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IS TOPICAL FLUORIDE SAFE FOR CHILDREN?

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Figure index :

Abbreviations:

DMFT= Decayed, Missing, and Filled Teeth index
DMF= Decay-missing-filled
DMFS= Abbreviation for decayed, missing, or filled tooth surfaces.
FDI= Federation dental international
CDC= US Centers for Disease Control
EAPD= European Academy of Pediatric Dentistry
FO= Outer fluoride
FS= Surface fluoride
FL= Liquid fluoride
Fa= Absorbed fluoride
CaF_2= Difluoro calcium
FHAP= Fluoro-hydroxy-apatite
FPA= Fluoro-hydroxy-apatite
APF= Acidulated phosphate fluoride
Ppm= Part per million
UEM= Universidad Europea de Madrid
PTD= Probable toxic dose
CAMBRA= Caries Management by Risk Assessment

I. RESUMEN / ABSTRACT

Desde su descubrimiento en 1886, la química del flúor ha evolucionado considerablemente. Su acción, ampliamente demostrada en la literatura científica, llevó a las autoridades sanitarias a introducirlo ampliamente como terapia en la prevención de la caries dental. Es por eso que el flúor se encuentra presente en muchos productos relacionados con la salud dental en la actualidad.

Aunque las autoridades sanitarias permiten el uso del flúor como medida preventiva de la caries dental, un consumo excesivo de este no deja de tener consecuencias negativas. Dependiendo de la dosis consumida, los efectos secundarios pueden producir una toxicidad aguda o crónica.

Por estas razones, en los últimos años, han surgido diferencias en torno al uso de fluoruro. En concreto, en cuanto a los métodos de administración, la edad óptima del paciente, la naturaleza sistemática o no sistemática de la suplementación y la vía de administración elegida.

Esta revisión tiene como objetivo aclarar, con base en la literatura actual, el balance riesgo / beneficio del flúor tópico en niños. Tras revisar su acción y las modalidades de suplementación con flúor, los autores analizan la situación y dan una reflexión sobre su uso racional.

Concluimos que la suplementación con flúor, con el objetivo de prevenir el desarrollo de caries, solo puede iniciarse después de establecer una evaluación personalizada del flúor (realizada por la profesión médica).

Since its discovery in 1886, the chemistry of fluorine has evolved considerably. Its action, widely demonstrated in scientific literature, led the health authorities to widely introduce it as therapy in the prevention of dental caries. This is the reason why fluoride has found his full place in many health products today.

Although health authorities consider the action of fluoride in preventing dental caries to be established, excess fluoride is not without consequences. It may be responsible, depending on the dose, of significant acute and chronic toxicity. For those reasons, differences around the use of fluoride have raised lately, in particular on the administration methods, the optimal age, the systematic or unsystematic nature of the supplementation and the preferred route of administration.

This paper aims to clarify, based on the current literature, the balance benefit/risk of topical fluoride in children. After reviewing its action and the modalities of fluoride supplementation, authors analyze the situation and give a reflection on its rational use.

After a meticulous review of the current literature, it appears that fluoride supplementation, with the aim of preventing caries development, can only be initiated after establishing a personalized fluoride assessment (carried out by the medical profession) and a reasonable prescription following the European guidelines.

II. INTRODUCTION:

A. Context

The prevention of oral diseases is a major public health issue. According to the World Health Organization, it affects around five billion people worldwide, making it the fourth largest global disease in terms of prevalence (1). Oral diseases continue nowadays to be problematic in industrialized and less industrialized countries causing in individuals: pain, functional impairment and reduced quality of life. The management of these pathologies constitutes a significant cost, since they represent 5 to 10% of health expenses in these countries (2) (3).

The development of these diseases is quite recent and is due, among other factors, to the evolution of our lifestyles and particularly the introduction of refined sugar in food (4)(3).

B. Dental caries and Mondial prevention plan

Described since antiquity in the collections of papyri of EBBERS, dental caries is nowadays considered as "a localized, post-eruptive, pathological process of external origin, involving softening of the hard tooth tissue and proceeding to the formation of a cavity" (5). From a pathophysiological point of view, the dental caries is a chronic multifactorial bacterial disease, linked to the presence of cariogenic bacteria that adhere and colonize the dental surfaces. Cariogenic bacteria use carbohydrates as an energetic substrate: through glycolysis, they transform these sugars in organic acids which are ultimately responsible for the dissolution of the inorganic fraction of the teeth. Caries is therefore an acid demineralization process originating from a bacterial infection. It comes across as a loss of tissue first microscopic, and finally macroscopic, revealing a clinically detectable defect. This particular pathological process of necrosis and centrifugal disorganization results in loss of substance and finally to the destruction of the dental organ (6).

In the 21st21st century, social, environmental and lifestyle factors play a great influence on health and especially in oral health. Indeed, tooth decay becomes a major public health problem in industrialized countries affecting 60 to 90% of children and the vast majority of adults. WHO ranks it among the 10 most common chronic diseases in humans (1). It’s also the most prevalent condition included in the 2015 Global Burden of Disease Study, ranking it in the first place for decay of permanent teeth (2.3 billion people) and 12th for deciduous teeth (560 million children) (3).

Although tooth decay is the most common chronic disease in the world, the lack of reliable data is striking. The data available are often obsoleted and/or not representative of a whole country. To solve this problem and standardize the data in the studies, an epidemiological index allowing aa qualitative and quantitative measure of the oral health of an individual /sample of the population, was introduced in 1936 by Klein and Palmer (7). The DMFT 12 index (decayed, missing or filled teeth) measures the caries history of the permanent dentition at the age of 12 (4). Now widely used internationally, this indicator makes it possible to assess and monitor the state of oral health of a population in its majority (8).

Nevertheless, in recent years, the distribution of caries disease seems somewhat disparate in different parts of the world. Indeed, for 30 years, the prevalence decay significantly decreased in the industrialized countries while in others, where the socio-economic level is more precarious, it remains elevated and / or has continued to increase (9). In the early 1980s, WHO and the International Dental Federation (FDI) had already clearly established the objectives to be achieved the year 2000 with the aim of improving the level oral care for children from 6 to 12 years old. If the most of the so-called "favored" countries have largely met these objectives, it is not the case for most of the least developed countries (10).

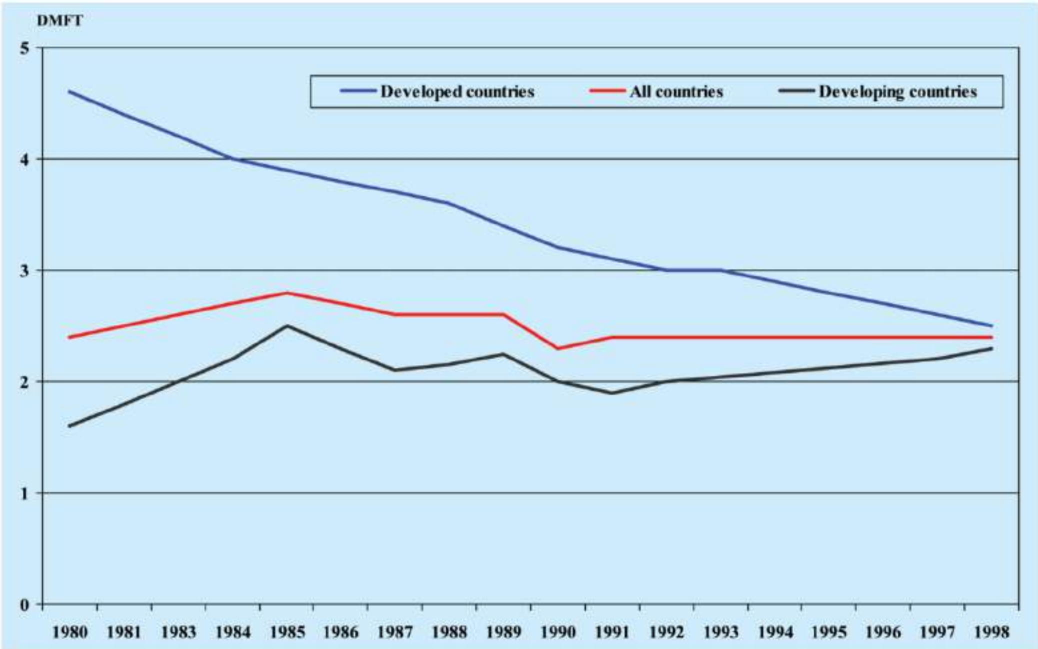

Figure 1. Changing levels of dental caries experience (DMFT) among 12-year-olds in developed and developing countries. The World Oral Health Report 2003: Continuous improvement of oral health in the 21st century - The approach of the WHO.

According to health professionals, the decline of decay in industrialized countries could be explained by the establishment of a new dental philosophy that shifted from “drill and fill” to “prevent and immune” following the evolution of the studies about dental decay process (11). The establishment of the various prevention strategies depends on both individual and group programs. Individual practices bring together oral hygiene habits, eating habits and prophylaxis performed by dental professionals. Collective programs are of two types: collective “active” strategies for individual prevention (promotion of good oral hygiene habits, free diagnosis in some populations..), and introduction of a “passive” supplementation prevention such as the use of fluorinated water (12). This development of new protocol management and discovery of new products conduct to a new preventive vision of dentistry. One of these is based on the use of the anticariogenic properties of fluoride (13).

C. Fluoride (history, chemistry and interest in public health)

Its name comes from the Latin "fluor" - meaning flow - because from the 15th century it was used to facilitate the smelting of ores by reducing the temperature required for the transition of state. Fluoride is an abundant natural oligo-element found in nature in several forms.

It is always combined with other elements and is therefore never found in the free state. Fluorine is found naturally mainly in three minerals: fluorite (or fluorspar) (CaF_2), cryolite (AIF3) and fluorapatite. The mineral which represents the most important source of fluorine is fluorite which is a calcium fluoride (CaF_2). It consists of approximately 47% of fluorine (14).

The discovery of fluoride did not happen overnight. Indeed, a succession of Chemists worked on it for almost a century. It is possible to summarize the history of this discovery in some key dates, beginning in 1886 with the French chemist Henri Moissan (14). He succeeded in obtaining difluor (F2) by producing electrolysis of a mixture of anhydrous hydrofluoric acid and hydrogen fluoride potassium, which earnt him the Nobel Prize for Chemistry in 1906 (15). To appreciate better the issues of this study, it is interesting to understand that the fluorine found in the oral environment can be classified into 5 categories (Figure 2):

—Fo: considered to be the external fluoride, the one found outside the tooth tissue (in the biofilm or saliva).

—Fs: also called fluorapatite, is present in the solid phase of the crystals.

—Fl: in the enamel fluid.

—Fa: on the crystalline surface.

—CaF_2: is the one deposited on the enamel and the biofilm after application of highly concentrated fluorinated products. It acts as a reservoir for fluoride and calcium at a neutral pH (13).

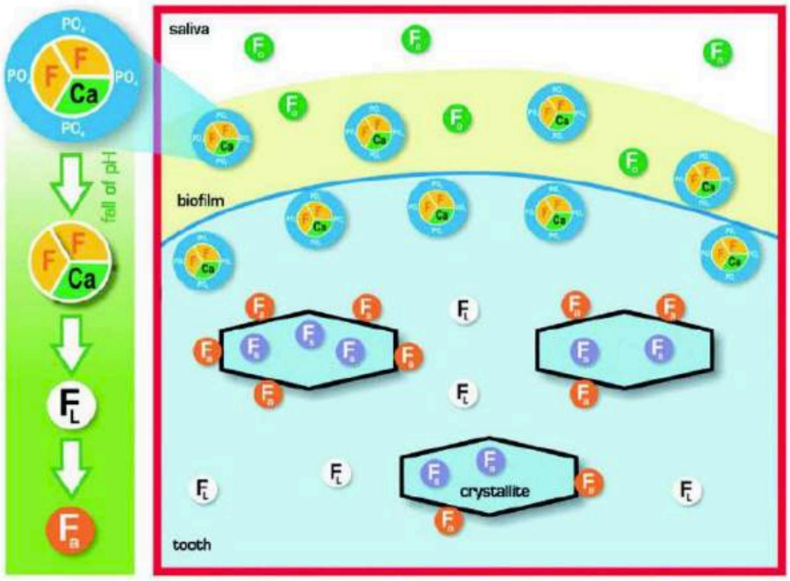

Figure 2 Schematic representation of the different forms of fluoride found in the oral environment (13)

The use of fluoride has recently raised interest thanks to its effectiveness against cavities. Several interesting options from a cost-effectiveness point of view agreed on discussion on making fluoride available to populations. Politically, it rushed governments of several countries to take the opportunity to use it for public health. It can and should be applied depending on regional realities and country laws.

The prophylactic value of fluoride in the prevention of caries disease is scientifically proven (13). Fluoride is now established as the best defense against tooth decay, and water fluoridation is considered by the US Centers for Disease Control (CDC) as one of the most important public health measures of the 20th century (16).

It is therefore essential to optimize fluoride intakes, in order to obtain maximum protection of the child's teeth and a minimum prevalence of secondary risks. This requires following the ideal fluoride recommendations of the WHO (1) and the European Academy of Pediatric Dentistry (EAPD) (17):

⇒ Rapid deposit of maximum amount of fluoride

⇒ Great affinity for the surface layers of the enamel

- ⇒ Sufficient cariostatic activity
- ⇒ Ease of local application
- ⇒ Lowest handling time possible
- ⇒ Absence of deleterious effects at useful does
- ⇒ Chemical stability allowing storage
- ⇒ Bearable costs in all forms of vectors
- ⇒ Cost price compatible with the cost of the fluoride program
- ⇒ Long decline in cario-prophylactic results recorded

These requirements are difficult to meet at the same time, but it can help and guide the practitioner in his choice of fluoride to apply, in terms of efficacy, handling, conservation and toxicity (17).

D. Anatomical reminder and the action of fluoride on the different structures

i. Enamel

a) Definition and structure

Enamel is a mineralized, acellular tissue built up during amelogenesis. It contains over 85% of the mineral element in its mature form, defining it as the most mineralized and hardest structure in the body (13).

It plays a protective role by covering dental crowns and preserving the dentin-pulp complex. And gives teeth their appearance and function in the oral cavity.

Its organization is complex; crystals are organized in prisms and interprismatic substance. Their smallest units (crystal of hydroxyapatite) lean against each other to form crystallites at the base of the enamel microstructure (13). Hydroxyapatite crystals represent 96% of the mass of the enamel, or 85% of its volume (13). This rigorous organization gives enamel a certain strength and resilience, which allows it to respond to the constant biomechanics the oral cavity.

b) Composition

Enamel is an acellular tissue unique to vertebrates. It is formed by major elements, such as: calcium, phosphate, carbonates, sodium, magnesium, chlorine and potassium. And minor elements like fluorine, strontium, and zinc mainly coming from the environmental contamination (18).

Water (12% volume) (13) is mainly present in enamel in two forms: a free form (1% of tissue weight) found in interprismatic spaces and a bound form (2.4% of the tissue weight) forming a protein shell around the crystallites. This hydrated matrix is essential for exchanges and ionic dissemination and is the place where de- and remineralization reactions occur (18). The organic phase represents 0.6 to 1% of the tissue weight in mature enamel or 3% of volume (13). It is composed of residual non-amelogenin proteins and phospholipids. The proteins are mainly glycoproteins different from keratin.

c) Effect of fluor

Recently, studies have revealed that the protection/healing of the enamel is increased in the presence of fluorine. This is explained by various phenomena:

- **Limitation of demineralization** by decreasing the acid-sensitivity of the enamel. When fluoride interacts with the mineral or solid component of teeth, it produces a fluoro-hydroxy-apatite (FHAP or FAP) mineral, where the hydroxyl group (OH-) is substituted by fluoride ions (F). As a result of this reaction, the mineral compound becomes denser, decreasing enamel solubility (11) (18).
- **Enhancement of Remineralization** thanks to the buffering effect of fluorine on the pH of the oral environment. The dissolution of hydroxyapatite in enamel, or

demineralization, takes place when saliva can no longer play its buffering role, and its pH then drops below the critical threshold of 5.5. If this condition arises and fluoride is present even in small quantities, the hydroxyapatite in the enamel is still dissolved, but at the same time fluorapatites are formed (until pH 4.5). Fluoride therefore make it possible to block demineralization by promoting remineralization even at low pH (4.5 <pH <5.5) (19). These fluorapatites thus formed are more stable, less soluble and will therefore be more resistant to acid attacks and caries (13) (11).

- **Re-precipitation of mineral ions on the enamel** and formation of acid-fast layers of calcium fluoride or fluorapatite. The formation of CaF_2 is a two-step reaction. Initially, a slight dissolution of the enamel surface should occur to release Ca^{2+} which, in a second step, will react with the applied fluoride, thus forming CaF_2 globules. These globules precipitate not only on the enamel surfaces but also and especially on the porosities.
- **Bacteriologic regulation.** Although the main action of fluoride on the dynamics of caries is on the processes of demineralization and remineralization, it has been shown that they can also affect the metabolism of bacterial cells (20).

  With decreases in pH, the sensitivity of bacteria to fluoride is increased. Indeed, in acidic conditions, HF (pka = 3.5) will form and will be able to diffuse inside the bacteria. Because the bacterial intra-cytoplasmic pH is more alkaline, HF will go back to its initiate form as dissociate in H+ and F—and exert their action on the bacterial metabolism. The main intracellular targets of fluoride that will be inhibited are enolase (the enzyme of glycolysis), and the "proton pump". They will thus lead to a decrease in the production of acids as well as a decrease in the tolerance of these bacteria to acidic environments (20).

ii. Dentin

a) Aspect

The dentin is a mineralized, non-vascularized connective tissue that represents the most important mass of the tooth. It is yellowish and is responsible for the color of the crown.

Although more mineralized than bone, it is significantly softer than enamel: about 70% minerals and 30% organic components and water. Its coronal part is covered by enamel and the root part is covered by cement. The dentin is traversed by hundreds of thousands of fine canaliculi or tubuli which can reach a density of 50,000 / mm^3.

There are several varieties of dentins depending on the periods in which they are formed: Primary dentin is the mass of dentin formed from the first layer until maturation, the end of the root building. Dentin development then continues throughout life, but at a slower pace; thus, the secondary dentin is formed. Chronic irritations, pathological or therapeutic, are at the origin of tertiary dentin; this can be tubular or amorphous. If secondary dentin settles all the way around the primary dentin, tertiary dentin only forms in the irritated area.

b) Composition

Permanent dentin contains (by volume) 47% apatite, 33% organic components and 20% water (13). The composition of the mineral is similar to enamel in terms of hydroxyapatite compounds but the crystallites have much smaller dimensions giving dentin surfaces a higher susceptibility to caries attack than enamel surfaces. (13).

c) Effect of Fluoride

Fluoride given topically will build up on the outer layer of dentin. As with enamel, fluoride will reduce the solubility of dentin and inhibit its demineralization in a caries lesion.

However, the fluoride concentration required to inhibit demineralization is 10 times greater than that required for enamel.

When demineralization takes place in the presence of fluoride, the outer layer of dentin is retained and the mineral loss from the lesion is deeper (beyond the surface layer). Without fluoride, demineralization leads to the formation of an erosion-type defect, while with fluoride, the lesion is of the sub-surface type (18).

iii. Fluoride incorporation and concentration in teeth

There is no homeostatic balance to maintain a constant concentration of fluoride regardless of the part of the human body. Regular exposure to fluoride (systemic or topical) is therefore necessary to maintain a constant concentration of fluoride in the oral environment and in particular in the dental biofilm. Incorporation of fluoride in all mineralized tissues will vary depending on the actual intake concentration and the length of time during which such an intake has taken place (18).

After the eruption, enamel finish its formation by a phase of maturation that will last up to 2 years. By this time, enamel undergoes an alternation of phases of demineralization and remineralization that will reshape its surface. When the topical fluoride intake is regular, saliva, dental plaque and oral mucous membranes become loaded with fluoride ions. They then constitute a real reservoir of fluoride ions near the enamel surfaces.

In enamel, the highest concentration of fluoride is found at the surface. Then there is a drop in concentration to about 100 µm from the surface and then stabilization up to the enamel/dentin junction. In dentin, the fluoride concentration is overall greater than that of enamel and only increases up to the dentin-pulpal interface. As dentin slowly continues to form over the course of life, fluoride is therefore fixed at this interface. Figure 3.

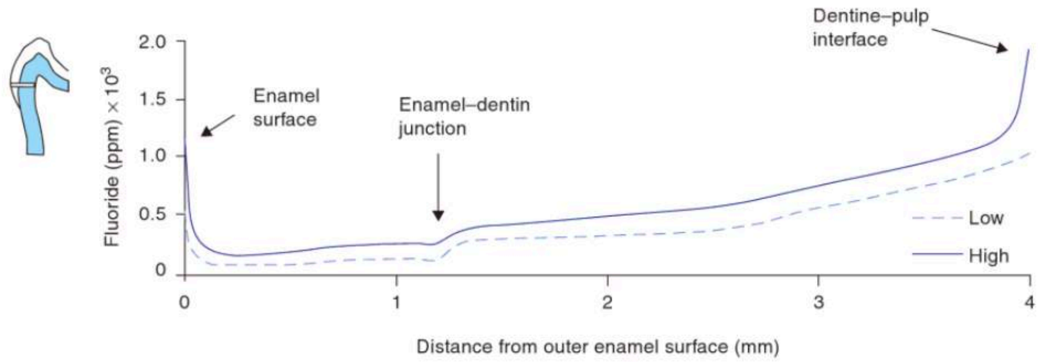

Figure 3. Fluoride concentrations in enamel and dentin, from the tooth surface to the dentin-pulp interface, in subjects with low and high levels of fluoride (18).

