la carie dentaire par les comprimés fluorés : premiers résultats. *Bull. schweiz. Akad. med. Wiss.*, **10**, 249
22. Held, A.-J. & Piguët, F. (1956) Prophylaxie de la carie dentaire par les comprimés fluorés. *Bull. schweiz. Akad. med. Wiss.*, **12**, 453
23. Held, H. R. (1952) Der Durchtritt des Fluors durch die Placenta und sein Übertritt in die Milch. *Schweiz. med. Wschr.*, **82**, 297
24. Hilleboe, H. E. et al. (1956) History of the Newburgh-Kingston caries-fluorine study. *J. Amer. dent. Ass.*, **52**, 291
25. Hodge, H. C. & Smith, F. A. (1954) *Some public health aspects of water fluoridation*. In : Shaw, J. H., ed., *Fluoridation as a public health measure*, Washington, D.C., p. 79 (Publication of the American Association for the Advancement of Science)
26. Hurme, V. O. (1949) Developmental opacities of teeth in a New England community : their relation to fluorine toxicosis. *Amer. J. Dis. Child.*, **77**, 61
27. Hutton, W. L., Linscott, B. W. & Williams, D. B. (1951) The Brantford fluorine experiment : interim report after five years of water fluoridation. *Canad. J. publ. Hlth*, **42**, 81
28. Hutton, W. L., Linscott, B. W. & Williams, D. B. (1956) Final report of local studies on water fluoridation in Brantford. *Canad. J. publ. Hlth*, **47**, 89
29. Largent, E. J. (1952) Rates of elimination of fluorides stored in the tissues of man. *Arch. industr. Hyg.*, **6**, 37
30. Largent, E. J. (1954) *Metabolism of inorganic fluorides*. In : Shaw, J. H., ed., *Fluoridation as a public health measure*, Washington, D.C., p. 49 (Publication of the American Association for the Advancement of Science)
31. Leone, N. C. et al. (1955) Review of the Bartlett-Cameron survey : a ten year fluorine study. *J. Amer. dent. Ass.*, **50**, 277
32. McCauley, H. B. & McClure, F. J. (1954) Effect of fluoride in drinking water on the osseous development of the hand and wrist in children. *Publ. Hlth Rep. (Wash.)*, **69**, 671
33. McClure, F. J. (1946) *Nondental physiological effects of trace quantities of fluorine*. In : Moulton, F. R., ed., *Dental caries and fluorine*, Washington, D.C., p. 74 (Publication of the American Association for the Advancement of Science)
34. McClure, F. J. et al. (1945) Balances of fluorine ingested from various sources in food and water by five young men ; excretion of fluorine through the skin. *J. industr. Hyg.*, **27**, 159
35. Moulton, F. R., ed. (1946) *Dental caries and fluorine*, Washington, D.C. (Publication of the American Association for the Advancement of Science)
36. Muegge, O. J. (1954) *Engineering aspects of fluoridation installation*. In : Shaw, J. H., ed., *Fluoridation as a public health measure*, Washington, D.C., p. 193 (Publication of the American Association for the Advancement of Science)
37. Neuman, W. F. et al. (1950) The surface chemistry of bone. II. Fluoride deposition. *J. biol. Chem.*, **187**, 655
38. Ockerse, T. (1944) *Endemic fluorosis in South Africa*, Pretoria (Thesis, University of the Witwatersrand). Abstract in *Bull. Hyg. (Lond.)*, 1945, **20**, 20
39. Ockerse, T. (1944) *Report on the incidence of dental caries among school children in South Africa*, Pretoria (Union of South Africa, Department of Public Health). Abstract in *Bull. Hyg. (Lond.)*, 1945, **20**, 21