E. Topical application and its different administrable forms

Oral topical products are considered to be drugs intending to act locally/externally on soft tissues (skin, mucous membranes) or hard tissues (enamel, dentin) of the orofacial sphere.

Topicals are composed of one or more active ingredients incorporated into an excipient intended to ensure their retention on the treated surface and/or to promote their local penetration. Their action in the affected areas is immediate. However, their contact at target areas is limited in time, hence a renewal of their application is necessary (19). The different topical applications of fluor will be later detailed in this project.

The action of fluoride is located at two levels: the systemic route, during the mineralization of the teeth, and the topical route, after the eruption of the teeth.

—The systemic or general route aims to incorporate fluoride into dental tissues during their formation. It involves phenomena related to the metabolism of fluorine in the body: absorption, diffusion of fluorine driven in biological fluids up to mineralized tissues (skeleton and teeth in the process of mineralization) where it is captured, because of its great affinity for calcium.

The prophylactic action of fluoride by the systemic route will therefore be essentially effective during the development of tooth germs (19).

—The topical or local route involves interactions between fluoride and dental surfaces and their environment. The topical route therefore occurs when the teeth have erupted.

These two pathways are interdependent and complementary. In fact, products administered orally (tablets for example), will have a certain topical action due to their intra-oral transit even if it is brief (19). In addition, part of the fluoride ingested is excreted in the salivary glands and released into the oral cavity, resulting in a secondary topical action. Reciprocally, products with topical action, when they are partially ingested, will be conveyed systemically. Especially in the very young child.

In Germany, Künzel and Fisher (1997) studied the prevalence of caries in two German cities, and correlated it with the fluoride content of ingested water. During the first thirty decades, the prevalence of caries was in correlation with the fluoride concentration in the water. However, since the end of the 1980s, a significant decrease in caries has been verified while the water was only very slightly fluoridated. One of the reasons put forward is the wide availability of products containing fluorine, which compensates the absence of water fluoridation.

Contemporary studies conclude that the “preventive” effect of fluoride on caries lesions is almost exclusively post-eruptive. In addition, epidemiologists are now questioning the scientific validity of old studies on fluoride (systemic effect). The concept of the post-eruptive effect of fluorine is, on the other hand, supported by in vitro and in situ research demonstrating that the mode of action of fluorine can be mainly attributed to its influence on the processes of de- and re-eruption. Mineralization of calcified tissue. Thus, the application of topical fluoride should be encouraged (21). It reduces dental caries by, on average, 26% (22).

i. Professional application

a) Aqueous solution and varnishes

There are mainly three types of fluoride solutions: 2% sodium fluoride (NaF), 8% or 10% stannous fluoride (SnF_2) and acidulated phosphate-fluoride (FPA). While citric acid causes solubilization of the constituent hydroxyapatite of the enamel, the fluorinated salts, for their part, reduce this solubilization phenomenon, thus allowing an anti-caries effect. (23) (19)

This technique involves applying a fluoride solution to the teeth (previously cleaned and isolated from saliva), using a small brush (19). Their effectiveness increases with the number of applications (from 1 to 4 applications per year) (23).

Studies have proven the effectiveness of these fluoridated solutions in preventing dental caries and also in stopping certain caries lesions with reductions of 30% to 40% in their incidence (23).

Fluorinated solutions are used less and less, because unlike fluoride varnishes, the product does not bind to the tooth and is therefore in contact with it for less time (23).

Their use is exclusively professional; the practitioner will apply the product to the teeth (previously cleaned and isolated from saliva) using the material provided by the manufacturer of the product (24). Depending on the varnish, the concentrations vary from 1000 ppm of fluoride (difluoro silane) to 56,300 ppm of fluoride (sodium fluoride/calcium fluoride 6%). The most widely used is sodium fluoride (NaF) varnish at 5% and 22,600 ppm of fluoride (X-Pur, Halo Duraflor...) (25) (11).

The varnish allows prolonged contact with the tooth surface and thus allows better penetration of the product. It was developed in order to adhere to the surface of the enamel for extended periods of time (up to 12 hours and more) in order to slowly discharge their fluoride towards the teeth while shortening the patient presence time in the chair.

Numerous studies have proven the effectiveness of fluoride varnishes in preventing or even intercepting dental caries (25) (26). As the risk of ingestion is limited and controlled by the practitioner, varnishes can be used on children under 6 years old but their use keeps still reserved for children who have a high individual caries risk (24) (22). The safety, effectiveness, speed and ease of use of fluoride varnishes award them an advantage over other fluoride topicals (24) (22).

b) Gel

Fluorinated gels are composed of acidulated phosphate fluoride (1.23% [12 300 ppm] fluoride), as 2% % neutral sodium fluoride compounds (containing 9,000 ppm fluoride), and as gels or foam of sodium fluoride (0.9% [9 040 ppm] fluoride) (27) (11).

The practitioner makes an individual thermoformed plastic splint perfectly fitting the patient's teeth, then incorporates a fluoride gel into the tray. He positions the tray into the mouth, holding it for 4 minutes (11). Once the time has elapsed, the practitioner removes the tray and the patient spits out the gel. It is recommended that you do not eat or drink within 30 minutes of applying the gel to prevent the patient from ingesting fluoride and to allow the product to act on the tooth as long as possible (27). This operation is to be carried out twice a year. It is indicated in cases of high individual caries risk (22).

The use of these procedures has been shown to reduce the amount of inadvertently swallowed fluoride to less than 2 mg, which can be expected to be of little consequence (28). However, it is not recommended the use of gels <6 years of age because the ratio benefit/risk balances to risk due to the danger of swallowing (17). Nowadays the use of these gels has mostly been replaced by the use of fluoride varnish (28).

ii. Self-application

a) Dentifrice

Fluoride dentifrices represent an unmatched method in their simplicity of use. Inexpensive, accessible to all, and with a widely proven effectiveness , it constitutes nowadays the very basis of oral hygiene for most people in developed countries (29). Many scientific authorities believe that the fall in caries prevalence during the last twenty-five years in most industrialized countries has been greatly conditioned by the extension of use of fluoridated toothpaste (29).

The primary function of a toothpaste is to supplement the mechanical action of brushing in the removal of dental plaque, debris and stains thanks to its different properties:

—**Therapeutic:** it eliminates dental plaque and inhibits its formation, reduces tartar deposits, polishes and cleans teeth by removing extrinsic stains and reduces mouth odor. When it contains specific active agents, it may have an anti-inflammatory or desensitizing action and thus increase resistance tissue, aid in the treatment of periodontal disease, treat dentinal hypersensitivity and remineralize superficial caries.

—**Cosmetics:** it should provide a feeling of cleanliness and freshness after use. This has a direct bearing on consumer psychology (30).

Although commercially available toothpastes appear, at first sight, to have very different chemical formulas, it always consists of a mixture of water and a number of agents present in a relatively constant amount. These agents give the product its consistency, its stability during storage or its taste. On the other hand, the active ingredients, which give the toothpaste its therapeutic or preventive properties, are present in variable concentration (30). Fluoride, nowadays present in almost all toothpastes, appears to be the major active ingredient.

There are two types of fluoride found in the composition of toothpaste:

—Mineral or inorganic fluoride (sodium, tin, potassium fluoride and sodium monofluorophosphate). They have multiple properties: they are cryostats, antibacterial and desensitizers, which makes them particularly useful in the treatment of periodontal disease and dentinal hypersensitivity.

—Organic fluoride (amine fluoride and nicomethanol hydrofluoride). They decrease the solubility of enamel as well as inhibit the formation of bacterial plaque (21).

b) Mouthwash

Fluoride mouth rinses are available for several decades as solutions containing 0.05% NaF (~226 ppm F) or acidulated phosphate fluoride (APF) for daily use; and 0.2% NaF (~900 ppm F) solutions for weekly use (19).

Their use is reserved for children with moderate/high caries risk and is complementary to brushing and the use of fluoride toothpaste (27). It achieves a modest reduction in caries compared with toothpaste used alone (28). It is not recommended for children under six years of age, since they cannot control the muscles for swallowing and might not be able to spit. prescribe. (19) (29) (27).

c) Gel

Fluoride gels are prescribed by the practitioner and are applied by the patient at home.

They are currently available as APF and neutral NaF products, containing 1.1% NaF (5 000 ppm F ion) (27).

They are indicated in the case of a highly individual caries risk or in patients under radiotherapy.

The protocol is the same as for the fluoride gel administered in the office. The practitioner will deliver individual thermoformed plastic trays and the patient, at home, will place the fluoride gel in the tray before placing it in the mouth for 4 minutes (27). For children, the supervision of the parents is mandatory to avoid any risk of ingestion (17) (27).

F. Balance benefit/risk

For healthcare professionals, choosing the best intervention among the various existing options is a crucial step before any act. It's defined—safe—by Oxford Dictionary: "protected from or not exposed to danger or risk; not likely to be harmed or lost". Medicines, developed with the aim of providing benefits, are never without side effects, zero risk does not exist. When a drug obtains a marketing authorization (MA), it has been concluded that, in the indications for which it is to be administered, the benefits expected must be greater than the expected risks (31). This is the reason why a drug is mainly characterized by the relationship between the benefit of the patient and/or for public health and the risks of side effects which may occur. This work will use this balance as a reference.

III. OBJECTIVES:

The aim of this exercise is to clarify, according to the dedicated and careful study of recent papers, the ratio benefice/risk of topical fluoride in the population of children. By this means, the review will be articulated in different parts: the first ones (present in the results section of the study) help understanding the issues exposed in the discussion. On the one hand, it will highlight the benefit established for a long time of fluoride in public health and confront it on another hand to its side effect and misuse. Finally, the study of all those positive and negative effects of fluoride will guide the review to discuss the balance benefit risk of fluoride, taking into account the safety considerations related to the use of this product. To achieve these major objectives, this project aims to develop a comparative review of the current literature about the use of topical fluoride in children. It is intended that the research findings will contribute to prove the importance of an appropriate and reasonable use of fluoride products but also its importance in clinical treatment. The research project also tends to explore how we can overcome the obstacles created by this health product.

Principal objective:

- To gather information from the literature and develop an up-to-date benefit-risk ratio of the use of topical fluoride in children.

Sub-objectives:

- To determine the clinical effectiveness of fluoride
- To evaluate the incidence of adverse effects and their manifestations
- To suggest rules for a correct usage of fluoride

IV. MATERIAL AND METHODS:

To achieve this goal, a literature review method has been chosen, which allows for a complete and synthesized research and helps obtain conclusions from this theme. To produce this review, six steps were used. Firstly, the guiding questions had to be defined in order to select articles. The second step was the definition of information to be extracted from selected articles and the analysis of the included studies and interpretations of results. At the end, the integrative review opened to a discussion, balancing the research. The literature review has been carried out online in the period from 1970 to 2020. The search was based on the following keywords: topical fluoride - children—child, topical application of fluoride - children—child, topical fluoride for toddlers, topical fluoride, topical fluoride varnish, topical fluoride for caries prevention, topical application of fluoride, topical application of fluoride varnish, topical fluoride treatments, topical fluoride gel, topical fluoride varnish, topical fluoride applications, topical fluoride treatment, topical fluoride definition, topical fluoride application procedures. The primary search was made using the online databases MEDLINE, PUBMED and the e-library of the UEM (Universidad Europea de Madrid). The combination of the keywords resulted in 103 publications. The criteria used for selecting the sample were: complete articles published and available online, open access, articles with abstract for initial assessment and studies written in English. The population studied is focused on children; it is agreed for that reason that only children from 0 to 18 have been assessed and therefore only articles treating this range of age have been studied. Also, as the studies evolve regularly, it was found convenient to select the articles based on the date of publication and focus more on new information. Of these last articles, 33, 21 studies were used to build the introduction of this study. To finalize the search, 37 additional reading texts were added to assist in understanding the subject. Thus, 59 publications were included in the review. Documents and articles considered interesting were downloaded in adobe pdf format, and were gathered within the Mendeley software. The files have been divided into categories, and their most important information was collected. The bibliography was then automatically integrated in the thesis Word document, in Vancouver format

V. RESULTS

A. Beneficial effect of fluoride

i. Direct repercussion: reduction in number of caries

a) Effect of fluoridation of drinking water

The great diversity of fluoride concentrations naturally encountered in drinking water has provided ethical opportunities to study and determine the relationship between the frequency of dental caries and fluoride intake. For decades, the efficacy and safety of fluoridation has been extensively studied and we now have over a thousand reports on the biological properties and their effects on bones and teeth (5).

In this regard, the United States of America deserves special mention as more than 3 million people live in communities where the content of natural fluoride in drinking water is equal to or greater than 1.0 mg of fluoride per liter. In this country Dean and his collaborators carried out meticulous epidemiological surveys involving 21 cities. In this series of works, 7,257 children between the ages of 6 and 14 were examined (32–34).

The first main experiment in controlled fluoridation of an urban water distribution system began in 1945 in Grand Rapids, Mich. (United States) (33); followed shortly after by further trials in Newburgh, New York (USA) (34), and in Brantford, Ontario (Canada) (32). In each of these cases, a sufficient fluoride amount was added to bring the concentration to 1.0-1.2 mg fluoride per liter, and a control zone was used as a comparison. The studies were carefully planned and monitored and the effect on general health were studied.

One of the first studies (1957), conducted over 15 years in Grand Rapids, Michigan, was planned for a period of ten years. This time allowed the first teeth and most of the permanent teeth to be subjected to the action of fluoride throughout their period of development and mineralization and let them be expose for a few years to the appearance of caries. It appeared that children who drank fluoridated water from birth suffered from 50 to 63% fewer cavities than those in localities where the drinking water was not fluoridated. Among those who were aged two years and under when the measure was adopted, cavities were 48–50% rarer than in the youth in the group control (33).

Table 3—General Comparison of Dental Caries Experience Rates for Deciduous (def) and Permanent (DMF) Teeth After 10 Years of Fluoridation in Grand Rapids, Mich., Brantford, Ont., and Newburgh, N. Y.

(Data from References 9–11)

Age (Last Birthday)	Grand Rapids, Mich. No. Children Examined		Per cent Reduction Caries Rate		Brantford, Ont. No. Children Examined		Per cent Reduction Caries Rate		Newburgh, N. Y.[1] No. Children Examined	Per cent Reduction Caries Rate
	1944	1954	def	DMF	1944	1955	def	DMF	1954 1955	DMF
6	1,789	561	54	75	556	485	57	60		
7	1,806	751	48	63	616	448	52	67	708	58
8	1,647	567	43	57	614	483	43	54	(6–9 yrs.)	
9	1,639	477	35	50	608	423	34	46		
10	1,626	515	17	52	565	301	33	41		
11	1,556	499	2	54	604	280	−2	39	521	53
12	1,685	260	—	52	658	336	—	48	(10–12 yrs.)	
13	1,668	224	—	48	531	247	—	42	263	48
14	1,690	250	—	38	307	93	—	36	(13–14)	
15	1,511	240	—	35 }	105	37	—	35	—	—
16	1,107	198	—	26 }					109	41

1. Results based on difference between Newburgh and Kingston after 10 years fluoridation and include both clinical and roentgenographic findings.

Figure 4 General Comparison of Dental Caries Experience Rates for Deciduous (DEF) and Permanent (DMF) Teeth After 10 Years of Fluoridation in Grand Rapids, Mich., Brantford, Ont., and Newburgh, N. Y.

On another experiment, in Newburgh, New York, in 1989, a vast program of pediatric research was also included. Children aged 4 to 15 were subjected to extensive dental examinations; these examinations were carried out for the first time before water fluoridation and were then repeated each year. the number of cases of dental caries in the areas benefiting from fluoridation was compared to the control group (Kingston, in the same state, where the water is deficient in fluoride). Ten years after fluoridation, the caries rate in children aged 6 to 9 of Newburgh, was 58% lower, compared to children of the same age in Kingston. In older children who had consumed fluoridated water for only a few years, the frequency of cavities was 41% lower than among young people who had not consumed fluoridated water. In

Newburgh, the 13–14 year old group had, after 15 years of fluoridation, a decay rate which was 70% lower than a similar group in the city of Kingston (34).

In a last study in Brantford, Ontario, adolescents aged 12 to 16 presented in 1959, 40% fewer cavities than young people their age in 1948 (date prior to fluoridation (32).

While it is well known that there are fewer decayed, absent or filled (CAD) teeth in children in fluoridated localities, it is often not known that the beneficial effects of this measure persist. According to several surveys, the number of adolescents free from cavities has increased considerably in the past 30 years. If we trust the most cautious, 20% of them should be in this case in agglomerations where drinking water is fluoridated, in other words six times more numerous than in hypo fluoridated localities.

b) Effect of brushing with a fluoride toothpaste

The authors of the Cochrane Group conducted a review up to date in 2018 (29). The review includes 96 studies: seven studies with 11,356 randomized participants reported the efficiency of toothpaste with fluoride concentrations up to 1,500 ppm on primary dentition; a study with 2,500 randomized participants reported the effects of toothpaste at 1,450 ppm fluoride on primary and permanent dentition; 85 studies with 48,804 randomized participants reported the effects of toothpaste at 2400 ppm fluoride on the permanent dentition of children aged up to 18 years; and three studies with 2675 randomized participants reported the effects of toothpaste with a concentration of 1100 ppm fluoride on the permanent teeth of adults. Most studies assessed the presence of tooth decay after 36 months of participants use of toothpaste.

In the primary dentition of young children, brushing teeth with toothpaste containing 1500 ppm fluoride reduced the development of new cavities compared to toothpaste without fluoride; the number of new cavities was similar with toothpaste having 1055 ppm fluoride compared to toothpaste having 550 ppm fluoride; and there was a slight reduction in the number of new cavities with toothpaste having 1450 ppm fluoride compared to toothpaste having 440 ppm fluoride.

On permanent in children and adolescents, it was found that there was less new cavities with the use of toothpaste containing 1000 to 1250 ppm or 1450 to 1500 ppm fluoride compared to non-fluoridated toothpaste, and brushing teeth with toothpaste containing 1450 to 1500 ppm fluoride reduces more the number of new cavities compared to using a toothpaste containing 1000 to 1250 ppm fluoride. We have seen a similar number of new cavities when children and adolescents used toothpaste containing 1700-2200 ppm fluoride or 2400-2800 ppm fluoride compared to toothpaste with 1450-1500 ppm fluoride (29).

c) Effect of applying a fluoride vanish

A review carried out by the Cochrane Oral Health Group screened 12,455 randomized children to receive treatment with fluoride varnish or placebo / no treatment (26). It appeared that the evidence produced is of moderate quality due to problems with the study designs. However, in the 13 trials that looked at children and adolescents with permanent teeth, the review found that youth treated with fluoride varnish experienced an average 43% reduction in decayed, missing, and filled tooth surfaces. In the 10 trials that examined the effect of fluoride varnish on deciduous teeth, evidence suggests a 37% reduction in decayed, missing and filled tooth surfaces (26).

d) Effect of applying fluoride mouthwash

In a study including more than 15,000 participants, children (ages six to 14) were treated with either fluoride mouthwashes, placebo (a mouthwash without the active substance) or did not receive treatment. Most children received sodium fluoride (NaF) solution, given at a concentration of 230 parts per million fluoride (ppm F) daily or at a higher concentration of 900 ppm F weekly or fortnightly. The studies lasted from two to three years (35).

This updated review confirmed that regular use of fluoride mouthwashes under supervision can limit the onset of dental caries in children and adolescents. The combined results of the 35 trials showed that, on average, there was a 27% reduction in decayed, missing and filled surfaces of permanent teeth with fluoride mouthwash compared with placebo or no mouth. This benefit is likely to be present even if children use fluoride toothpaste or liv -in areas where the water has been fluoridated. The combined results of 13 trials showed an average of 23% reduction in decayed, absent, and filled teeth (rather than tooth surfaces) on permanent teeth with fluoride mouthwashes compared with placebo or absence of mouthwashes (35).

ii. Indirect repercussion: reduction in the need of restorative treatments

The Decayed, missing (from tooth decay), filled teeth (DMFT), and Decayed, missing (from tooth decay), filled surfaces (DMFS) constitute indices of total caries. Thus, any decrease in these indices must result in a decrease in the number of restorative treatments and extractions. A study of the effects of fluoridation on childhood dental care was performed in Gainesville, Florida, USA, between 1954 and 1959 (37). Controlled fluoridation already existed in Gainesville for 4 years and 2 months when the study was undertaken. In the first round of dental care treatments, 35% of white children and 54% of black children between the ages of 5 and 16 had been consuming fluoridated water for about 5 years. The effect of fluoridation was manifested by a constant decrease in the DMF indices measured during successive rounds of treatment, while in the non-fluoridated water supply towns of Richmond and Woonsocket, the CAD indices remained relatively constant. Treatments for white children fell from an average of 2.9 temporary and permanent tooth fillings and 0.2 extractions per child in the first round of treatments to 1.7 fillings and 0.1 extraction in the fourth series. In black children, treatments were reduced from 2.1 fillings and 0.3 extraction on average per child in the first round of treatments to 1 filling per child and no extraction in the fourth set. In the city of Woonsocket, not supplied with fluoridated water, 4.67 fillings of temporary and permanent teeth had been done and 0.90 extractions on average per child during the first series of treatments (36).(36)

From these observations, we can note that:

a) The fluoridation operation carried out for 4 1/2 years in Gainesville resulted in a 38% (1.77) reduction in the number of fillings needed per child, and a 78% reduction (0, 7) in the number of extractions required per child at the time of the first treatment.

b) After an additional 30 months of fluoridation, plus a full course of treatment, the gain in Gainesville, compared with the town of Woonsocket which did not benefit from fluoridation, amounted to 3.94 fillings per child (reduction of 66%) and 0.61 extraction per child (reduction of 75%) (36).

iii. Optimal dose for optimal benefits

The optimal daily dose of fluoride is the total amount of fluoride from various sources that can be ingested daily and provides protection against tooth decay while minimizing the risk of dental fluorosis. Dental fluorosis is a dysplasia (alteration in the development of structure and color) of teeth that occurs as a result of chronic fluoride poisoning during the period of tooth development occurring usually between birth and the age of 6 to 8 years (37)(38).

This dose has been defined for decades between 0,05 and 0,07 milligrams of fluoride per kilogram of body weight and per day (mg/kg/day) (13).

The origin of the optimal daily dose of fluoride is attributed to McClure, who in the 1940s believed that the daily food intake contained between 1.0 and 1.5 mg of fluoride and thus provided approximately 0.05 mg / kg / day in children aged 1 to 12 (38). Since the 1980s, the dose of 0.05 to 0.07 mg / kg / day is used as a recommendation for the optimal daily intake of fluoride (39). The optimal daily dose of fluoride has also been the subject of studies and research by Health Canada and by the United States Environmental Protection Agency. According to these organizations, with exposure to a daily dose of fluoride less than or equal to 0.122 mg / kg / day, it is unlikely to have moderate to severe dental fluorosis. The origin of the optimal daily dose of fluoride is attributed to McClure, who in the 1940s believed that the daily food intake contained between 1.0 and 1.5 mg of fluoride and thus provided approximately 0,05 mg/kg/day in children aged 1 to 12 (38). Since the 1980s, the dose of 0,05 to 0,07 mg/kg/day is used as a recommendation for the optimal daily intake of fluoride (39). The optimal daily dose of fluoride has also been the subject of studies and research by Health Canada and from the United States Environmental Protection Agency. According to these organizations, with exposure to a daily dose of fluoride less than or equal to 0.122 mg/kg/day, it is unlikely to have moderate to severe dental fluorosis.

In addition, a longitudinal study published in 2009, was conducted to assess the optimal daily dose of fluoride (40). In this study, the authors evaluated the amount of fluoride ingested by 9-year-old children without dental fluorosis in permanent dentition or decay in primary and permanent dentition. The authors observed that children who had consumed slightly less than 0,05 mg/kg/d of fluoride had dental decay, while those who had generally consumed just over 0,05 mg/kg/d of fluoride exhibited fluorosis. The authors thus evaluated that the optimal mean daily dose of fluoride in young children during the first 48 months of life was of 0,05 mg/kg/day or less (38) (40). However, this study, which is the only recent assessment of the optimal daily dose of fluoride, has certain limitations, which are attributable to the great variability of individual fluoride intakes.

B. Negative repercussion of the misuse of fluoride

i. Acute toxicity

A single large dose of fluoride, i.e., one teaspoon of pure sodium fluoride (5 to 10 mg) causes death within 2 to 4 hours (reference).

The greatest morbidity and mortality from fluoride poisoning has occurred in the Oregon State Hospital, the USA. Powdered milk has been mistaken for a fluorine-based insecticide when preparing scrambled eggs. 263 cases of acute poisoning were reported including 47 deaths (41).

a) Intoxication

Most cases of acute poisoning in humans described in the literature are associated with accidental or deliberate ingestion of insecticides and other fluorinated products for domestic use. The most important scandal surrounding fluoride poisoning was the one of the Meuse Valley in the 1930s. Between the years 1873 to 1935, thousand cases of acute pulmonary attacks occurred. At first unclear, Roholm was one of the first pointing between the neighboring fluorine industry and the poisoning of this population. In total, Roholm reviewed 1211 cases which occurred in this period. Of this total, 60 fatal cases (42).

More recently, acute fluoride poisoning has been reported in humans by several authors. In the most detailed analysis of the American Association of Poison Control Centers it's indicated that of all reported cases of fluoride intoxication, 68% were related to fluoride dentifrice ingestion, 17% to fluoride mouth rinses, and 15% to fluoride supplements. Also, the proportion of children younger than 6 years old reported for fluoride intoxication account for more than 80% of all the reports (37). In the report of 2009, while 1146 patients were suffering from minor bothersome sign or symptoms, 378 cases of fluoride intoxication landed to emergency rooms (43).

Reports to Poison Control Centers in U.S.
Due to Excessive Ingestion of Fluoride Toothpastes
Data from: Bronstein (2009, 2010) & Watson (2003)

Year	Product	# Reports	# Treated in Emergency Room	Medical Outcome*				
				None	Minor	Moderate	Major	Death
2009	F Toothpaste	24,547	378	4,781	1,146	42	2	0
2008	F Toothpaste	23,468	383	4,395	1,119	43	1	0
2002	F Toothpaste	24,087	411	4,852	1,218	40	1	1

* ***Minor effect:*** Minimally bothersome signs or symptoms that generally resolved without residual disability or disfigurement (e.g. self-limiting gastrointestinal symptoms). ***Moderate effect:*** More pronounced or prolonged signs or symptoms, or more of a systemic nature than minor systems. While the symptoms are not life-threatening (e.g., disorientation or high fever that responds readily to treatment), some form of treatment is indicated. ***Major effect:*** Signs and symptoms that are life-threatening or result in significant residual disability or disfigurement. (Shulman and Wells 1997)

Figure 5. Reports to Poison Control Centers in the U.S.

In acute poisoning, all organs and systems can be potentially affected. Symptomatic manifestations include vomiting (sometimes bloody), diffuse abdominal pain of spasmodic type, diarrhea, cyanosis, severe asthenia, dyspnea, muscle spasms, paresthesia and paralysis, cardiovascular disorders, convulsions and coma (37)(38).In acute poisoning all organs and systems can be potentially affected. Symptomatic manifestations include vomiting (sometimes bloody), diffuse abdominal pain of spasmodic type, diarrhea, cyanosis, severe asthenia, dyspnea, muscle spasms, paresthesia and paralysis, cardiovascular disorders, convulsions and coma (37) (38).

In acute fluoride poisoning, death occurs generally as a result of blockage of the normal cell metabolism. Fluoride inhibits enzymes involved in essential processes, leading to the dysfunction of vital and non-vital functions through bad generation and transmission of nerve impulses. These symptoms result in generalized or localized muscle tetany especially of hand and feet (44). The disruption can be even more important if it gets linked with functions regulated by calcium. Indeed, the strong affinity of fluorides for calcium results in impressive hypocalcemia and ultimately results in inhibition of physiological nerve functioning (44). Fluorides can also combine with other metal ions and block various biochemical mechanisms (proteolytic and glycolytic enzymes) contributing to an electrolyte imbalance, a state of hypovolemic shock, and decreased blood pressure (44). Furthermore, hyperkalemia or ventricular fibrillation are also linked with fluoride toxicity, which may result in ventricular arrhythmias and cardiac arrest. Massive functional impairment of vital organs leads to cell damage and necrosis characteristic of a shock syndrome.

Not all of the compounds of fluoride are equally toxic. The toxicity will depend on the mode of penetration in the organism and the physico-chemical properties of the compound. Also, the symptoms won't be the same according to the patient, the age/weight, and the elapsed time between the exposure and the beginning of management of the intoxication (44).

Fluoride is considered toxic with a minimal dose of 5 mg/kg body weight and the lethal dose of fluoride has been set at 15 mg/kg. (42.45) But those values need to be nuanced; if a child ingests a dose of fluoride in excess of 15 mg F/kg, death is likely but a dose as low as 5 mg F/kg can also be fatal in some children. Thus, the probable toxic dose (PTD), defined as the limit does that can cause serious and potentially fatal signs and symptoms, and which requires emergency medical treatment as well as hospitalization, is 5 mg F/kg.

The probably toxic doses are estimated for each dental health product. If these doses are exceeded, emergency treatment and hospitalization are necessary:

- ➔ Toothpaste at 1500 ppm, ingestion of 33g by a one year old child (importance of learning to sputum) (46) (38)
- ➔ Fluoride tablets: ingestion of 50 tablets (46).
- ➔ Topical gels: in general, 1.2 to 6.5g are applied by the practitioner, but a quantity of 5g (123mg of fluoride) corresponds to twice the probably toxic dose in a two-year-old child. Toxicity is reached if the child swallows half of this gel! Symptoms of toxicity may appear in a 10 kg child after ingestion of a teaspoon (5mL) of topical gel professional (38).Topical gels: in general, 1.2 to 6.5g are applied by the practitioner, but

a quantity of 5g (123mg of fluoride) corresponds to twice the probably toxic dose in a two-year-old child. Toxicity is reached if the child swallows half of this gel! Symptoms of toxicity may appear in a 10 kg child after ingestion of a teaspoon (5mL) of topical gel professional (38).

➔ Mouthwash: 500ml of 0.005% fluoride mouthwash contains 122mg of fluorine. This is 2.4 times the probably toxic dose for a child weighing 10 kg (about one year) if he ingests this amount (46).

ii. Chronic toxicity

a) Dental fluorosis

Fluoride plays a key role in the prevention and control of tooth decay. Fluorosis has therefore been considered a "side effect" of benefits of prevention and protection against decay provided by fluoride. Indeed, until the 1990s, the toxic effect of excess fluoride on teeth was considered as a "cosmetic" problem(47). (47)

Dental fluorosis is a dysplasia (alteration in the development of structure and color) of teeth that occurs as a result of chronic fluoride poisoning during the period of tooth development occurring usually between birth and the age of 6 to 8 years (37) (38).

During fluorosis, there is a decrease in the activity of matrix proteases, which leads to a buildup of proteins (especially amelogenins) during the maturation phase of the fluorotic enamel. This retention of amelogenins will delay the final mineralization phase of enamel matrix, resulting in the formation of subsurface hypo-mineralization characteristic of fluorotic enamel (39).During fluorosis, there is a decrease in the activity of matrix proteases, which leads to a buildup of proteins (especially amelogenins) during the maturation phase of the fluorotic enamel. This retention of amelogenins will delay the final mineralization phase of enamel matrix, resulting in the formation of subsurface hypo-mineralization characteristic of fluorotic enamel (39)

It appears clinically as stains of the enamel (Figure 6), ranging from mottled areas to mottling, streaking, diffuse opaque bands overlaying a chalky white or brown/black background. The dark coloration would be post-eruptive by incorporation of extrinsic materials in the enamel porosities. Fluorosis also presents as a sink in severe forms, following loss of surface enamel (48). The opacities appear in the form of bands following the lines of development of the enamel and present a certain symmetry with the contralateral tooth.

Figure 6 Whitish spots included by fluorosis (Naulin-Ifi, 2011) Include complete reference

Investigation of the different sources of fluoride ingestion will confirm the clinical diagnosis. A fluoride assessment is carried out through questioning of the parents and makes it possible to highlight one or more sources of fluoride in accordance with the clinical signs. The period, duration of ingestion and the accumulation of fluorinated sources confirm the diagnosis: the affected surfaces correspond to the mineralization phases.

The Dean's Index is the historical index, it has been and still is widely used. It has six levels, classifying the appearance of fluorotic enamel from "normal" to "severe". Its limitations are that it is too vague for the lower levels of fluorosis and that it lacks sensitivity for fluorosis of the "severe" level. Moreover, it does not give information regarding the number of affected teeth (18). The clinical examination is first performed by examining both arches as a whole to determine the presence or absence of fluorotic lesions. If these are detected, the score for the person examined is based on the two most affected teeth.

- **Normal 0**

The enamel exhibits its usual translucency.

- **Doubtful 1**

In endemic areas with a prevalence of more than 75% of fluorosis, it is sometimes difficult to determine if the enamel is normal or has very low fluorosis. In this case, the examiner classifies the subject as “doubtful”. Typical “doubtful” lesions appear as thin lines, or irregular opaque white spots in the incisal third of the upper incisors.

- **Very low 2**

Presence of small opaque white areas irregularly arranged on the surface of the tooth. These spots are found mainly on the buccal and lingual surfaces and occupy up to 25% of the surface of the affected tooth.

- **Low 3**

White opaque areas occupy at least half of the tooth surface. Posterior tooth surfaces are prone to attrition and show fine white streaks. Light brown spots are sometimes visible, usually on the upper part of the incisors.

- **Moderate 4**

There is no change in the shape of the tooth, but all tooth surfaces are generally affected. The attrition surfaces are marked. There is a frequent presence of brown spots and pits on the vestibular surfaces. Colors vary from light brown to chocolate and take up no more than half of the surface.

- **Severe 5**

The hypoplasia is so marked that the shape of the tooth is sometimes affected. Older children have a slight incisal or occlusal abrasion. The wells are deep and confluent, which results in loss of surface enamel and gives a corroded appearance to the tooth. The spots are extensive and range from a chocolate brown to almost black color.

The severity of the alterations is multifactorial and depends on the dose ingested, the time of exposure (phase of enamel formation), the duration of impregnation and the variability between individuals. Thus the amount of fluoride exposure necessary to cause dental fluorosis is largely unknown (38).

Prevalence comparison of the different studies carried out in Europe is difficult because of the differences in water consumption, climate, diet, standard of living and availability of fluoride sources. In addition, the studies use different methods and indices. Many biases are possible: inter and intra-examiner bias, drying and cleaning of teeth, type of light used. However, the overall results tend to show an increase in the prevalence of fluorosis and diffuse opacities in fluoridated areas (48). When fluoridated supplements like fluoride tablets are used in non-fluoridated areas, the prevalence of fluorosis and opacities approaches that of fluoridated areas (49).

Unlike decay, dental fluorosis is not a public health problem, however, its aesthetic damage justifies prevention. This is a dental damage that can easily be avoided carrying out a personalized fluoride checkup and educating parents about the child's exposure to fluoride agents ensures this prevention.

b) Skeletal fluorosis

Chronic exposure to high levels of fluoride can cause bone fluorosis, which results from the gradual build-up of fluoride in the bones over many years. Intense exposure to high levels of fluoride is rare and usually due to accidental contamination of drinking water or from fires or explosions. Chronic exposure at a moderate level (greater than 1.5 mg / liter of water - WHO reported value for fluoride in water) is more common (1,2). Chronic exposure to high levels of fluoride can cause bone fluorosis, which results from the gradual build-up of fluoride in the bones over many years. Intense exposure to high levels of fluoride is rare and usually due to accidental contamination of drinking water or from fires or explosions. Chronic exposure at a moderate level (greater than 1.5 mg/liter of water—WHO reported value for fluoride in water) is more common (1.2)

Bone fluorosis, much more dangerous than dental fluorosis, initially results in an increase in bone mass and fluoride concentrations that can reach 2 to 5 times normal, that is to say from 3 to 5 g/kg. Symptoms that appear next are pain and hardening of the joints followed by osteosclerosis which can ultimately lead to skeletal deformity through calcification of the ligaments, osteoporosis of the long bones and neurological problems due to hyper-calcification (38). In this final step, the level of fluoride in the bones can reach or even exceed 10 g/kg. Skeletal fluorosis appears after taking 10 to 80 mg of fluoride per day, for a period of ten to twenty years. For example, skeletal fluorosis may be encountered in adult subjects who have always lived in an area where the water drunk comes from sources or wells containing fluorine levels greater than 13 ppm (41).

Currently, in developed countries, skeletal fluorosis is no longer encountered thanks to the protection of workers and the pollution prevention measures implemented in the industry. The Food & Nutrition (USA) study showed that such cases are extremely rare in the United States, even when the water contains up to 2 mg/L (50).

Skeletal fluorosis has disappeared in developed countries but persists in developing countries such as China. Skeletal fluorosis is known in this country and is found in less developed rural areas in the north and southwest, especially due to the presence of fluorine in the coal particles emitted by mining industry and power stations, which then contaminate the air and grain. There is evidence from India and China of excess risk of skeletal fluorosis and bone fractures at a total fluoride intake of 14 mg/day, and suggestive evidence of increased risk of skeleton effects at a total intake above about 6 mg/day (1).

c) Other chronic toxic effects of fluoride, contradictory in the scientific literature

- Relationship between fluorine and cancer

Many studies have tried for years to demonstrate the long-term toxicity of the ingestion of fluoride at low doses.

The cancer mortality rate has been subject of a considerable number of comparative epidemiological studies. To establish the relationship between fluoridation water and cancer, a systematic review (51) and a case-control study (52) was reviewed.

The included studies are not conclusive in establishing an association between water fluoridation, at concentrations of 0.6 to 1 ppm and global incidence of cancer when compared to the non-fluoridation of water (51)(53). The studies are not conclusive in establishing an association between water fluoridation, at concentrations of 0.6 to 1 ppm and global incidence of cancer when compared to the non-fluoridation of water (51) (53). Although the study by Bassin et al. shows a significant association between fluoride exposure in drinking water and incidence of osteosarcoma with a peak between 6–8 years in men diagnosed before 20 years of age (52). Low quality methodological study makes us look at these results with caution (54). The authors found no type of association in women.

- Relationship between fluoride and bone fractures

A systematic review (51) and a cross-sectional study (55) were undertaken in order to establish the effect of the fluoridation of drinking water over the bone mineral density (BMD) and bone fracture. A systematic review (51) and a study cross-sectional (55) were included as evidence to establish the effect of the fluoridation of drinking water over the density bone mineral (BMD) and bone fracture.

These studies conclude that water fluoridation at levels to prevent tooth decay has no adverse effect on BMD or incidence of fractures. (51,53)

They conclude that water fluoridation at levels to prevent tooth decay has no adverse effect on BMD or incidence of fractures. Only one study that showed an increase in the incidence of fractures but at levels 4 times higher than the levels considered optimal (51). In the study from Sowers, the control of the variables confusing was poor, which indicates that this association could be due to another confounding factor and not just the concentration of fluorine in the water (55). The evidence is also not conclusive in establishing that water fluoridation may have a protective effect on the incidence of fractures bone (51.53)

VI. DISCUSSION

A. Balance benefit-risk

There is an ongoing debate on fluoride supplementation. An upsurge in cases of dental fluorosis due to fluoride over-prescription in North America and Australia (48) has revived fears of a misuse of this product. In 2002, Belgium took the decision to ban the sale of fluoridated food supplements. These findings, along with too much advice on fluoro-prophylaxia, are currently confusing patients and prescribers.

On the one hand, nothing proves the safety of water fluoridation more convincingly than the existence of large populations (3 million people in the United States of America, 1/2 million in England) who have drunk naturally fluoridated water at a rate of 1 mg / l or more without harm throughout their existence /(33). In these groups, water consumption was obviously not controlled and, as elsewhere, there were healthy infants and sick children, vigorous young adults and frail old people. Practicing physicians and specialists in these areas have never observed or defined any systematic deviation from normal which could be attributable to the ingestion of fluoride (with the exception of speckled enamel in endemic areas) (39).

Moreover, the detailed pediatric observations which were continued for several years in Newburgh-Kingston, and which focused among other things on growth, blood cell counts and X-ray images of the skeleton, unequivocally attest to the good health of the children who drank water containing 1 mg of fluoride per liter (34).

large-scale epidemiological studies don´t show toxicity, and accidental ingestion remains happening in isolated cases which can be avoided by increased supervision of children and knowledge of the risks associated with large ingestion.

On the other hand, the benefit that fluorine brings to public health is unequivocal.

The effects obtained after ten years of controlled fluoridation in the three cities studied above show remarkable uniformity between them (32–34). In children who have constantly resided in the treated area, and who have therefore drunk since birth a water rich in fluoride, the frequency of caries of permanent teeth is 60% lower than that observed in homologous subjects before fluoridation and that which we found in the control city chosen for each experiment. The frequency of decay of deciduous teeth is also lower, the reduction being between 50 and 60%.

The results obtained during the three experiments confirmed the hypothesis according to which the consumption of drinking water containing 1 mg of fluoride per liter gives identical effects on the teeth and on the general condition, as fluoride is naturally present or have been added artificially (32–34).

On an other hand, it is also known that fluoride is part of the family of halogens, which gives it a very high reactivity (it is the most reactive chemical element)(44). Fluoride toxicity is considered to be close to lead and arsenic. Anti-fluoride opposition claims that fluor encountered in a toothpaste tube is sufficient to murder a child (46). As written by Whitford: “The concentrations and quantities of fluoride in selected dental products are discussed in relation to the PTD. It is concluded that, as these products are currently packaged, most of them contain quantities of fluoride sufficient to exceed the PTD for young children” (46,56). But, it is also known that fluoride is part of the family of halogens, which gives it a very

high reactivity (it is the most reactive chemical element) (44). Fluoride toxicity is considered to be between lead and arsenic. Anti-fluoride opposition claims that fluor countered in a toothpaste tube is sufficient to murder a child (46). As written by Whitford: “The concentrations and quantities of fluoride in selected dental products are discussed in relation to the PTD. It is concluded that, as these products are currently packaged, most of them contain quantities of fluoride sufficient to exceed the PTD for young children.” (46.56)

A disturbing fact, however, is that even part of a toothpaste for children contains sufficient amounts of fluoride to kill a child. Indeed, as. As shown in the following table, the ingestion of just 40% of a “Colgate for Kids” is enough to kill an average-weighing 2-year-old child.