40. Perkinson, J. D., jr, et al. (1955) Metabolism of fluorine 18 in domestic animals. *Amer. J. Physiol.*, **182**, 383
41. Pindborg, J. J. (1957) The effect of 0.05 per cent dietary sodium fluoride on the rat kidney. *Acta pharmacol. (Kbh.)*, **13**, 36
42. Roholm, K. (1937) *Fluorine intoxication: a clinical-hygienic study, with a review of the literature and some experimental investigations*, London
43. Russell, A. L. & Elvove, E. (1951) Domestic water and dental caries. VII. A study of the fluoride-dental caries relationship in an adult population. *Publ. Hlth Rep. (Wash.)*, **66**, 1389
44. Savchuck, W. B. & Armstrong, W. D. (1951) Metabolic turnover of fluoride by the skeleton of the rat. *J. biol. Chem.*, **193**, 575
45. Schlesinger, E. R. et al. (1956) Newburgh-Kingston caries-fluorine study. XIII. Pediatric findings after ten years. *J. Amer. dent. Ass.*, **52**, 296
46. Sebrell, W. H. et al. (1933) Changes in the teeth of white rats given water from a mottled enamel area compared with those produced by water containing sodium fluoride. *Publ. Hlth Rep. (Wash.)*, **48**, 437
47. Smith, F. A., Gardner, D. E. & Hodge, H. C. (1950) Investigations on the metabolism of fluoride. II. Fluoride content of blood and urine as a function of the fluorine in drinking water. *J. dent. Res.*, **29**, 596
48. Smith, F. A., Gardner, D. E. & Hodge, H. C. (1953) Age increase in fluoride content in human bone. *Fed. Proc.*, **12**, 368
49. Smith, M. C., Lantz, E. M. & Smith, H. V. (1931) The cause of mottled enamel, a defect of human teeth. *Science*, **74**, 244
50. Steinberg, C. L. et al. (1955) Comparison of rheumatoid (ankylosing) spondylitis and crippling fluorosis. *Ann. rheum. Dis.*, **14**, 378
51. Syrrist, A. (1951) Kariesforholdene i Valle Herrod, Setesdalen (En reundersøkelse). *Odont. Fören. T.*, **58**, 523
52. Taylor, F. B., sr (1954) Engineering aspects of water fluoridation. *Publ. Hlth News (Trenton, N.J.)*, **35**, 24
53. United States Public Health Service, Division of Dental Public Health (1957) Status of controlled fluoridation in the United States, 1945-56. *Publ. Hlth Rep. (Wash.)*, **72**, 464
54. Van Burkalow, A. (1946) Fluorine in United States water supplies. *Geogr. Rev.*, **36**, 177
55. Venable, F. S. (19—) *An investigation of the health hazard associated with the handling of sodium fluoride at a Texas municipal water plant*, Austin, Tex. (Texas State Department of Health, Bureau of Sanitary Engineering)
56. Wallace-Durbin, P. (1954) The metabolism of fluorine in the rat using F¹⁸ as a tracer. *J. dent. Res.*, **33**, 789
57. Weaver, R. (1944) Fluorine and dental caries: further investigations on Tyneside and in Sunderland. *Brit. dent. J.*, **77**, 185
58. Wespi, H. (1956) *Fluor-Vollsalz zur Kropf- und Cariesbekämpfung*, Basel
59. Ziegler, E. (1956) Über die Milchfluorierung. *Bull. schweiz. Akad. med. Wiss.*, **12**, 466
60. Zimmermann, E. R. (1954) Fluoride and nonfluoride enamel opacities. *Publ. Hlth Rep. (Wash.)*, **69**, 1115
61. Zufelt, J. C. (1950) Fluorides in air of water plant feeding sodium fluoride. *Wat. Sewage Wks*, **97**, 335

Annex**LIST OF SUPPORTING DOCUMENTS ***

WHO/DH/2	First results of fluoridation of water in Brazil, by P. da Silva Freire
WHO/DH/3	Geographical distribution of fluorides in water, by H. Trendley Dean
WHO/DH/4	Safety of water fluoridation, by H. C. Hodge
WHO/DH/5	Engineering problems in water fluoridation, by F. J. Maier
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WHO/DH/8	Some possible reasons why public and professional acceptance of water fluoridation has been slow, by C. A. Metzner
WHO/DH/9	Metabolism of inorganic fluorine compounds, by A. J. Held
WHO/DH/10	Recent data on the physiological effects of small doses of fluorine, by Y. Ericsson
WHO/DH/11	Dental effects of fluoride, by J. W. Knutson
WHO/DH/12	Fluoride references, by H. C. Hodge
WHO/DH/13	Water fluoridation in Brazil and other Latin American countries, by P. da Silva Freire
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Report of a joint committee convened by WHO with the participation of United Nations, ILO and UNESCO	75	1/9	0.25	1.—
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Nursing Education, Working Conference on				
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Third report	72	1/6	0.20	0.80
Fourth report	97	3/6	0.60	2.—
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Occupational Health, Joint ILO/WHO Committee on				
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Report of a study group	114	3/6	0.60	2.—