Minimum Lethal Dose of Fluoride Contained in One Tube of "Colgate for Kids" Toothpaste

Age of Child	Average Weight	Threshold for Lethal Fluoride Dose	Percent of “Colgate for Kids” toothpaste which, if swallowed, could kill child**
2 years	~12 kg	60 mg	**42% of tube**
3 years	~15 kg	75 mg	**53% of tube**
4 years	~16 kg	80 mg	**56% of tube**
5 years	~18 kg	90 mg	**63% of tube**
6 years	~20 kg	100 mg	**70% of tube**
7 years	~22 kg	110 mg	**77% of tube**
8 years	~25 kg	125 mg	**87% of tube**
9 years	~28 kg	140 mg	**98% of tube**

**The fluoride concentration in Colgate for Kids toothpaste is 1,100 ppm. At 130 grams of paste in the average tube, this equals 143 milligrams of fluoride.

Figure 7 Minimum lethal dose of fluoride contained in a tube of Kids toothpaste

Or in children's toothpaste available products there are endless sweet and tangy flavors to make brushing teeth less unpleasant. Despite the laudable intention of the manufacturers, these little tips can also have a perverse effect: confusing toddlers between toothpaste and candy. For example, according to a study by the Centers for Disease Control and Prevention in the United States, 40% of children aged 3 to 6 use too much toothpaste. However, at this age, and driven by the delectable flavors, many - will swallow this toothpaste, exposing themselves to the ingestion of too much fluoride, which can lead to serious intoxication. The victims are children in 90% of cases.

According to Whitford, the dose causing toxic effect is approximately 6 to 9 mg/kg (56) (46). And for Heifetz and Horowitz, the toxic dose would be 8 mg/kg and the lethal dose would be 32 to 64 mg/kg (23). The scientific community agrees that the ingestion of 5 to 10 g of fluoride causes death in 24 hours in a 70 kg man.

In the United States, a 27-month-old child ingested fewer than 100 fluoride tablets containing 0.5 mg of fluoride each. He vomited immediately and recovered completely. Four hours later the child collapsed again and died five days later (reference). Another case is that of a 3 year old child who died three hours after the application of a 4% fluoride gel, followed by the ingestion of a 4% mouthwash (435mg of fluoride) (23).

It is also important to highlight that fluoride is organic cumulative. In fact, it has been established that approximately 50% of the fluoride ingested by adults, and up to 80% for children, will be stored in the body, mainly in the teeth and bones (37). So even if the concentration of fluoride intake is low, it should not be forgotten that fluorine is accumulated throughout life and that the sources are nowadays very variated (47). Therefore, the risk of being affected by long-term fluoride build-up is real. The recognized effects of excessive fluoride intake are dental fluorosis, bone problems such as bone fluorosis or increased bone fragility, among others (37,52).It is also important to remain that fluoride is organic cumulative.

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When it became evident that slightly increased concentrations of fluoride in enamel was associated with a decrease in cavities, the method of Dean became an important tool in trying to establish fluorine concentration optimal, the one that gave a maximum reduction of dental caries without causing unacceptable dental fluorosis in the population. This led to the discussion, still ongoing, of the definition of such an optimal dose. Dental fluorosis is the first clinical sign of the toxic effect of fluoride on children. But in public health, many health promoters consider dental fluorosis only from a cosmetic point of view; it is to say that it only poses a public health problem if it leads to an increase in cosmetic problems. This point of view has led to confusion as to the biological effects of fluorine on the human body.

About the relation between fractures and fluoride intake only one study showed an increase in the incidence of fractures (but at levels of fluoridation 4 times higher than the levels considered optimal) (51). In the study from Sowers et al. in 2005, the control of the variables was poor, which indicates that this association could be due to another confounding factor and not just the concentration of fluorine in the water (55). The evidence is also not conclusive in establishing that water fluoridation may have a protective effect on the incidence of fractures in bones.

Some authors also explored the relation between cancer and fluoride. The study by Bassin et al. showed a significant association between fluoride exposure in drinking water and incidence of osteosarcoma with a peak between 6–8 years in men diagnosed before 20 years of age (52). Another work published two years later states that the low quality of this methodological study should prompt us to look at these results with caution (54). The authors found no type of association in woman.

B. Towards a rational use of fluoride

i. Ideal concentration and ideal timing

a) Toothpaste

Studies show that toothpaste prevention is even more effective that the concentrations exceeding 1000 ppm of fluoride. But, the recommendations for a dental use should take into account the aforementioned risk of developing fluorosis (29).

In addition, it should also be taken into account that children swallow a lot of toothpaste. It is therefore important to check the fluoride content as mentioned on the packaging, since not all "children's" toothpastes contain a content suitable in fluoride. A comparative study carried out on children between 1.5—and 2.5-years old shows that the average percentage of toothpaste ingested varies from 64 to 84% and that 36 to 70% of children swallow 80–100% of the applied toothpaste. Whatever the concentration, a pea-sized amount of toothpaste is considered more than enough to children (57).

- From the eruption of the first temporary tooth and for children up to 2 years old, it is recommended to brush teeth twice a day with children's toothpaste (500 to1000 ppm) (57).
- Between 2 and 6 years old, the same recommendation of twice a day remains valid but with a concentration of 1000 to 1450 ppm (57) (58).
- For children over six years of age and throughout life, it is recommended to brush your teeth twice a day with toothpaste containing 1450 ppm (58)

Up to a concentration of 1450/1500 ppm, toothpastes are considered cosmetics. There are also toothpastes that contain a higher concentration of fluoride. In general, they are not intended for routine use and are considered to be medication. They can only be obtained from pharmacies. These products are preferably used only on the advice of a doctor or dentist.

b) Varnish

The application of fluoride varnish is indicated for very young children, EAPD recommends its use as soon as the teeth erupt (25). This would avoid the early childhood caries that could predispose to new decay of temporary and permanent teeth (27). The use of fluoride varnishes is recommended, on temporary and permanent teeth, 2 to 4 times per year, combined with daily use of fluoride toothpaste (58). The targets of this caries prevention program are vulnerable groups(58). The targets of this caries prevention program are groups vulnerable at high caries risk (25). The cumulative effect of fluoride should be taken into account for children under 6 years of age, depending on the balance between the maximum protective effect against caries and the minimum risk of fluorosis, and the balance between the practitioner's expertise and family preferences (24).

Three types of concentration are available in Europe.

- The weakest concentration corresponds to 0.1% of difluorosilane, i.e. 1000 ppm of fluorine (Fluor Protector®, Ivoclar Vivadent) (19) (26).
- The intermediate concentration is 5% sodium fluoride, i.e. 22,600 ppm of fluorine found in Duraphat® varnishes, Enamelast® (Ultra Dent), Clin Pro® (3M, ESPE) or Profluorid® (Voco). MI varnish® (GC) has the same concentration of fluorine and it also contains Amorphous Casein Calcium Phosphate Phosphopeptide (CCP-ACP) (26).
- Most concentrates are bifluorides that contain 6% sodium fluoride and 6% sodium calcium fluoride, i.e. 56,000 ppm of fluorine such as Bifluorid 10® (Voco,) (26) (19).

The use of agents with a high concentration of fluorine, such as products for professional use, is recommended for patients at high risk of caries (25). Fluorinated agents that release a large dose at the start would be the most effective (24). But a high concentration of fluoride on the surface of the enamel would physically prevent Ca^{2+} ions from reaching the deeper layers (24).

Products with a high fluoride concentration are quite effective in inhibiting lesion formation through the secondary prevention plan (24), while frequent application of low fluoride agents is considered to be the most effective regimen in controlling the progression of initial lesions, thus helping the primary prevention. The continued presence of a low concentration of fluoride ions promotes remineralization (13.19)

c) Gel

The fluoride gel can be applied by a professional, using a splint, worn for a few minutes, every 6 months. It can also be used individually, during daily brushing (59). The gel for professional use usually contains 12,300 ppm of fluorine and can go up to 20,000 ppm, it can be acidic or neutral (27). (27). The gel for personal use contains 1800 to 13,500 ppm F.

In Europe, the fluoride gel for professional use is indicated for adults only (Fluocaril bifluoré 2000®). Fluoride gels for individual use are related to toothpastes and are reserved for patients over 6 years for Fluocaril bifluoré 180®, over 10 years for Fluocaril bifluoré 250®, over 12 years for Fluodontyl®, and over 16 years for Duraphat®, on the advice of the dentist.

Fluoride gel presents a greater risk of ingestion than fluoride varnish, which is why it cannot be used for children under 6 years old.

d) Mouthwash

Fluoride mouthwash is a topical intended for children over 6 years old (19). It includes 200 to 900 ppm. Its use can be individual or supervised, daily or weekly. Its efficiency is questioned nowadays (18).

ii. Ideal administration form

Fluoride varnishes are easy to use and quick to apply. They require little material and rapid tooth preparation. Its adhesion to the enamel surface and its rapid setting after application result in a reduced risk of ingestion. This risk of limited ingestion is of particular interest in young children. For this reason, fluoride varnish may be preferred for very young and young patients at risk of caries who cannot spit. The generally recommended frequency is twice a year, 6 months apart (26).

Professional fluoride gels are applied in the office using trays. Their application time is several minutes, this technique is therefore contraindicated in young children because it is difficult to control excess gel during the application and therefore to avoid ingestion (27).

iii. Adapted prescription of fluoride

All patients are not equal in risk when it comes to caries disease, which is why the management must be adapted and individual. The treatment plan therefore requires an evaluation phase of these factors, commonly called “evaluation of the caries risk”. Many risk assessment methods have been developed such as the system Caries Management by Risk Assessment (CAMBRA) and the Cariogram (24). Both are based on the identification of variables that can be grouped in different ways, for example: unchanging factors, represented by risk groups (elderly, disabled, low socio-economic level), versus factors modifiable by the patient and/or the practitioner; environmental factors versus behavioral and biological factors.

It is also important to assess the child’s fluoride intake, it is essential to know its weight and the daily intake quantity of fluoride:

—fluoridated intakes from drinking water. The fluorine concentrations in the distribution of water by municipalities were collected from the departments and a list of bottled waters with their fluorine concentration is available on online platforms.

—intake by fluoridated salt during meals.

—fluoride intakes through drug supplementation: prescriptions and self-medication.

iv. Safety considerations

In order to ensure the healthy use of fluorides, some recommendations apply generally to all children. First, toothbrushing should be done under parental supervision so that only the recommended doses of toothpaste are used (pea size up to twice a day for children under 6). six).

It is also important to keep products containing fluoride out of the reach of children, in a dry storage place and at room temperature. The product packaging or the instruction for use provides information on the risks and the ideal dosage. In case of manifestation of side effects, it would be interesting to turn to drug safety or pharmacovigilance agencies to advise them.

VII. CONCLUSION

During the 20th century, fluoride played a major role in significantly reducing the prevalence of dental caries worldwide.

Victim of its own success and growing market demands, fluoride administration methods have multiplied and diversified over time (drinking water, salt, food, toothpaste, etc.), leading to an often unintentional overconsumption of fluorides and therefore consequently an increase in the prevalence of its side effects.

One of its major negative repercussion is dental fluorosis. It is caused by excessive ingestion of fluorides during the first years of life. This excess fluoride causes an incomplete crystal development in the tissues, resulting in the formation of a porous fluorotic enamel.

Faced with the hypothesis of these toxicity, many people wonder whether fluoride is good or bad. This binary thought often makes discussion impossible. Indeed, the answer is neither the one nor the other and both at the same time. Fluoride has a definite beneficial effect on the prevention of dental caries. On the other hand, at a certain concentration, it exhibits toxicity. It's the accumulation and ignorance of the various sources of fluoride intake that are often the cause of these negative experiences.

To prevent the occurrence of this toxicity, it is the responsibility of all healthcare professionals to check before each prescription that fluoride supplementation is suitable. It is therefore essential to carry out an individualized fluoride assessment.

VIII. RESPONSABILITY

Oral health is an essential and integral component of health in general; its degradation represents thus a major public health problem, due to its human and social impact. That is all the more important when it comes to the oral health of a child, since it directly influences their development and quality of life. It is clear that oral diseases are obviously a history linked to the life course. That is to say that from early childhood to the last years of life, people will be affected by oral diseases. This is a very important component when government establishes public health strategies. In this context, it is important not to relax the efforts put to prevent the onset of caries disease in children and delay the appearance of caries.

The insufficient knowledge of parents about the issues and risks at an early stage of children's development contribute to maintain a high level of early childhood caries. Their therapeutic management is difficult because of their young age and the lack of trained and informed practitioners. Recommendations are needed for health professionals and parents to change behaviors towards oral health. Data from the international scientific literature allows to establish recommendations on certain strategies that have been shown to be effective in improving the oral health of young children. Thus, oral prevention is a way to improve dental health, to detect risk factors, detect lesions as soon as they appear so that they can be treated quickly reduce the carious index of children and reinforce health education, prevent the occurrence of subsequent pathologies.

Despite the numerous scientific data showing the harmlessness and the efficiency of fluorine, a lot of erroneous information, even dangerously far-fetched, circulate on the Internet and social networks. These "fake news", as they are called, are propagated by "anti-fluorine" groups that question its harmlessness. Some of them rely on the possible confusion between fluorine (an irritating gas, totally absent from oral hygiene products) and fluorides, the fluoride salts present in toothpastes. Unfortunately, anti-fluorine fake news sow doubt in people's minds and the consequences on oral health are very visible. Used in a reasoned way, fluorine is a very precious ally for the health of teeth and especially not an enemy to be fought at all costs. Years of experience are there to prove it, fluorine is the most effective anti-caries active. It is therefore our responsivity of caregiver to reestablish a scientific truth and relativize the controversies.

The social determinants of oral health are well known. Depending on the living area, the education received, and the progress through education and work etc., people will be exposed to more or less oral problems. So oral diseases are today a marker of social inequalities. The richer people are, the better educated they are, the better the oral health. All this to tell that fluoride may seem to be a solution. Combined with other oral preventive measures, fluoride salt offers a potential for improving oral health, particularly in developing countries where it may be the only affordable supplementation solution. This vector of fluoride intake can reach a large population, given its universal consumption with a limited risk of side effects. Fluorosis would not be a public health problem in the context of a salt fluoridation program, although the benefit/risk ratio must be systematically assessed. The effectiveness of salt fluoridation depends on the rate of use in the population, and therefore particularly on the communication policy used to promote it.

IX. BIBLIOGRAPHY

1. World Health Organization. The World Oral Health Report 2003. Community Dent Oral Epidemiol. 2003;31 Suppl 1:3–23.
2. Petersen PE. The World Oral Health Report 2003: Continuous improvement of oral health in the 21st century - The approach of the WHO Global Oral Health Programme. Community Dent Oral Epidemiol. 2003;31(SUPPL. 1):3–24.
3. Vos T, Allen C, Arora M, Barber RM, Brown A, Carter A, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016;388(10053):1545–602.
4. Bener A, Al Darwish MS, Tewfik I, Hoffmann GF. The impact of dietary and lifestyle factors on the risk of dental caries among young children in Qatar. J Egypt Public Health Assoc. 2013;88(2):67–73.
5. Standardization of reporting dental diseases and conditions. Vol. 196, Nature. 1962. p. 1155.
6. Conrads G, About I. Pathophysiology of Dental Caries. Monogr Oral Sci. 2018;27:1–10.
7. Public US. Caries Attacks. Public Health. 1936;243–56.
8. Shulman JAYD, Cappelli DP. Chapter 1 E pidemiology of Dental Caries CARIES EPIDEMIOLOGY THE SCIENCE OF CARIES POPULATION-BASED MEASURES OF. 2010;
9. Truin GJ, König KG, Bronkhorst EM, Frankenmolen F, Mulder J, Van 'T Hof MA. Time Trends in Caries Experience of 6- and 12-Year-Old Children of Different Socioeconomic Status in the Hague. Caries Res. 1998;32(1):1–4.
10. Hobdell M, Petersen PE, Clarkson J, Johnson N. Global goals for oral health 2020. Int

Dent J. 2003;53(5):285–8.

11. Mazyad O, marakby A, Sorour Y, ghannam M, Salem M, Salamah M, et al. Topical Application of Fluoride and Its Anti-Cariogenic Effect. Int J Adv Res. 2017;5(12):1483–8.

12. Petersen PE, Ogawa H. Prevention of dental caries through the use of fluoride – the WHO approach. Community Dent Health. 2016;33(2):66–8.

13. Buzalaf MAR, Pessan JP, Honório HM, Cate JM ten. Mechanisms of Action of Fluoride for. Monogr Oral Sci. 2011;22:97–114.

14. Peter Meiers. The discovery of fluoride and fluorine [Internet]. [cited 2020 Nov 10]. Available from: http://www.fluoride-history.de/fluorine.htm

15. Tressaud A. Henri Moissan: Winner of the Nobel Prize for Chemistry 1906. Angew Chemie - Int Ed. 2006;45(41):6792–6.

16. CDC report. Achievements in Public Health, 1900-1999: Fluoridation of Drinking Water to Prevent Dental Caries [Internet]. [cited 2020 Nov 10]. Available from: https://www.cdc.gov/mmwr/preview/mmwrhtml/mm4841a1.htm

17. Toumba KJ, Twetman S, Splieth C, Parnell C, van Loveren C, Lygidakis N. Guidelines on the use of fluoride for caries prevention in children: an updated EAPD policy document. Eur Arch Paediatr Dent [Internet]. 2019;20(6):507–16. Available from: https://doi.org/10.1007/s40368-019-00464-2

18. Ole Fejerskov BN and EK. Dental Caries: The Disease and Its Clinical Management. Br Dent J. 2015;3(11):239.

19. Bertrand-Krajewski JL, Briat P, Scrivener O, Ackers P. A literature review. Vol. 32, Journal of Hydraulic Research. 1994. 312–316 p.

20. Marquis RE. Oral Bacteria. Can J Microbiol. 1995;964:955–64.

21. Sh Priyadarshini1, Ramya Raghu1, Ashish Shetty1, PM Gautham1, Satyanarayana

Reddy1 RS. Effect of organic versus inorganic fluoride on enamel microhardness. 2011;8(2):95–101.

22. Lo EC, Tenuta LM, Fox CH. Use of professionally administered topical fluorides in Asia. Adv Dent Res. 2012;24(1):11–5.

23. Horowitz HS, Heifetz SB. The current status of topical fluorides in preventive dentistry. Council on Dental Therapeutics. J Am Dent Assoc. 1970;81(1):166–77.

24. Seale NS, Daubert DM. The Use and Efficacy of Professional Topical Fluorides. 2013;

25. Azarpazhooh A, Main PA. Fluoride varnish in the prevention of dental caries in children and adolescents: A systematic review. J Can Dent Assoc (Tor). 2008;74(1):73–9.

26. Marinho VCC, Worthington H V., Walsh T, Clarkson JE. Fluoride varnishes for preventing dental caries in children and adolescents. Cochrane Database Syst Rev. 2013;2013(7).

27. Adair SM. Evidence-based use of fluoride in contemporary pediatric dental practice. Pediatr Dent. 2006;28(2):133–42.

28. Pollick H. The Role of Fluoride in the Prevention of Tooth Decay. Pediatr Clin North Am [Internet]. 2018;65(5):923–40. Available from: https://doi.org/10.1016/j.pcl.2018.05.014

29. Walsh T, Glenny AM, Worthington H V., Marinho VCC, Appelbe P. Fluoride toothpastes of different concentrations for preventing dental caries in children and adolescents. Cochrane Database Syst Rev. 2009;(3).

30. Davies R, Scully C, Preston AJ. Dentifrices - An update. Med Oral Patol Oral Cir Bucal. 2010;15(6):976–82.

31. Dalla Torre Di Sanguinetto S, Heinonen E, Antonov J, Bolte C. A Comparative Review of Marketing Authorization Decisions in Switzerland, the EU, and the USA. Ther Innov Regul Sci. 2019;53(1):86–94.

32. Ontario. Report of the committee appointed to inquire into and report upon the fluoridation of municipal water supplies. 1961;177 p.
33. ARNOLD FA. Grand Rapids fluoridation study; results pertaining to the eleventh year of fluoridation. Am J Public Health. 1957;47(5):539–45.
34. Newbrun E. Effectiveness of Water Fluoridation. J Public Health Dent. 1989;49(5):279–89.
35. Marinho VCC, Worthington H V., Walsh T, Chong LY. Fluoride gels for preventing dental caries in children and adolescents. Cochrane Database Syst Rev. 2015;2015(6).
36. FRANK JE, LAW FE, SPITZ GS, GALAGAN DJ. School Dental Care in a Community With Controlled Fluoridation. Public Heal reports (Washington, DC 1896). 1964;79:113–24.
37. Martínez-Mier EA. Fluoride: Its metabolism, toxicity, and role in dental health. J Evidence-Based Complement Altern Med. 2012;17(1):28–32.
38. Warren JJ, Levy SM. Current and future role of fluoride in nutrition. Dent Clin North Am. 2003;47(2):225–43.
39. Bronckers ALJJ, Lyaruu DM, Denbesten PK. Critical review in oral biology and medicine: The impact of fluoride on ameloblasts and the mechanisms of enamel fluorosis. J Dent Res. 2009;88(10):877–93.
40. Buzalaf MAR. Fluoride and the oral environment. Fluoride Oral Environ. 2011;22:1–178.
41. Hodge, H. C. & S. Occupational Fluoride Exposure. Journal of Occupational and Environmental Medicine.
42. J.H Simons. Fluorine Chemistry [Internet]. [cited 2021 Jan 5]. Available from: https://books.google.fr/books?id=88hr0Pyovk4C&pg=PA3&lpg=PA3&dq=1873+to+1935+roholm&source=bl&ots=Nkq0ooT-

1J&sig=ACfU3U0NxlkUF08UVNbSXkOIOofnNtCyzQ&hl=fr&sa=X&ved=2ahUKEwjFjPOHpoXuAhUDuRoKHWYuCukQ6AEwAXoECAEQAg#v=onepage&q=1873 to 1935 roholm&f=false

43. Bronstein AC, Spyker DA, Cantilena LR, Green JL, Rumack BH, Giffin SL. 2009 annual report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 27th annual report. Clin Toxicol. 2010;48(10):979–1178.

44. Ullah R, Zafar MS, Shahani N. Potential fluoride toxicity from oral medicaments: A review. Iran J Basic Med Sci. 2017;20(8):841–8.

45. Shulman JD, Wells LM. Acute fluoride toxicity from ingesting home-use dental products in children, birth to 6 years of age. J Public Health Dent. 1997;57(3):150–8.

46. Whitford GM. The metabolism and toxicity of fluoride. Monogr oral Sci 13, 1-160.

47. Aoba T, Fejerskov O. D f : c b. Crit Rev Oral Biol Med. 2002;13(2):155–70.

48. Directrices L, Clinique DEP, Clark DC. CLINICAL PRACTICE GUIDELINES on the Evaluation of Current Recommendations Concerning Fluorides. 1993;149(12).

49. Whelton HP, Ketley CE, MSweeney F OMD. A review ofluorosis in theEuropean Union prevalence,risk factors and aesthetic issues - Whelton 2004. Community Dent Oral Epidemiol. 2004;32(5):9–18.

50. Tressaud A HG. Fluorine and health: molecular imaging, biomedical materials and pharmaceuticals.1st ed. Oxford: Elsevier; 2008. 32. In.

51. National Health and Medical Research Council. SUMMARY REVIEW / CARIES A systematic review of the efficacy and safety of fluoridation. :39–43.

52. Bassin EB, Wypij D, Davis RB, Mittleman MA. Age-specific fluoride exposure in drinking water and osteosarcoma (United States). Cancer Causes Control. 2006;17(4):421–8.

53. Marian S McDonagh, Penny F Whiting, Paul M Wilson, Alex J Sutton, Ivor Chestnutt

JC, Kate Misso, Matthew Bradley, Elizabeth Treasure JK. Systematic review of water fluoridation. Guangxue Jingmi Gongcheng/Optics Precis Eng. 2008;16(12):2358–65.

54. Douglass CW, Joshipura K. Caution needed in fluoride and osteosarcoma study. Cancer Causes Control. 2006;17(4):481–2.

55. Sowers MF, Whitford GM, Clark MK, Jannausch ML. Elevated serum fluoride concentrations in women are not related to fractures and bone mineral density. J Nutr. 2005;135(9):2247–52.

56. Whitford GM. Fluoride in Dental Products: Safety Considerations. J Dent Res. 1987;66(5):1056–60.

57. Ellwood RP, Cury JA. How much toothpaste should a child under the age of 6 years use? Eur Arch Paediatr Dent. 2009;10(3):168–74.

58. Archives E. European Archives of P ae d i a t r i c De n t i s t r y Guidelines on the use of fluoride in children : an EAPD policy document . European Archives of P ae d i a t r i c De n t i s t r y. 2009;10(3):129–35.

59. Marinho VCC, Higgins JPT, Logan S, Sheiham A. Systematic Review of Controlled Trials on the Effectiveness of Fluoride Gels for the Prevention of Dental Caries in Children. J Dent Educ. 2003;67(4):448–58.

Buzalaf MAR (ed): Fluoride and the Oral Environment.
Monogr Oral Sci. Basel, Karger, 2011, vol 22, pp 1–19

Fluoride Intake of Children: Considerations for Dental Caries and Dental Fluorosis

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Abstract

Caries incidence and prevalence have decreased significantly over the last few decades due to the widespread use of fluoride. However, an increase in the prevalence of dental fluorosis has been reported simultaneously in both fluoridated and non-fluoridated communities. Dental fluorosis occurs due to excessive fluoride intake during the critical period of tooth development. For the permanent maxillary central incisors, the window of maximum susceptibility to the occurrence of fluorosis is the first 3 years of life. Thus, during this time, a close monitoring of fluoride intake must be accomplished in order to avoid dental fluorosis. This review describes the main sources of fluoride intake that have been identified: fluoridated drinking water, fluoride toothpaste, dietary fluoride supplements and infant formulas. Recommendations on how to avoid excessive fluoride intake from these sources are also given.

Fluorides play a key role in the prevention and control of dental caries. In the middle of the previous century, it was generally believed that fluoride had to be incorporated into dental enamel during development to exert its maximum protective effect. It was then considered unavoidable to have a certain prevalence and severity of fluorosis in a population to minimize the prevalence and severity of caries among children. In the 1980s, a paradigm shift regarding the cariostatic mechanisms of fluorides was proposed [1]. This considered that the predominant, if not entire, explanation of how fluorides control caries development is their topical effect on the de- and re-mineralization processes that occur at the interface between the tooth surface and the adjacent dental biofilm. This concept became widely accepted [2–6], and made it possible to obtain very substantial caries protection without significant ingestion of fluorides. With this in mind and being aware of the increase in the prevalence of dental fluorosis in both fluoridated and in non-fluoridated areas [7–9], researchers around the world turned their attention toward controlling the amount of fluoride intake.

The most important risk factor for fluorosis is the total amount of fluoride consumed from all sources during the critical period of tooth development. Thus, it is important not only to know the main sources of fluoride intake, but also the critical periods of formation in which the teeth are more susceptible to the effects of fluoride and the levels of fluoride intake above which dental fluorosis is expected to occur. The purpose of this review is to discuss the levels of fluoride intake

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Fluoride gels for preventing dental caries in children and adolescents (Review)

Marinho VCC, Worthington HV, Walsh T, Chong LY

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Fluoride gels for preventing dental caries in children and adolescents.
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Grand Rapids Fluoridation Study—Results Pertaining to the Eleventh Year of Fluoridation

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As long as the adoption of water fluoridation is to be left to the vagaries of public or popular decision—and it is one of the few public health protective devices that is subject to such unpredictable action—every bit of scientific evidence of fluoridation's value should be readily at hand for persuasive use. This is the second of four important papers, "New Developments in Water Fluoridation." The remaining two will appear serially in succeeding issues.

The control of dental caries by water fluoridation has been the subject of articles and reports for more than a decade. Relatively complete bibliographies on this subject are included in previous review dissertations.[1–4] It may be stated that all recognized scientific studies have demonstrated the certainty of this method as a public health procedure for securing better dental health for a community.

Although many of the studies on water fluoridation have been in progress long enough to evaluate the soundness of the procedure, much is to be learned concerning its various public health aspects. The purpose of the present paper is to review briefly the results of 10 years of one of these research projects; to summarize the findings of the eleventh year of the study, particularly those observations which pertain to dental health programs; and to evaluate the findings in respect to the results of other independent investigations of similar character. For this reason the results of three of these studies covering the first 10 years of operation will be discussed.

Study Plan

Generally speaking, all of the studies referred to are designed to evaluate what, if any, effect fluoridation of a public water supply will have on the general health of the community using this supply. This public health responsibility has been foremost in the minds of all people concerned and has been recognized by everyone involved in initiating or endorsing such programs. The technical methods of evaluation used in these different research projects have been described previously.[5–8]

Particularly, the study plans were designed to determine the prevalence of dental caries in a community prior to fluoridation and to evaluate the effects by subsequent annual oral examinations. In each of these studies due attention has been paid to determining whether fluoridation has any effect upon the general health, in addition to the dental health, of the population using the fluoride water.

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This paper was presented before a Joint Session of the Dental Health and School Health Sections of the American Public Health Association at the Eighty-Fourth Annual Meeting in Atlantic City, N. J., November 15, 1956.

DENTAL FLUOROSIS: CHEMISTRY AND BIOLOGY

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ABSTRACT: This review aims at discussing the pathogenesis of enamel fluorosis in relation to a putative linkage among ameloblastic activities, secreted enamel matrix proteins and multiple proteases, growing enamel crystals, and fluid composition, including calcium and fluoride ions. Fluoride is the most important caries-preventive agent in dentistry. In the last two decades, increasing fluoride exposure in various forms and vehicles is most likely the explanation for an increase in the prevalence of mild-to-moderate forms of dental fluorosis in many communities, not the least in those in which controlled water fluoridation has been established. The effects of fluoride on enamel formation causing dental fluorosis in man are cumulative, rather than requiring a specific threshold dose, depending on the total fluoride intake from all sources and the duration of fluoride exposure. Enamel mineralization is highly sensitive to free fluoride ions, which uniquely promote the hydrolysis of acidic precursors such as octacalcium phosphate and precipitation of fluoridated apatite crystals. Once fluoride is incorporated into enamel crystals, the ion likely affects the subsequent mineralization process by reducing the solubility of the mineral and thereby modulating the ionic composition in the fluid surrounding the mineral. In the light of evidence obtained in human and animal studies, it is now most likely that enamel hypomineralization in fluorotic teeth is due predominantly to the aberrant effects of excess fluoride on the rates at which matrix proteins break down and/or the rates at which the by-products from this degradation are withdrawn from the maturing enamel. Any interference with enamel matrix removal could yield retarding effects on the accompanying crystal growth through the maturation stages, resulting in different magnitudes of enamel porosity at the time of tooth eruption. Currently, there is no direct proof that fluoride at micromolar levels affects proliferation and differentiation of enamel organ cells. Fluoride does not seem to affect the production and secretion of enamel matrix proteins and proteases within the dose range causing dental fluorosis in man. Most likely, the fluoride uptake interferes, indirectly, with the protease activities by decreasing free Ca^{2+} concentration in the mineralizing milieu. The Ca^{2+}-mediated regulation of protease activities is consistent with the *in situ* observations that (a) enzymatic cleavages of the amelogenins take place only at slow rates through the secretory phase with the limited calcium transport and that, (b) under normal amelogenesis, the amelogenin degradation appears to be accelerated during the transitional and early maturation stages with the increased calcium transport. Since the predominant cariostatic effect of fluoride is not due to its uptake by the enamel during tooth development, it is possible to obtain extensive caries reduction without a concomitant risk of dental fluorosis. Further efforts and research are needed to settle the currently uncertain issues, *e.g.*, the incidence, prevalence, and causes of dental or skeletal fluorosis in relation to all sources of fluoride and the appropriate dose levels and timing of fluoride exposure for prevention and control of dental fluorosis and caries.

Key words. Fluorosis, fluoride, enamel, matrix proteins, proteases, mineralization, caries prevention.

(1) Introduction

Fluoride plays a key role in the prevention and control of dental caries. Ever since the excellent work of Dean and his collaborators (Dean 1934, 1942; Dean and Elvovo, 1935), in which the association between fluoride in drinking water and the occurrence of disturbances of tooth formation (mottling of enamel or dental fluorosis), as well as a concomitant reduction in caries experience, was demonstrated, dental fluorosis has been a central issue in all programs seeking to harness the unique property of fluorides to control and prevent caries. In the middle of the previous century, the paradigm was that, to exert its maximum cariostatic effect, fluoride had to become incorporated into dental enamel during development, and hence it was inevitable to have a certain prevalence and severity of fluorosis in a population to minimize the prevalence and severity of caries among children. Dental fluorosis was then regarded as an unfortunate side-effect of fluoride's caries-protective benefits, and attempts to "play down" the possible toxic effect of fluoride on developing dental enamel often led the dental profession to present dental fluorosis as merely a cosmetic problem.

Much of what is perpetuated world-wide in caries-preventive programs today is derived from the beliefs and paradigms concerning fluorides generated in the 1950s and '60s, but now we are at a time in science where "evidence-based medicine" is becoming a central issue for evaluating the scientific achievements during the last decades concerning our understanding of how fluoride affects mineralizing and mineralized dental hard tissues. The last 25 years have presented major breakthroughs in basic research on how fluoride affects the mineralization of teeth and how fluoride exerts its cariostatic effect (for reviews, see Fejerskov *et al.*, 1981; Ten Cate and Featherstone, 1996). It is remarkable, however, that the dramatic decline in dental caries which we have witnessed in many different parts of the world (for reviews, see Glass, 1982; Fejerskov and Baelum, 1998) has occurred without the dental profession being fully able to explain the relative role of fluoride in this intriguing process. It is a common belief that the wide distribution of fluoride from toothpastes may be a major explanation (Bratthall *et al.*, 1996), but serious attempts to assess the role of fluoridated toothpastes

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ORIGINAL PAPER

Age-specific fluoride exposure in drinking water and osteosarcoma (United States)

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Abstract
Objective We explored age-specific and gender-specific effects of fluoride level in drinking water and the incidence of osteosarcoma.
Methods We used data from a matched case–control study conducted through 11 hospitals in the United States that included a complete residential history for each patient and type of drinking water (public, private well, bottled) used at each address. Our analysis was limited to cases less than 20 years old. We standardized fluoride exposure estimates based on CDC-recommended target levels that take climate into account. We categorized exposure into three groups (<30%, 30–99%, >99% of target) and used conditional logistic regression to estimate odds ratios.
Results Analysis is based on 103 cases under the age of 20 and 215 matched controls. For males, the unadjusted odds ratios for higher exposures were greater than 1.0 at each exposure age, reaching a peak of 4.07 (95% CI 1.43, 11.56) at age 7 years for the highest exposure. Adjusting for potential confounders produced similar results with an adjusted odds ratio for males of 5.46 (95% CI 1.50, 19.90) at age 7 years. This association was not apparent among females.
Conclusions Our exploratory analysis found an association between fluoride exposure in drinking water during childhood and the incidence of osteosarcoma among males but not consistently among females. Further research is required to confirm or refute this observation.

Keywords Osteosarcoma · Fluoride · Fluoridation · Case–control

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Introduction

Osteosarcoma is a very rare primary malignant tumor of bone. Although uncommon, primary malignant bone tumors comprise the sixth most common group of malignant tumors in children and the third most common malignant tumor for adolescents, with an annual incidence rate of 5.6 per million for Caucasian children under 15 years old [1]. Osteosarcoma is the most common tumor of bone and for patients less than 20 years old more than 80% of these tumors tend to occur in the long bones of the appendicular skeleton which are undergoing rapid growth [2]. The incidence of osteosarcoma is slightly higher in males than females with an annual incidence rate of approximately 3.5 per million for males and 2.9 per million for females under the age of 24 years [3].

CRITICAL REVIEWS IN ORAL BIOLOGY & MEDICINE

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The Impact of Fluoride on Ameloblasts and the Mechanisms of Enamel Fluorosis

ABSTRACT

Intake of excess amounts of fluoride during tooth development cause enamel fluorosis, a developmental disturbance that makes enamel more porous. In mild fluorosis, there are white opaque striations across the enamel surface, whereas in more severe cases, the porous regions increase in size, with enamel pitting, and secondary discoloration of the enamel surface. The effects of fluoride on enamel formation suggest that fluoride affects the enamel-forming cells, the ameloblasts. Studies investigating the effects of fluoride on ameloblasts and the mechanisms of fluorosis are based on *in vitro* cultures as well as animal models. The use of these model systems requires a biologically relevant fluoride dose, and must be carefully interpreted in relation to human tooth formation. Based on these studies, we propose that fluoride can directly affect the ameloblasts, particularly at high fluoride levels, while at lower fluoride levels, the ameloblasts may respond to local effects of fluoride on the mineralizing matrix. A new working model is presented, focused on the assumption that fluoride increases the rate of mineral formation, resulting in a greater release of protons into the forming enamel matrix.

KEY WORDS: fluoride, enamel fluorosis, amelogenin, ameloblasts, review.

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INTRODUCTION

An excess ingestion of fluoride induces multiple changes in the developing enamel, and is referred to as enamel fluorosis. Changes vary from chalky white opaque areas, resulting from subsurface hypomineralization, to pits and grooves, and with increased severity, post-eruption staining. Fluorotic enamel is softer and chips easily (for reviews, see Fejerskov *et al.*, 1977, 1994; Giambro *et al.*, 1995). Enamel fluorosis is observed in young children at fluoride intakes as low as 0.03 mg F/kg body weight, and there is a clear linear relationship between fluoride dose and the development of dental fluorosis, regardless of whether fluoride is ingested from drinking water, from supplements, or from other sources (Fejerskov *et al.*, 1994; Warren *et al.*, 2009). Although fluoride may have different effects in the various stages of enamel formation, its effect is greatest when exposure occurs during all stages of formation (Ishii and Suckling, 1986; DenBesten, 1999; Hong *et al.*, 2006).

During the last four decades, many experimental animal and organ culture studies, as well as more recent cell culture studies, have investigated mechanisms by which fluoride affects ameloblasts and enamel formation. In these and future studies, important issues to consider include: how fluoride causes these changes in forming enamel, how fluoride affects different stages of development, and how fluoride affects ameloblast function. The effects of fluoride are highly dose-dependent, and proper interpretation of the cellular effects of fluoride, including effects on the ameloblasts, requires a careful analysis of the *in vivo* or *in vitro* model systems and the dose of fluoride used. The present review is focused on studies aimed at elucidating the effects of fluoride on the ameloblasts, and the objectives of the review are:

(1) to evaluate the efficacy of animal model systems for the study of enamel fluorosis in humans;

(2) to define the relevance of various fluoride doses in studies related to enamel fluorosis and how fluoride doses relate to fluoride plasma levels;

(3) to describe which stages of enamel development are sensitive to fluoride and what types of mineralization disturbances occur at each stage; and

(4) to present a working model that explains the observed effects of fluoride on the developing enamel organ.

MODEL SYSTEMS USED TO STUDY THE EFFECTS OF FLUORIDE ON HUMAN TOOTH DEVELOPMENT

The effects of fluoride on enamel development have been studied in a wide range of animal species and tooth types. In most studies, rat incisors

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LETTER TO THE EDITOR

Caution needed in fluoride and osteosarcoma study

Chester W. Douglass · Kaumudi Joshipura

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This issue of *Cancer Causes and Controls* includes a paper with results from an analysis of a subset of participants in our ongoing study of fluoride and osteosarcoma. The paper, ''Age-specific fluoride exposure in drinking water and osteosarcoma'', presents a partial view of this ongoing study. We would like to advise the readers to be especially cautious when interpreting the findings of this paper for several reasons. The authors themselves have already raised a flag of caution in their final paragraph with the note that they are aware of additional findings from other incident cases that appear not to replicate the findings from the cases presented in their paper.

The Harvard School of Dental Medicine study of fluoride and osteosarcoma has been a 15-year collaboration among NIEHS, NCI, NIDCR, and Harvard. Two sets of cases have been collected each with their own control groups. The study started in 1992. The first set of cases was recruited from existing cases between 1989 and 1992, and the second set of cases was recruited from new incident cases between 1993 and 2000. The Bassin et al paper reports age-specific results among only the cases from 1989 to 1992. We are also finding some positive associations between fluoride and osteosarcoma in the overall (not age-specific) analysis of the first set of cases. However, our preliminary findings from the overall analysis of the second set of cases (1993–2000) do not appear to replicate the overall findings from the first part of the study. Our findings currently being prepared for publication, do not suggest an overall association between fluoride and osteosarcoma. This seems particularly important since the cases had been accrued essentially from the same hospitals within the same orthopedic departments with the same providers, and the same pathology departments making the diagnosis of the osteosarcoma and also using similar methods of fluoride exposure.

In addition to fluoride intake history, many of the cases and controls that were accrued in the 1993–2000 time period agreed to provide bone specimens. The cases provided bone that was obtained proximal to the osteosarcoma lesion as well as from their contra lateral hip. The control group of non-osteosarcoma cancer patients provided bone specimens. Our preliminary analysis of the fluoride content of the bone specimens suggests that the fluoride level within the bone is not associated with excess risk of osteosarcoma. We are grateful to Dr. Bassin and her coauthors for mentioning at the end of their paper that we are not finding a positive association from the bone specimens in the second set of cases.

Obtaining and analyzing sufficient numbers of bone specimens has been a laborious and a time consuming effort by many people throughout the hospitals and research teams. The analysis of these specimens has included quality control procedures on laboratory techniques, pilot studies to test reliability, many runs of small batches of specimens, the double checking of specimen transport procedures, and the preparation of data sets for analysis.

We are now in the possession of the complete analytic data sets and are pursuing previously planned analysis and comparisons with the earlier set of collected cases. We

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How much toothpaste should a child under the age of 6 years use?

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Abstract

AIM: To discuss current concepts in the use of fluoride and to determine how much fluoride is sufficient for caries prevention but also how much is too much. Use of fluoride by young children is a balance between maximising caries efficacy and minimising the risk of fluorosis. **METHODS:** Review of the current literature. This review considers the importance of amount, concentration and dose of fluoride applied from toothpaste and the implications for risk and benefit. **RESULTS:** Dental fluorosis is dependent on local fluoride levels in the extra cellular fluid surrounding the tooth during its development. These fluoride levels are determined by the plasma concentration that in turn is a function of the daily intake of fluoride. Fluoride released from bone during remodelling may also contribute to fluoride levels in the tissue. There is evidence to suggest that the effects of fluoride resulting in fluorosis prior to eruption of the tooth are cumulative and dependent on the amount and duration of exposure rather than a specific window of vulnerability. In contrast to dilution of ingested fluoride in the large volume of plasma, dilution of toothpaste in oral fluids is relatively small. Hence, for a given dose of fluoride, higher fluoride levels can be achieved in the oral environment using small amounts of toothpaste with higher fluoride concentrations rather than larger amounts with lower fluoride concentrations. **CONCLUSION:** It is concluded that for young children fluoride ingestion needs to be carefully controlled during the first six years of life and the best balance between risk and efficacy might be achieved by using small amounts of high fluoride toothpaste under close supervision from parents.

Introduction

Fluoride (F) toothpastes are one of the few preventive interventions used in dentistry that withstand the close scrutiny of systematic reviews of efficacy. Marinho et al. [2003] conducted a comprehensive systematic review of fluoride toothpastes for children in association with the "The Cochrane Collaboration" and concluded that:

> "Supported by more than half a century of research, the benefits of F-toothpastes are firmly established. Taken together, the trials are of relatively high quality, and provide clear evidence that F-toothpastes are efficacious in preventing caries,"

However, it has long been accepted that the appropriate use of F-toothpaste by young children is a balance between the risk of fluorosis [Pendrys, 2000] and anticaries benefit. Therefore when considering the amount of toothpaste a child should use an understanding of both the key determinants of risk and efficacy is required, before appropriate advice can be given.

Risk of fluorosis. Dental fluorosis is a developmental defect of enamel caused by ingestion of F prior to eruption of the tooth into the oral cavity. The effect is systemic and depends on the F concentration around the developing tooth during enamel formation. The risk of fluorosis and its severity is dependent on a wide range of factors such as the timing of the F ingestion, amount ingested, its bioavailability, the developmental stage of the tooth, duration of the exposure and the body weight of the child. The body weight of the child is important as this determines the dilution of a dose ingested. For a constant dose the resultant concentration in plasma will be higher for a low body weight than a higher and hence the effects of a particular dose on a 1 year old, weighing approximately 10 kg, will be greater than on a 5-6 year old weighing 20 kg. To take account of this, the risk of fluorosis, for a particular dose of fluoride, is qualified as a dose per kg body weight (mg F/kg).

In terms of risk there are two important questions that need to be addressed; firstly at what stage during the development of the enamel does F exert its effect and secondly how much fluoride needs to be ingested and absorbed to elicit fluorosis of different severities.

Developmental stage of the dentition. Our understanding of the mechanism of action of F resulting in dental fluorosis is far from complete, but there is good evidence that F exerts its main effect in the maturation phase of tooth development [Andersen et al., 1986; Richards et al., 1986]. However, although the main effect is thought to be on enamel maturation there is also evidence to suggest that continuous intake of F during and after the secretory phase may also increase fluorosis risk [Aoba and Fejerskov, 2002].

It should be appreciated that initially, even when the crown is fully formed, the mineral density is low (30%) [Robinson et al., 1996]. Maturation of the enamel occurs up to the time

Key words: fluoride, toothpaste, fluorosis, caries

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Guidelines on the use of fluoride in children: an EAPD policy document.

SUMMARY

The EAPD strongly endorses that the daily use of fluoride should be a major part of any comprehensive preventive program for the control of dental caries in children. Regardless of the type of program, community or individually based, the suggested use of fluoride must be balanced between the estimation of caries risks and the possible risks for toxic effects of the fluorides. Such a preventive program should be re-evaluated at regular intervals and adapted to a patient's needs and risks. For the majority of European communities, the EAPD recommends the use of appropriate fluoride toothpaste in conjunction with good oral hygiene to be the basic fluoride regimen.

Key words: Fluoride, Caries, Child

1. Background considerations

The European Academy of Paediatric Dentistry (EAPD), in collaboration with the Hellenic Division of EAPD, organised a workshop in Athens, Greece (June, 1997), aiming at drawing up guidelines for future use of fluorides among European children. The first draft of these guidelines was published in the EAPD newsletter, and members were invited to make comments and suggestions. The revised first draft was then presented at the biannual EAPD Congress in Sardinia (1998), where it was discussed in great detail, so that members' viewpoints were taken into consideration. The major concepts of the proposed guidelines were approved, and a working group, consisting of the authors of the original paper, was authorised to finalise and publish the recommendations [Oulis et al., 2000]. In November 2008 the EAPD organised another workshop, again in Athens, Greece, to update the original fluoride guidelines. These updated fluoride guidelines employed the evidence-based SIGN (Scottish Intercollegiate Guidelines Network) methodology for ranking the levels of evidence and the grades of recommendations [SIGN 83, 2005; SIGN 50, 2008].

2. Introduction

Evidence suggests that the cariostatic effect of fluoride is mostly exerted by its topical rather than systemic effect [Featherstone, 1999]. This effect might be even greater when combined with good oral hygiene, such as when practised as comprehensive tooth brushing with a fluoride toothpaste [Rolla et al., 1991]. Concern about the prevalence of dental fluorosis in some children has mostly been related to the use of fluoride supplements, especially during the first 6 years of life [Ismail and Bandekar, 1999]. However, it has also been shown that early exposure to fluoride toothpaste might be a risk factor [Levy et al., 1995; Mascarenhas and Burt, 1998]. Studies that have summarised the risks for dental fluorosis have concluded that the risk is highest when the exposure takes place in both the secretory and the maturation phases of enamel formation [DenBesten, 1999; Evans and Stamm, 1991]. Therefore, three age groups can be considered in terms of having a risk for enamel mottling, namely:

0-4 years

Babies and infants under the age of 4 years of age are considered to be at risk of dental fluorosis of permanent incisors and first molars because the calcification and maturation of these teeth occurs during this period of life. More specifically, the period spanning from 15 to 30 months of age is called the "susceptibility window" as this has been estimated as the highest risk period [Evans and Stamm, 1991]. It is during this period when the use of fluorides must be carefully monitored and balanced with the need to prevent the occurrence of early childhood caries. Special attention should be given to the use of topically applied fluorides during this period of life, because of the inadequate control of the swallowing reflex.

4-6 years

The posterior teeth (premolars and second molars) are calcifying and maturing during this period and at risk of dental fluorosis. Nevertheless, when this occurs it represents less of an aesthetic problem, which needs to be weighed against the marked benefit of caries prevention brought about by the use of fluoride.

6 years and above

The risk for enamel mottling during this period is negligible, with the exception of third molars.

3. Guidelines

The following guidelines are recommended as an integral part of preventive programs for children. It must be emphasised, however, that any dentist supervising a child's oral care must address individual needs.

Systematic review of water fluoridation

Marian S McDonagh, Penny F Whiting, Paul M Wilson, Alex J Sutton, Ivor Chestnutt, Jan Cooper, Kate Misso, Matthew Bradley, Elizabeth Treasure, Jos Kleijnen

Abstract

Objective To review the safety and efficacy of fluoridation of drinking water.

Design Search of 25 electronic databases and world wide web. Relevant journals hand searched; further information requested from authors. Inclusion criteria were a predefined hierarchy of evidence and objectives. Study validity was assessed with checklists. Two reviewers independently screened sources, extracted data, and assessed validity.

Main outcome measures Decayed, missing, and filled primary/permanent teeth. Proportion of children without caries. Measure of effect was the difference in change in prevalence of caries from baseline to final examination in fluoridated compared with control areas. For potential adverse effects, all outcomes reported were used.

Results 214 studies were included. The quality of studies was low to moderate. Water fluoridation was associated with an increased proportion of children without caries and a reduction in the number of teeth affected by caries. The range (median) of mean differences in the proportion of children without caries was −5.0% to 64% (14.6%). The range (median) of mean change in decayed, missing, and filled primary/permanent teeth was 0.5 to 4.4 (2.25) teeth. A dose-dependent increase in dental fluorosis was found. At a fluoride level of 1 ppm an estimated 12.5% (95% confidence interval 7.0% to 21.5%) of exposed people would have fluorosis that they would find aesthetically concerning.

Conclusions The evidence of a beneficial reduction in caries should be considered together with the increased prevalence of dental fluorosis. There was no clear evidence of other potential adverse effects.

Introduction

In the white paper, *Saving Lives: Our Healthier Nation*, the UK government highlighted the commonly held belief that there is strong evidence that water fluoridation improves and considerably reduces inequality in dental health.[1] The government also acknowledged that "the extensive research linking water fluoridation to improved dental health was mostly undertaken a few years ago," and as a result this study was commissioned to provide a comprehensive systematic review of the safety and efficacy of fluoridation of the public water supply.

We focused on the two main objectives: the effects of fluoridation of drinking water supplies on the incidence of caries and whether fluoridation has negative effects. The full report is available elsewhere.[2]

Methods

Search strategy

We searched 25 specialist databases, including Medline, Embase, TOXLINE, and Current Contents (Science Citation Index) from inception of the database to February 2000. In addition, we hand searched Index Medicus (1945-63) and Excerpta Medica (1955-73). Further searches included the world wide web and bibliographies of all included studies. We sought additional references from individuals and organisations through a dedicated web site for this review (www.york.ac.uk/inst/crd/fluorid.htm includes the full report) and through members of a specifically designated advisory panel. Published and unpublished studies in any language were included. Full details of the search strategy are reported elsewhere.[2]

Inclusion criteria

We applied two types of inclusion criteria. The first was the level of evidence, based on the risk of bias. Studies were classified into the levels of evidence. Evidence rated below level B (moderate quality evidence, moderate risk of bias) was not considered in the evaluation of efficacy. In the assessment of safety all levels of evidence were considered. If a study met only one or two of three criteria for a given level of evidence, it was assigned the next level down. Details of both types of inclusion criteria can be found on the *BMJ*'s website.

Data extraction and assessment of study quality

Inclusion criteria were assessed independently by at least two reviewers. Extraction of data from studies and assessment of validity was independently performed by two reviewers and checked by a third reviewer. Disagreements were resolved through consensus. We assessed study validity formally using a published checklist modified for this review.[3] Each item on the checklist was given one point, with a total of eight points possible for all study designs except case-control studies, which could attain a total of nine points.[2]

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continued over

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Additional material comprising criteria for inclusion, members of the advisory panel, references (w1 etc) for included studies, and meta-regression table can be found on the BMJ's website

Effectiveness of Water Fluoridation

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Abstract

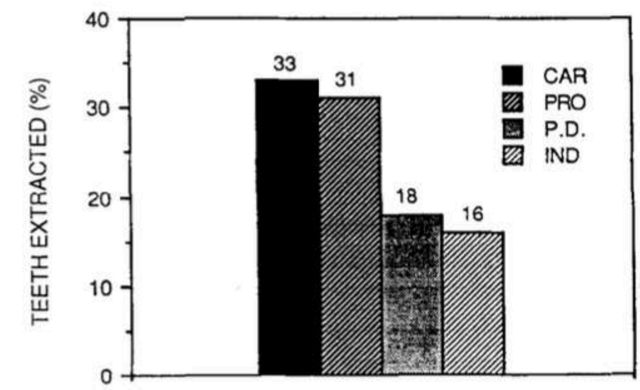
The efficacy of communal water fluoridation in reducing dental caries has been reviewed based on surveys conducted in the last decade of caries prevalence in fluoridated and nonfluoridated communities in the United States as well as in Australia, Britain, Canada, Ireland, and New Zealand. The efficacy is greatest for the deciduous dentition, with a range of 30-60 percent less caries in fluoridated communities. In the mixed dentition (ages 8 to 12), the efficacy is more variable, about 20-40 percent less caries. In adolescents (ages 14-17), it is about 15-35 percent less caries. Current data on caries prevalence in adults and seniors are extremely limited and include several populations living in communities with higher than optimal fluoride levels. For these adults and seniors, a range of 15-35 percent less caries would also apply. Viewed in toto, the current data for children, adolescents, adults and seniors show a consistently and substantially lower caries prevalence in fluoridated communities. For an accurate measurement of the efficacy of water fluoridation in reducing dental caries, it is essential that only persons with a record of continuous or long-term residency in fluoridated versus nonfluoridated areas be included in such assessments. Because of the high geographic mobility in our society and the widespread use of fluoride dentifrices, supplements, and other topical fluoride agents, such comparisons are becoming more difficult to conduct. Accordingly, the effectiveness (rather than the efficacy) of water fluoridation has decreased as the benefits of other forms of fluoride have spread to communities lacking optimal water fluoridation.

Key Words: dental caries, effectiveness, fluoridation.

Introduction

Americans spent almost $30 billion in 1986 to treat all their dental and oral woes (1). A major portion of this amount was for the treatment of decayed teeth or the sequelae of caries. Caries is the most prevalent dental affliction of childhood. According to a 1979-80 survey (2), the average American child had an average of one decayed, missing or filled surface by age 8; four by age 12; and 11 by age 17. A more recent study (3), which surveyed US children during 1986-87, found 36 percent less dental caries than in the 1979-80 survey. While these findings are encouraging, it is important to remember that caries continues to be the leading cause of loss of teeth (Figure 1). As reported recently in the United States, France, Finland, and the Netherlands (4-8), caries exceeds prosthetic reasons, periodontal disease, and other miscellaneous causes for tooth extraction.

FIGURE 1
Causes of tooth extraction in male adults, aged 45 to 90, in the United States. Most common cause was caries, followed closely by prosthetic needs. Periodontal disease and other indeterminate causes were much less frequent reasons for extraction. (Adapted from Chauncey et al. [4].)



The decline in dental caries observed in children during the late 1970s, and more recently in the 1980s, has not benefited all children equally. In the 1979-80 US survey, 25 percent of the children had five or more DMFT. Similarly, in the National Preventive Dentistry Demonstration Program, 20 percent of the children accounted for nearly 60 percent of all decay found (9). This phenomenon, in which a small number of the total population have a higher proportion of disease, has been termed "polarization" (10).

Accordingly, about 20 percent to 25 percent of children are at relatively high risk of caries, in spite of the declining caries prevalence in the "fluoride generation." Moreover, most adults of the "prefluoridation generation" continue to be at risk of recurrent decay and root caries, and most often lose their teeth because of caries. Therefore, caries

School Dental Care in a Community With Controlled Fluoridation

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PREVIOUS STUDIES of accumulated and maintenance dental care needs of school children, such as those conducted in Woonsocket, R.I., and Richmond, Ind. (*1–5*), have provided communities a basis for estimating dental care requirements in child population groups where the prevalence of caries is high or moderate. Introduction of controlled fluoridation to a public water supply, however, can create a situation to which the aforementioned studies are not applicable for forecasting dental needs of children.

This report is based on a study of regular clinical maintenance care needs of the school population of Gainesville, a city of moderate size in north central Florida, which had been controlling the fluoride level of its drinking water at 0.8 ppm since 1949. Our study, started in January 1954 and completed in 1959, 5½ years later, was made to determine the level and character of dental needs of children and the professional time and service required to meet these needs in a community having the benefit of water fluoridation. The Gainesville school system offered a group of approximately 5,000 children who were experiencing steadily diminishing dental care requirements. Our study was designed to provide complete dental care, except orthodontics, for all children having parental consent in grades one through six.

Each school was visited four times, in turn, during this study. The first treatment series required 17 months, the second took 18½ months, and the third required 16 months. After completion of the accumulated backlog of dental care, the time element was gradually reduced to 14 months for the fourth series.

A cooperative project of the Alachua County Health Department, the Gainesville Board of Public Instruction, and the Public Health Service, the program also was supported and assisted by the Florida State Health Department, State and local dental societies, and the parent-teacher association.

Dr. Frank is now a regional radiological health consultant in Chicago, Dr. Law has retired, and Mrs. Spitz is with the Nursing Homes and Related Facilities Branch, Division of Chronic Diseases, Public Health Service. All were in the Division of Dental Public Health and Resources, Public Health Service, at the time of the study. Dr. Galagan is chief of the Division of Dental Public Health and Resources, Public Health Service.

Facilities and Personnel

It was apparent from the beginning that the rapidly expanding school population would prohibit the allocation of suitable space to house a dental clinic in all schools. Thus the Alachua County Health Department provided a new structure, approximately 26 by 36 feet, to serve as a portable clinic building that could be moved from school to school as required. It was designed to provide maximum light to work areas, a well-engineered laboratory storage area, a darkroom, space for six dental units, a place for record keeping and administration, and a reception area. Equipment was supplied by the Public Health Service.

Basic equipment for each of the dentists assigned to the project included two standard dental units with lights, air, automatic water

Elevated Serum Fluoride Concentrations in Women Are Not Related to Fractures and Bone Mineral Density[1]

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ABSTRACT Epidemiologic studies of the relations between drinking-water fluoride levels and bone mineral density (BMD) and fracture are characterized by disparate conclusions and an absence of information about individual circulating fluoride levels. This study relates serum fluoride concentrations, which reflect individual fluoride exposures, to BMD and bone fractures. Data are from 1300 female residents of 3 small communities in which the water fluoride concentrations were 52.6 or 210.4 μmol/L. Circulating serum fluoride concentrations were assessed by ion-specific electrode. Fluoride intake was estimated from interviews describing water and water-based beverage consumption and duration of residence in the community. BMD was measured by dual-energy X-ray densitometry and single-photon densitometry. Self-reported fractures were confirmed by medical record abstraction. The mean serum fluoride concentration in the high-fluoride community, 2.11 $\pm$ 0.05 μmol/L, was significantly higher than serum fluoride concentrations in the control and high-calcium communities with water fluoridation to 52.6 μmol/L. The mean serum fluoride concentrations in these latter 2 communities were 1.6 $\pm$ 0.04 and 1.22 $\pm$ 0.05 μmol/L, respectively. Serum fluoride was not significantly related to BMD after adjusting for covariates including age and body size. The mean distal radius BMD, however, was significantly higher in the high-fluoride community. Serum fluoride concentrations were not related to incident osteoporotic fractures with 4 y of observation. Serum fluoride concentrations were not associated with BMD or osteoporotic fractures among female residents of communities with water fluoride concentrations of 52.6 or 210.4 μmol/L. J. Nutr. 135: 2247–2252, 2005.

KEY WORDS: • *water fluoride* • *serum fluoride* • *bone mineral density* • *bone fracture*

Fluoride is a trace element that is ubiquitously distributed throughout the environment in a wide range of concentrations. After its absorption from the gastrointestinal tract, it is rapidly incorporated into calcified tissues, which contain 99% of the body burden (1). Fluoride has the ability to prevent the formation and progression of dental caries and to stimulate the formation of new bone. In pharmacologic doses for the treatment of osteoporosis, fluoride was shown to increase bone mineral density (BMD) (2,3). With such doses, there is concern about atypical mineralization (4,5) and increased risk of fracture (6,7) when steady-state serum fluoride concentrations are chronically above the "therapeutic window" of 5–10 μmol/L (8,9).

There is also uncertainty about the skeletal effects of fluoride at considerably lower intakes from the diet and drinking water. Some epidemiologic studies found no association with BMD or bone fracture among women whose drinking water contained fluoride at <15.8–52.6 μmol/L (10,11) when the fluoride exposures were defined by fluoride concentrations in drinking water at its processing source. In contrast, an increased risk of bone fracture was reported in a community in which the naturally occurring water fluoride concentration was 210.4 μmol/L compared with one in which the water concentration was 52.6 μmol/L (12). None of these studies of BMD and/or fracture, however, included measures of individual circulating fluoride exposure, which is considered the best indicator of body burden and varies widely among residents of the same region. Because these and other studies (10–15) were conducted at the ecologic level with its inherent limitations, there is growing interest in using biomarkers, such as serum fluoride concentrations, to assess individual exposures (16). Serum fluoride concentrations correlate well with long-term levels of intake and with skeletal fluoride concentrations because of the steady-state relation between the concentrations in the exchangeable pool of bone and the extracellular fluids (17–21), although bone biopsies could provide a more direct assessment if they could actually be done in large population-based studies such as these.

Understanding the health effect of relatively low fluoride exposures, from dietary sources and dental products, has substantial public health importance. There are large geographic areas in the United States in which naturally occurring water fluoride levels approach or exceed 105.2 μmol/L, particularly in the southwestern region of the United States but also in

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U.S. Public Health Service Recommendation for Fluoride Concentration in Drinking Water for the Prevention of Dental Caries

U.S. Department of Health and Human Services Federal Panel on Community Water Fluoridation

Through this final recommendation, the U.S. Public Health Service (PHS) updates and replaces its 1962 Drinking Water Standards related to community water fluoridation—the controlled addition of a fluoride compound to a community water supply to achieve a concentration optimal for dental caries prevention.[1] For these community water systems that add fluoride, PHS now recommends an optimal fluoride concentration of 0.7 milligrams/liter (mg/L). In this guidance, the optimal concentration of fluoride in drinking water is the concentration that provides the best balance of protection from dental caries while limiting the risk of dental fluorosis. The earlier PHS recommendation for fluoride concentrations was based on outdoor air temperature of geographic areas and ranged from 0.7–1.2 mg/L. This updated guidance is intended to apply to community water systems that currently fluoridate, or that will initiate fluoridation, and is based on considerations that include:

- Scientific evidence related to the effectiveness of water fluoridation in caries prevention and control across all age groups,
- Fluoride in drinking water as one of several available fluoride sources,
- Trends in the prevalence and severity of dental fluorosis, and
- Current evidence on fluid intake of children across various outdoor air temperatures.

BACKGROUND

Because fluoridation of public drinking water systems had been demonstrated as effective in reducing dental caries, PHS provided recommendations regarding optimal fluoride concentrations in drinking water for community water systems in 1962.[2,3] The U.S. Department of Health and Human Services (HHS) is releasing this updated PHS recommendation because of new data that address changes in the prevalence of dental fluorosis, the relationship between water intake and outdoor temperature in children, and the contribution of fluoride in drinking water to total fluoride exposure in the United States. Although PHS recommends community water fluoridation as an effective public health intervention, the decision to fluoridate water systems is made by state and local governments.

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COMMUNITY DENTISTRY AND ORAL EPIDEMIOLOGY

A review of fluorosis in the European Union: prevalence, risk factors and aesthetic issues

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Whelton HP, Ketley CE, McSweeney F, O'Mullane DM. A review of fluorosis in the European Union: prevalence, risk factors and aesthetic issues. Community Dent Oral Epidemiol 2004; 32 (Suppl. 1): 9–18. © Blackwell Munksgaard, 2004

Abstract – Fluoride has played a key role in caries prevention for the past 50 years but excessive ingestion of fluoride during tooth development may lead to dental fluorosis. Throughout Europe many vehicles have been, and are currently, employed for optimal fluoride delivery including drinking water, toothpaste, fluoride supplements, salt and milk. Several indices, both descriptive and aetiological, have been developed and used for measuring fluorosis. This factor, combined with the lack of use of a standardized method for measurement of fluorosis, has made comparison between studies difficult and assessment of trends in fluorosis prevalence unreliable. Overall the evidence would appear to indicate, however, that diffuse enamel opacities are more prevalent in fluoridated than in nonfluoridated communities and that their prevalence at the very mild level may be increasing. In addition to fluoridated drinking water, risk factors for fluorosis include inadvertent ingestion of fluoride toothpaste and the inappropriate use of fluoride supplements. The risk is of aesthetic concern primarily during the period of enamel development of the permanent central incisors, although this largely appears to be a cosmetic rather than a public-health issue. It is concluded that there is a need to co-ordinate studies measuring fluorosis throughout Europe and that development of a standardized photographic method would be useful. Furthermore, the aesthetic importance of fluorosis needs to be determined in more detail in each country in the light of each country's respective risk factors and dental health policies.

Key words: aesthetics; Europe; fluorosis; indices; prevalence; risk factors

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Fluoride has played a central role in oral health promotion for the past 50 years but the ingestion of excessive fluoride during tooth development, particularly at the maturation stage, may result in dental fluorosis, which has an extensive range of clinical signs. Mildly fluorosed enamel is fully functional and may present as barely detectable whitish surface striations (1, 2) whereas severely fluorosed enamel is more prone to wear and fracture and may present as pitted, stained and porous enamel (3). Fluorosis may occur in either the primary or permanent dentition, this paper reviews studies of fluorosis of the permanent dentition.

Currently the various vehicles for and sources of fluoride include drinking water, toothpaste, fluoride supplements, fluoridated salt, fluoridated milk, processed drinks and foods. Optimal water fluoridation is that concentration which provides the maximum protection against caries with the least clinically observable fluorosis. Some areas have naturally optimally fluoridated water supplies (0.7–1.5 ppm F) including the Bordeaux region in France, Mouscron in Belgium and Hartlepool in the UK. Water fluoridation schemes are currently operating in Ireland, Spain, Switzerland and the UK (4). In Ireland fluoridation (0.8–1.0 ppm F) began in 1964, serves approximately 74% of the population and is mandatory by law (5). Spain began fluoridation in 1986 and it now serves in excess of 3.3 million people (4). Under the UK Water Fluoridation Act of 1985 the decision to fluoridate is made locally and currently 10% of the UK population receives fluoridated water

Fluoride in Dental Products: Safety Considerations

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This review summarizes the nature of acute fluoride toxicity, its time-course, and the fluoride doses that are involved. The generally accepted "certainly lethal dose" range for 70 kg adults, i.e., from 5 to 10 g of sodium fluoride or from 32 to 64 mg fluoride/kg, is discussed. Based on recent case reports of fluoride-induced fatalities, it is concluded that this dose range has little utility in cases involving young children. The concept of a "probably toxic dose" (PTD) is advanced. The PTD, 5.0 mg F/kg, is defined as the dose of ingested fluoride that should trigger immediate therapeutic intervention and hospitalization because of the likelihood of serious toxic consequences. The concentrations and quantities of fluoride in selected dental products are discussed in relation to the PTD. It is concluded that, as these products are currently packaged, most of them contain quantities of fluoride sufficient to exceed the PTD for young children. Recommendations are made to reduce the risk of toxicity associated with their use.

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Introduction.

During the first four decades of this century, the search for the etiologic factor responsible for endemic dental mottling in localized regions of the United States led to the discovery that fluoride is a potent cariostatic agent (Dean, 1942). Soon thereafter, studies of laboratory animals and humans indicated that topically applied forms of fluoride could also reduce the rate of caries development in many individuals. Today, a wide variety of fluoride-containing products designed for professional application or home use is available.

The purpose of this brief review is to discuss the concentrations and amounts of fluoride that are found in the most commonly used of these products. This information will be related to our current knowledge about the quantities of ingested fluoride that may be associated with episodes of acute fluoride toxicity.

Acute fluoride toxicity.

When sufficiently large amounts of fluoride are ingested as a single dose, a catastrophic chain of events rapidly develops (Hodge and Smith, 1965). The first effects experienced by the victim usually include nausea, vomiting, and burning or cramp-like abdominal pains. There may be excessive salivation and tearing, mucous discharges from the nose and mouth, a generalized weakness, paralysis of the muscles of swallowing, carpo-pedal spasms or spasm of the extremities, tetany, and generalized convulsions. The pulse may be thready or not detectable. Blood pressure often falls to dangerously low levels at some point during the course of the toxic episode. As respiration is depressed, a respiratory acidosis develops. Plasma potassium levels are elevated, indicating a generalized toxic effect on cell membrane function. Cardiac arrhythmias may develop in association with the hyperkalemia. Plasma calcium levels are typically depressed, sometimes to extraordinarily low values (5 mg% or less). Extreme disorientation or coma usually precedes death, which often occurs within the first few hours after the fluoride dose.

The literature contains a wide range of estimates for the acute lethal oral dose of fluoride in humans, most of which were based on cases involving adults. They range from 6-9 mg F/kg (Dreisbach, 1980) to over 100 mg F/kg (Lidbeck, 1943). This confusing situation undoubtedly stems, in part, from uncertainties about the quantities of fluoride ingested. The different chemical forms of fluoride vary in their toxic potentials as well, chiefly because of differences in the rate or degree of absorption from the gastro-intestinal tract. Thus, fluoride from sodium or potassium fluoride, compounds which are relatively soluble, is more toxic than that from compounds which contain di- or trivalent cations such as calcium, magnesium, or aluminum. Similarly, there is evidence from two studies with rats that monofluorophosphate (Na_2PO_3F or MFP) is less toxic than equimolar amounts of sodium fluoride (Shourie *et al.*, 1950; Lim *et al.*, 1978). A more recent study, however, has failed to confirm the differential toxicity of MFP and sodium fluoride (Whitford *et al.*, 1987). Stannous fluoride has been reported to be slightly more toxic than sodium fluoride (Lim *et al.*, 1978). Further, individual humans as well as laboratory animals differ in their susceptibility to acute fluoride toxicity, largely for reasons that have not yet been identified.

The most frequently cited range for the "certainly lethal dose" (CLD) of sodium fluoride in humans was offered by Hodge and Smith (1965). Based on a review of case reports, they concluded that "a dose range of 5-10 g of sodium fluoride can be cited as a reasonable estimate of a certainly lethal dose for a 70-kg man." This corresponds to an ingested fluoride dose range of from 32 to 64 mg F/kg of body weight.

Several points must be made about this estimated range for the CLD. First, it is the equivalent of an LD_{100}. That is, *every* 70-kg adult who ingests from 5 to 10 g of sodium fluoride would be expected to die. This is important information but, from the public health and clinical perspectives, values such as an LD_{10}, LD_{33}, or LD_{50} as well as the maximum "certainly safe dose" would be more instructive. For humans, as would be expected, these values are not known. Second, it is not clear why Hodge and Smith selected that particular CLD range. An examination of their data shows that, in most cases, the fluoride doses that caused death were not known. Their data include two deaths caused by "*ca.* 3-4 gm" of sodium fluoride and one, which involved a three-year-old child, caused by "*ca.* 0.5-0.7 gm" of sodium silicofluoride (from 300 to 425 mg of fluoride ion). This raises the third point, which is whether it is appropriate to extrapolate the estimated CLD for adults to children.

It is known from studies with rats that younger animals are more resistant to the lethal effects of fluoride (Mornstad, 1975). This may not be the case for humans. Dukes (1980) reported that a 27-month-old male child experienced respiratory failure after the ingestion of fewer than 100 sodium fluoride tablets, each containing 0.5 mg of fluoride. Gastric lavage yielded four

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A systematic review of the efficacy and safety of fluoridation

Australian National Health and Medical Research Council. Canberra: Australian Government; 2007

Scope and purpose The systematic review was commissioned by the Australian National Health and Medical Research Council (NHMRC) to evaluate the scientific literature relating to the health effects of fluoride and fluoridation. The systematic review's research questions relate to the caries-reducing benefits and associated potential health risks of providing fluoride systemically (via addition to water, milk and salt) and the use of topical fluoride agents, such as toothpaste, gel, varnish and mouthrinse. Although the review summarises the recent evidence, it does not constitute health policy or clinical practice recommendations.

Data sources A literature search was undertaken using the Medline and Embase databases (via www.embase.com). In addition, the Cochrane Systematic Review and Clinical Trial databases were searched to help identify additional systematic reviews and original studies. Because of the availability of recent systematic reviews, searches were limited to publications from 1996 onwards . The search was conducted in December 2006 and limited to English-language publications.

Study selection Based on types of intervention (individual or population) and the outcomes assessed (efficacy or safety), the hierarchy of study types considered most relevant for answering each of the clinical questions defined in this review was chosen (Table 1). The levels of evidence used by NHMRC for intervention and aetiological studies are summarised in Table 2.

Data extraction and synthesis Screening of eligible studies was conducted by three reviewers. Data were extracted for all of the included systematic reviews and individual studies using standardised data-extraction forms. This included information about the study design, NHMRC level of evidence, population, intervention, comparator, outcome definitions and results. Information relating to potential biases and study quality were also extracted. Where appropriate, study results were pooled using standard meta-analysis techniques.

Results In total, 5418 nonduplicate citations were identified. After applying the inclusion and exclusion criteria, 408 citations were considered potentially eligible for inclusion in the review. After the review of the full papers of potentially eligible articles, 77 citations were included in the review. The summary of findings was presented in the context of the research questions (Table 3).

Recommendations Fluoridation of drinking water remains the most effective and socially equitable means of achieving community-wide exposure to the caries prevention effects of fluoride. It is recommended (see also www.nhmrc.gov.au/news/media/rel07/_files/fluoride_flyer.pdf) that water be fluoridated in the target range of 0.6–1.1 mg/l, depending on the climate, to balance reduction of dental caries and occurrence of dental fluorosis.n particular with reference to care in hospital for those following stroke.

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Commentary

This systematic review of fluoridation is the fourth of the reviews commissioned by the NHMRC in Australia. The first two were carried out in 1985[4] and 1991[5] and focussed on the effectiveness of water fluoridation. The third one[6] included a review of fluoride intake from discretionary fluoride supplements in addition to water fluoridation. The third review was published in 1999, and is presently available on the website of Australian Dental Association (www.ada.org.au/app_cmslib/media/lib/0703/m50958_v1_nhmrc%20fluoride.pdf). The fourth review[7] published in 2007 has once again expanded its scope by including other methods of fluoride delivery, such as milk, salt, toothpaste, gel, varnish and mouthrinse. Fluoride supplements such as drops, chewable tablets and chewing gum tablets have not been explicitly included in the current review, however.

The aim of the most recent review was to synthesise the highest level of evidence to answer each clinical question. It should be noted that the levels of evidence accepted for fluoride intervention at the population level was based on those chosen for the systematic review of water fluoridation by McDonagh et al.[2]

The inclusion and exclusion criteria for the current review were explicit. The search strategy used to identify relevant studies could not be considered to be comprehensive as no controlled vocabulary was used in searching the electronic databases. Moreover, the range of electronic databases searched was rather limited and restricting studies to those published in the English language may also affect the findings. During the literature search, three reviewers assessed the eligibility of abstracts (approximately one third each). It is not clear whether study selection or data extraction was carried out independently or in duplicate.

Included studies were clearly laid out in table format in the appendix. This included information about the study design, population, intervention, comparator, outcomes and results. The quality of studies was assessed using the key questions from the NHMRC.[7] For those study designs such as cross-sectional studies and ecological studies which had no guidance on assessment from the NHMRC, a summary of various factors relating to potential biases was provided. In addition, a global quality rating was given to each individual study. Post-hoc statistical analysis was carried out when necessary.

Two systematic reviews[2,8] and one additional, relevant, original study[9] were identified in the literature search on water fluoridation and dental caries. The York review[2] was chosen to form the evidence base for the effect of water fluoridation on dental caries in the current review, as it provided more detailed and comprehensive results than those shown in the review by Truman et al.[6] It should be noted that 12 of the 21 studies included in the latter were among the 26 studies included in the York review.[2] The lack of overlap between the two reviews is largely because the Truman review[8] assessed both "fluoridation *vs* no fluoridation" and "fluoridation *vs* fluoridation at a lower level" whereas the York review[5] assessed only "fluorida-

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Current and future role of fluoride in nutrition

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It is almost universally known and accepted by all reputable health organizations that fluoride is effective in preventing one of the most common of human diseases: dental caries. Although the actual substance was unknown to him at the time, McKay [1], in the early 1900s, was the first to note the caries-preventive effects of a presumably water-borne substance. Subsequently, the substance in the water supply with caries-preventive properties was identified as fluoride, and further research by Dean et al [2,3] established 1.0 parts per million (ppm) as the optimal water fluoride concentration. In 1945, fluoride was added to the water supply of Grand Rapids, Michigan for the express purpose of caries prevention and, since that time, fluoridation has become widespread in North America.

It was once believed that fluoride primarily was effective in caries prevention through systemic ingestion during tooth development, and fluoridated water and dietary fluoride supplements were developed to accommodate this mechanism of action [4]. Current evidence strongly suggests that fluorides work primarily by topical means through direct action on the teeth and dental plaque [4]. Thus, ingestion of fluoride is not essential for caries prevention, although as discussed below, water fluoridation and dietary supplements have been found to be very effective in caries prevention. In addition, some ingestion is inevitable with topical agents (such as dentifrice) and, due to a number of factors, there are many sources of fluoride in the diet. Moreover, there are consequences to excessive fluoride ingestion. Therefore, it is important to monitor fluoride as a component in the diet and as part of human nutrition.

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Acute Fluoride Toxicity from Ingesting Home-use Dental Products in Children, Birth to 6 Years of Age

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Abstract

Objectives: *This paper analyzes reports to the American Association of Poison Control Centers (AAPCC) of suspected overingestion of fluoride by children younger than 6 years of age between 1989 and 1994, and estimates the probably toxic amounts of various home-use fluoride products in children younger than 6 years of age.* ***Methods:*** *Annual incidence rates of reported fluoride exposures attributed to dietary supplements, toothpaste, and rinses were calculated. Probably toxic amounts of each product were calculated using the frequently cited dose of 5 mg/kg.* ***Results:*** *Children younger than 6 years of age accounted for more than 80 percent of reports of suspected overingestion. While the outcomes were generally not serious, several hundred children were treated at health care facilities each year. A 10 kg child who ingests 50 mg fluoride (10.1 g 1.1% NaF gel; 32.7 g 0.63%* SnF_2 *gel; 33.3 g 1,500 ppm F toothpaste; 50 g 1,000 ppm F toothpaste; and 221 mL 0.05% NaF rinse) will have ingested a probably toxic dose.* ***Conclusions:*** *Overingestion of fluoride products in the home is preventable. Dentists and other health care providers should educate parents and child care providers about the importance of keeping fluoride products out of reach of children. Manufacturers should be encouraged by the ADA and the FDA to use child-resistant packaging for all fluoride products intended for use in the home. [J Public Health Dent 1997;57(3):150-8]*

Key Words: fluoride, fluoride toothpaste, fluoride toxicity, fluoride mouthrinse, fluoride supplements, self-applied fluorides, fluoride gels.

In 1994, the American Association of Poison Control Centers (AAPCC) recorded 10,596 calls about suspected overingestion of fluoride (reported exposures), approximately one-half percent of all reports to participating poison control centers (1). The exposures were attributed to dietary supplements (33.4%), toothpaste (31.5%), vitamins (23.5%), and mouthrinses (11.5%) (1).

The use of flavored consumer fluoride products increases the possibility that a child will ingest a toxic dose of fluoride. Acute fluoride toxicity can occur rapidly after the single ingestion of a large amount of fluoride. Soluble fluoride compounds, such as sodium fluoride, are rapidly and almost completely absorbed from the gastrointestinal tract (2). Recent studies also have found that most of the fluoride in ingested toothpaste is absorbed, although absorption can be delayed or reduced by the presence of food or milk (3-6). Blood plasma levels of fluoride generally peak within an hour of ingestion and excretion occurs almost exclusively in the urine (2,7,8).

Symptoms of acute fluoride toxicity vary depending on how much fluoride is ingested. At lower dosages, acute fluoride toxicity appears as nausea, upset stomach, and vomiting (9). As the amount of ingested fluoride increases, blood plasma levels also increase and the symptoms become severe and possibly life-threatening. Convulsions, tetany, and decreased myocardial contractility are associated with hypocalcemia caused by fluoride binding of circulating calcium. Hyperkalemia, also associated with toxic fluoride levels, can lead to ventricular arrhythmias and cardiac arrest. Death is usually the result of respiratory or cardiac failure.

Estimates of the lethal oral dose of sodium fluoride vary substantially. Based on a review of fluoride poisonings, Hodge and Smith (10) estimated that the certainly lethal dose (CLD) for adults ranged from 32 to 64 mg F/kg body weight. Within this range, every 70 kg adult would be expected to die. Whitford (11) reviewed several reports and concluded that more than 15 mg F/kg would likely be fatal for a small child.

Estimates of the probably toxic dose (PTD) also vary substantially. Whitford defines the PTD as "the minimum dose that could cause toxic signs and symptoms, including death, and that should trigger immediate therapeutic intervention and hospitalization" (11). From the findings of Hodge and Smith (10), Heifetz and Horowitz (9) concluded that a dose of 8 mg F/kg body weight could be safely tolerated. Bayless and Tinanoff (12) stated that oral doses of fluoride up to 5 mg F/kg generally produce mild gastrointestinal symptoms while doses of more than 5 mg F/kg could cause serious systemic toxicity. Whitford (11) reviewed reports by Eichler et al. (13), Dukes (14), and Bayless and Tinanoff (12), and concluded that the PTD of fluoride is 5 mg/kg body weight and that the different estimates of the toxic oral dose are largely due to "uncertainties about the quantities of fluorides ingested."

To reduce the likelihood of accidental poisoning among children, the American Dental Association (ADA) recommends that no more than 120 mg of elemental fluoride, or 264 mg of sodium fluoride, be dispensed in one container of fluoride rinse, nonabrasive gel, or dietary supplement. This 120-milligram maximum was based on an extrapolation of the data in the Hodge and Smith report (15). The

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Fluoride: Its Metabolism, Toxicity, and Role in Dental Health

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Abstract

Fluoride is a naturally occurring element with multiple implications for human health. This review discusses its metabolism and toxicity, along with the current understanding of the mechanism of action of fluoride and its role as a safe and effective agent in the prevention of dental caries. The relationship between excessive fluoride intake during periods of dental enamel formation and the development of dental fluorosis is also reviewed.

Keywords

fluoride, dental caries, dental fluorosis

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Fluorine is an electronegative, naturally occurring element and is the 13th most abundant on earth. The range of fluorine-containing compounds is extensive since fluorine is capable of reacting with all the elements except helium and neon. The reduced form of fluorine (or its anion) is designated as fluoride both when present as an ion and when bonded to other elements. Fluorides are naturally occurring and are found in all water sources in small but traceable amounts.

Absorption, Distribution, Secretion, and Excretion of Fluoride

Fluoride-containing compounds are extremely diverse. For that reason it is not possible to generalize on their metabolism, which depends on their reactivity and structure, solubility, and ability to release fluoride ions. The ionic form of fluoride, which can be either generated within the body by the biochemical modification of the different fluoride-containing compounds or ingested directly, is metabolized by the body in a simple manner (see Figure 1 for a schematic of fluoride metabolism).

Fluoride mostly enters the body via the gastrointestinal tract and is absorbed quickly in the stomach without the need of specialized enzymatic systems.[1] It crosses epithelia in the form of undissociated acid (hydrogen fluoride). The diffusibility of hydrogen fluoride explains the physiological behavior of fluoride. At low pH (<3.5), the more undissociated form hydrogen fluoride predominates, whereas at higher pH the ionized form dominates.[2] Recent studies have indicated that in addition to crossing the stomach as undissociated acid, the majority of fluoride absorption occurs in the small intestine and is not pH dependent. Evidence suggests that there are several pH gradient-dependent, carrier-mediated mechanisms for fluoride transport in the intestine.[3-5]

The rate of fluoride absorption from the stomach is directly related to the acidity of its contents.[6] However, several other factors influence the rate of absorption, including the solubility of the ingested fluoride compound. More soluble compounds such as sodium fluoride (NaF) and hydrogen fluoride would result in faster absorptions, whereas less soluble fluoride compounds, such as calcium fluoride (CaF_2) and magnesium fluoride (MgF_2), would slow absorption.[7]

As soon as fluoride is absorbed, plasma fluoride levels increase (at 10 minutes), reaching peak levels at 60 minutes. A return to basal levels is achieved within 11 to 15 hours.[1] It is well documented that there are 2 forms of fluoride in plasma. One fraction is designated as ionic fluoride and the second is designated nonionic or bound fluoride, composed of lipid-soluble organic fluoro-compounds. The biological significance of the nonionic fraction is not well understood.[7]

Once fluoride reaches plasma, it is rapidly deposited in the skeleton or excreted via the kidneys. Fluoride skeletal uptake is also modified by factors such as the activity of bone modeling and remodeling and age.[8] The degree of fluoride retained in the

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Occupational Fluoride Exposure

Harold C. Hodge, Ph.D. and Frank A. Smith, Ph.D.

INTRODUCTION

Normal Intake

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

Air Quality

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

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

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2009 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 27th Annual Report

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Potential fluoride toxicity from oral medicaments: A review

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ABSTRACT

The beneficial effects of fluoride on human oral health are well studied. There are numerous studies demonstrating that a small amount of fluoride delivered to the oral cavity decreases the prevalence of dental decay and results in stronger teeth and bones. However, ingestion of fluoride more than the recommended limit leads to toxicity and adverse effects. In order to update our understanding of fluoride and its potential toxicity, we have described the mechanisms of fluoride metabolism, toxic effects, and management of fluoride toxicity. The main aim of this review is to highlight the potential adverse effects of fluoride overdose and poorly understood toxicity. In addition, the related clinical significance of fluoride overdose and toxicity has been discussed.

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Introduction

Fluoride is the 13th most abundant element present in the earth's crust. It belongs to the halogen group of elements and is found naturally in water, soil, animals, and plants (1). Fluoride is one of the most reactive and ubiquitously present in nature. It is present in trace amounts in all mineralized tissues of the body such as enamel, dentin, and bone. Fluoride is involved in a number of enzymatic reactions (2). In mineralized tissues and biomaterials, fluoride ions increase the stability of mineralized tissues and materials by decreasing the solubility of hydroxy-apatite mineral phase present in biomaterials and mineralized tissues (3). The protective effects of fluoride on dental health were first observed in 1930 as there was less tooth decay in communities consuming naturally fluoridated water compared to non-fluoridated areas (4). Due to these beneficial effects of fluoride, it was introduced into dentistry in 1940 and since then, it is being added to various consumer products. Water fluoridation is the most successfully adopted method (5-7). Fluoride delivery methods and related sources of dietary fluoride are:

Fluoridated water, beverages, and tea. Water is an important media for fluoride delivery. Fluoride exists either naturally or added during water fluoridation (8-11). Recommended optimal level of fluoride in drinking water is 0.7 mg/l; however, fluoride concentration in water varies based on geographical areas. For instance, fluoride content in drinking waters of Pakistan shows a large variation that ranges from < 0.1 ppm to >3 ppm (12). Another study demonstrated that natural water from certain geographical areas (e.g. Punjab, Pakistan) contains fluoride concentration of up to 21 ppm (13). Therefore, the data suggests a clear need for the careful selection of fluoride products to avoid toxic effects of fluoride (12).

Fluoride containing dentifrices such as tooth-paste, professionally used varnishes/gels, and mouth rinses. Fluoride tooth pastes are available as low fluoride (500 ppm), standard fluoride (1100-1500 ppm) and high fluoride toothpaste (>1500 ppm). Fluoride is added in different forms to toothpastes and mouth rinses such as sodium fluoride (NaF), mono-fluorophosphate (MFP), or stannous fluoride (SnF) (14, 15). The mouth rinses have an advantage over toothpastes because of their low viscosity that results in better delivery to least accessible areas of the teeth such as pits and fissures and interproximal areas (7, 16, 17).

Fluoridated milk including formula milk for infants and table salt fluoridation (7, 17). Fluoride delivery through milk fluoridation is not efficient as compared to other fluoride delivery methods. This is due to fluoride's tendency to form insoluble complexes with calcium, which makes fluoride absorption difficult.

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Editorial

Prevention of dental caries through the use of fluoride – the WHO approach

Poul Erik Petersen and Hiroshi Ogawa

Dental caries continues to pose an important public health problem across the world. The World Health Organization (WHO) emphasizes that the disease affects about 60–90% of schoolchildren, the vast majority of adults and that dental caries contributes to an extensive loss of natural teeth in older people globally (Petersen, 2008a; WHO, 2016). Meanwhile, in most westernized high income countries, an improvement in dental health has taken place over the past three decades in parallel with the introduction of prevention-oriented oral health systems. A decline in the prevalence and the severity of dental caries is particularly observed in countries having established public health programmes using fluoride for dental caries prevention, coupled with changing living conditions, healthier lifestyles, and improved self-care practices. In Eastern Europe and Central Asia dental caries levels are high and with health systems in transition the exposure of the population to fluoride for disease prevention has diminished dramatically. In low and middle income countries of Africa, Asia, and Latin America the lack of preventive programmes is further complicated by the fact that these countries have a shortage of oral health personnel and the capacity of health systems is mostly limited to treatment of symptoms or emergency care. In children and adults suffering from severe tooth decay, teeth are often left untreated or they are extracted to relieve oral pain or discomfort. In the future, tooth loss and impaired quality of life are therefore expected to increase as a public health problem in many developing countries.

The current global and regional patterns of dental caries largely reflect distinct risk profiles of countries which relate to structure of society, living conditions, lifestyles, and the existence of preventive oral health systems (Kwan and Petersen, 2010). The socio-behavioural risk factors in dental caries are found universally and they play significant roles in children, adults and older people. The disease level is relatively high among underprivileged population groups, i.e. people with low education background, poor living conditions, people with poor dietary habits and high consumption of sugars, and people with limited tradition of dental care. Unless serious efforts are made to tackle the social inequity by modifying risk factors and by establishing effective caries prevention programmes, the level of dental caries in disadvantaged populations and countries will unduly increase (Kwan and Petersen, 2010). Evidently, substantial population groups in low and middle income countries have not yet obtained the health benefit from fluoride in community prevention programmes. The reasons for not having been able to implement prevention programmes varies in nature ranging from lack of national policy for oral health to low awareness of the importance of oral health.

Fluoride and prevention of dental caries

The major reasons for the burden of dental caries in countries relate to the high consumption of sugars and inadequate exposure to fluoride (WHO, 2010; 2015). The use of fluoride is a major breakthrough in public health. Controlled addition of fluoride to drinking water supplies in communities where fluoride concentration is below optimal levels to have a cariostatic effect began in the 1940s and since then extensive research has confirmed the successful reduction in dental caries in many countries. Industrial production of fluoridated salt started in Switzerland in 1955 and its use expanded to several countries in various parts of the world with similar success as water fluoridation. Milk fluoridation has also been reported to be successful in dental caries prevention, particularly among children, and schemes have been developed in countries around the globe based on integration with school health and nutrition programmes (Jürgensen and Petersen, 2013). As no effort is required from the individual for ingesting fluoridated water, salt or milk these methods have been designated as automatic systems for dental caries prevention. Fluoride in toothpaste has also been available for decades and it is considered a main contributor to the decline in dental caries observed among people of industrialized countries; unfortunately, toothpastes are not universally used due to the cost factor which inhibits poor population groups from accessing such preventive measure. Finally, fluoride has been made available in products for professional application, including gels, varnishes and restorative materials. Fluoride mouth rinses incorporated in school health programmes have also been available for decades with various degrees of success in caries prevention.

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Caries Research

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Systemic versus Topical Fluoride

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Key Words
Caries prevention · Posteruptive fluoride · Pre-eruptive fluoride · Systemic fluoride · Topical fluoride

Abstract
The actual mechanism of fluoride action is still a subject of debate. A dogma has existed for many decades, that fluoride has to be ingested and acts mainly pre-eruptively. However, recent studies concerning the systemic effect of fluoride supplementation concluded that the caries-preventive effect of fluoride is almost exclusively posteruptive. Moreover, epidemiologists have cast doubt on the validity of the 'old' studies dealing with fluoride use. The concept of the posteruptive fluoride effect is supported by in vitro and in situ investigations demonstrating that the mode of action of fluoride can be attributed mainly to its influence on de- and remineralization kinetics of dental hard tissues. Therefore, topical fluoride application (e.g. in the form of fluoridated dentifrices) should be encouraged. There are still important questions open that need to be answered despite existing knowledge about the caries-preventive effect of fluoride.

Existing Information

Fluoride is still the cornerstone of modern non-invasive dental caries management. However, the actual mechanism of fluoride action remains the subject of debate. The belief that fluoride has to be ingested and acts preventively by becoming incorporated into tooth mineral during its development originated from the early studies of Dean et al. [1942] and McKay [1952]. At this time many clinical trials were designed to prove the pre-eruptive (systemic) mode of action of fluoride. It could be demonstrated that the prevalence of overt carious lesions in the permanent as well as in the primary dentition was lower in residents from areas with fluoridated drinking water compared to those living in non-fluoridated areas [Backer Dirks et al., 1978; Thylstrup et al., 1982; Newbrun, 1989; Ripa, 1993]. Additionally, laboratory analyses revealed that fluoride concentration in surface enamel was higher in teeth that developed under the influence of water fluoridation [Chan et al., 1989; Takeuchi et al., 1996]. It was also found that the prenatal administration of fluoride supplements could reduce caries prevalence in deciduous teeth [Glenn et al., 1982]. As early as 1955, Bibby et al. compared the caries-preventive efficacy of fluoride lozenges with fluoride pills in a group of 5- to 14-year-old children. While the lozenges were sucked, the coated pills were swallowed before any of the contained fluoride could come into contact with the teeth. They

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Geraldine M. Weinstein
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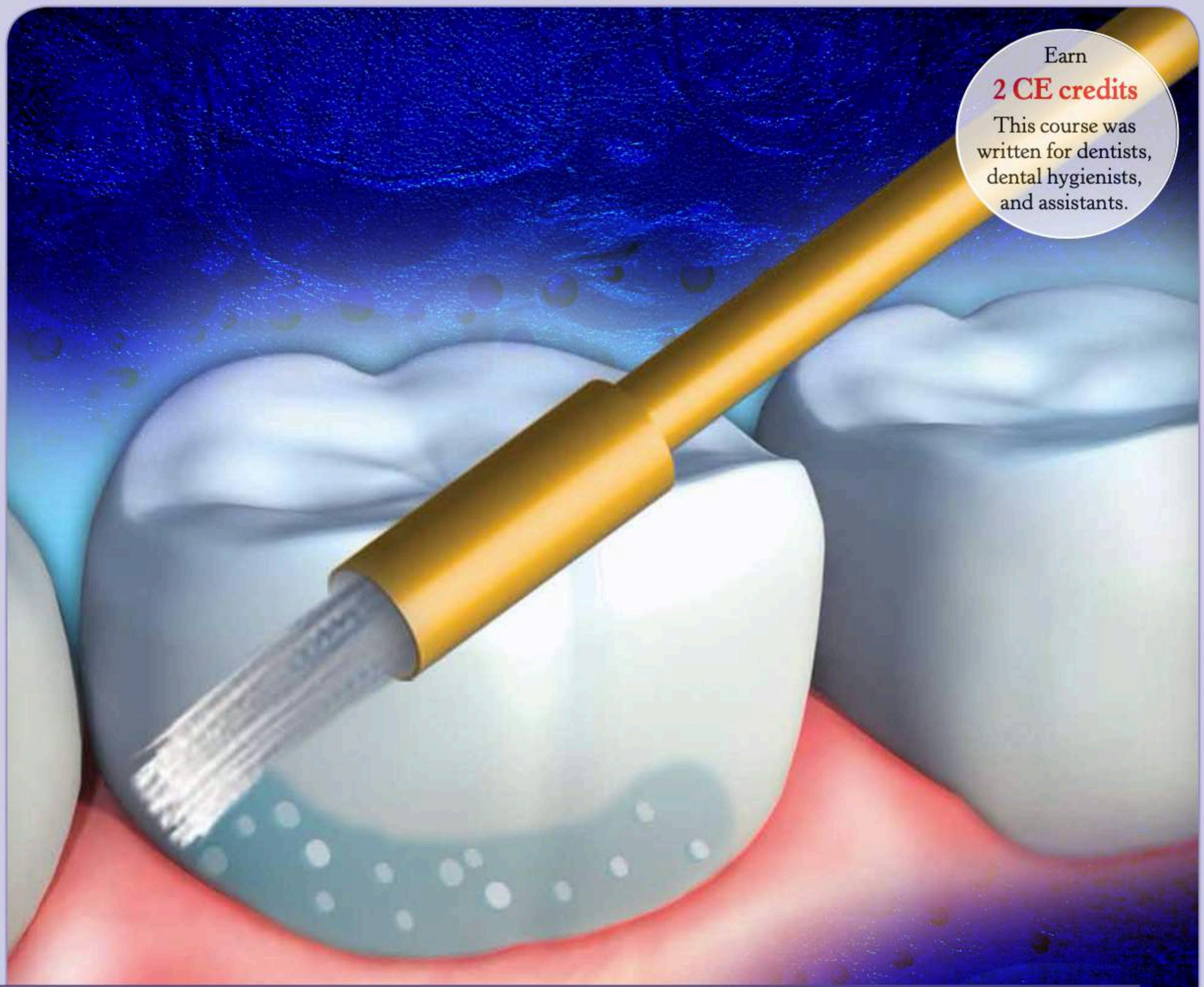

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RESEARCH ARTICLE

TOPICAL APPLICATION OF FLUORIDE AND ITS ANTI-CARIOGENIC EFFECT.

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Abstract

Most persons in industrial countries in addition to persons in some developing countries are suffering from dental caries (tooth decay) which is an infectious, multifactorial disease. Management of dental caries was shifted from “drill and fill” to “prevent and immune” after development of idea about the caries process. Many procedures and materials have been used for the preventive phase of dental caries. One of these materials was using the properties of fluoride with its anti-cariogenic properties. The incidence of dental caries (tooth decay) is reduced by using fluoride which slows, delays or arrests the progression of existingdental caries .This review article focused on different mechanism of action, types of topical applications and side effect of overdose use of fluoride compounds.

Introduction:-

Fluoride is a mineral that exists in all sources of the natural water and is the ionized form of the fluorine. Fluorine is ordinarily found in nature and reaches water sources by draining from soil and rocks into groundwater [1, 2]. Although fluoride compounds (e.g., calcium fluoride or sodium fluoride) represent a standard component of tooth enamel and bone, it can be also found in some plants. It is the most electro-negative element in the periodic table. Therefore, reactive with the strongest oxidizing action which binds to almost all other chemical elements. Many scientific papers reported the use of fluoride in improving oral health [3]. Fluoride likewise is created by some modern procedures that utilize the mineral apatite, a blend of calcium phosphate compound. In people, fluoride is primarily connected with calcified tissues (i.e., bones and teeth) as a result of its high affinity for calcium [4]. Fluoride's capacity to decrease the activity or even inverse the initiation and progression of dental caries is very much reported. The utilization of pre-adjusted fluoride in water for control of tooth decay began in 1945 and 1946 in the United States and Canada, at the point where fluoride concentration was balanced in drinking water providing four communities [5-8].

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Theme Papers

The global burden of oral diseases and risks to oral health

Poul Erik Petersen,[1] Denis Bourgeois,[1] Hiroshi Ogawa,[1] Saskia Estupinan-Day,[2] & Charlotte Ndiaye[3]

Abstract This paper outlines the burden of oral diseases worldwide and describes the influence of major sociobehavioural risk factors in oral health. Despite great improvements in the oral health of populations in several countries, global problems still persist. The burden of oral disease is particularly high for the disadvantaged and poor population groups in both developing and developed countries. Oral diseases such as dental caries, periodontal disease, tooth loss, oral mucosal lesions and oropharyngeal cancers, human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS)-related oral disease and orodental trauma are major public health problems worldwide and poor oral health has a profound effect on general health and quality of life. The diversity in oral disease patterns and development trends across countries and regions reflects distinct risk profiles and the establishment of preventive oral health care programmes. The important role of sociobehavioural and environmental factors in oral health and disease has been shown in a large number of socioepidemiological surveys. In addition to poor living conditions, the major risk factors relate to unhealthy lifestyles (i.e. poor diet, nutrition and oral hygiene and use of tobacco and alcohol), and limited availability and accessibility of oral health services. Several oral diseases are linked to noncommunicable chronic diseases primarily because of common risk factors. Moreover, general diseases often have oral manifestations (e.g. diabetes or HIV/AIDS). Worldwide strengthening of public health programmes through the implementation of effective measures for the prevention of oral disease and promotion of oral health is urgently needed. The challenges of improving oral health are particularly great in developing countries.

Keywords Mouth diseases/epidemiology; Tooth diseases/epidemiology; Oral manifestations; Dental care/economics; Dental caries/epidemiology; Mouth neoplasms/epidemiology; HIV infections/complications; Noma/epidemiology; Tooth erosion/epidemiology; Developmental disabilities/epidemiology; Fluorosis, Dental/epidemiology; Risk factors; Cost of illness (*source: MeSH, NLM*).

Mots clés Bouche, Maladie/épidémiologie; Dent, Maladies/épidémiologie; Manifestation buccale; Soins dentaires/économie; Carie dentaire/épidémiologie; Tumeur bouche/épidémiologie; Infection à VIH/complication; Noma/épidémiologie; Erosion dentaire/épidémiologie; Troubles développement enfant/épidémiologie; Fluorose dentaire/épidémiologie; Facteur risque; Coût maladie (*source: MeSH, INSERM*).

Palabras clave Enfermedades de la boca/epidemiología; Odontopatías/epidemiología; Manifestaciones bucales; Atención odontológica/economía; Caries dental/epidemiología; Neoplasmas de la boca/epidemiología; Infecciones por VIH/complicaciones; Noma/epidemiología; Erosión dentaria/epidemiología; Incapacidades del desarrollo/epidemiología; Fluorosis dentaria/epidemiología; Factores de riesgo; Costo de la enfermedad (*fuente: DeCS, BIREME*).

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Voir page 668 le résumé en français. En la página 668 figura un resumen en español.

Introduction

WHO recently published a global review of oral health (*1*) which emphasized that despite great improvements in the oral health of populations in several countries, global problems still persist. This is particularly so among underprivileged groups in both developing and developed countries. Oral diseases such as dental caries, periodontal disease, tooth loss, oral mucosal lesions and oropharyngeal cancers, human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS)-related oral disease and orodental trauma are major public health problems worldwide. Poor oral health may have a profound effect on general health, and several oral diseases are related to

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Conference Paper

Evidence-based Use of Fluoride in Contemporary Pediatric Dental Practice

Steven M. Adair, DDS, MS[1]

Abstract

Fluoride is an important and effective means of reducing the caries incidence in children. Multiple fluoride products are available to dentists for use with their patients at risk for dental caries. The purposes of this paper are to: (1) review clinically salient evidence, primarily systematic reviews and meta-analyses, for the effectiveness of fluoride options and, where possible, combinations of fluoride exposures; and (2) make recommendations to dental practitioners based on the available evidence for the use of these various approaches in contemporary practice, particularly regarding the use of multiple fluoride sources. The available data suggest that therapeutic use of fluoride for children should focus on regimens that maximize topical contact, preferably in lower-dose, higher-frequency approaches. Current best practice includes recommending twice-daily use of a fluoridated dentifrice for children in optimally fluoridated and fluoride-deficient communities, coupled with professional application of topical fluoride gel, foam, or varnish. The addition of other fluoride regimens should be based on periodic caries risk assessments, recognizing that the additive effects of multiple fluoride modalities exhibit diminishing returns. (Pediatr Dent 2006;28:133-142)

KEYWORDS: FLUORIDE, CARIES, PREVENTION, DENTAL PRACTICE

Prevention of dental caries in children is one of the hallmarks of contemporary pediatric dental practice. While there are multiple components of preventive dental programs developed by dentists for their child patients, perhaps none is as important and effective as the appropriate use of fluoride. Dentists have several options for optimizing the fluoride exposure of their child patients.

The purposes of this paper are to:

1. review clinically salient evidence, primarily systematic reviews and meta-analyses, for the effectiveness of fluoride options and, where possible, combinations of fluoride exposures;
2. make recommendations to dental practitioners based on the available evidence for the use of these various approaches in contemporary practice, particularly regarding the use of multiple fluoride sources.

The systemic paradigm

Fluoride's caries-protective action was first discovered in the 1920s and 1930s. Dental epidemiologists and practitioners discovered that naturally occurring fluoride in the water supply led to decreased rates of dental caries in the populations that consumed it.[1,2] They also noted that in areas with high fluoride levels in the water supply, significant numbers of individuals also exhibited a particular form of enamel mottling, later named "fluorosis."[3] From these observations, scientists deduced that fluoride exerts its effects systemically and that it must be ingested for these effects to occur.[4] This paradigm of systemic action led to the notion that significant caries reductions could be achieved in populations that consumed optimally fluoridated water. The success of the water fluoridation trials carried out in the 1940s and 1950s solidified the systemic paradigm for the next several decades.[5,6]

Fluoride dietary supplements

The efforts to extend the systemic benefits of fluoride to populations for whom water-borne fluoride was not available led to the development of fluoride dietary supplements. The intent was to provide a systemic dose of fluoride equivalent to that ingested by a child in an optimally fluoridated community. The developers of fluoride supplements had to wrestle with 2 problems inherent in this approach:

1. How much fluoride does a child in on optimally fluoridated community ingest daily?

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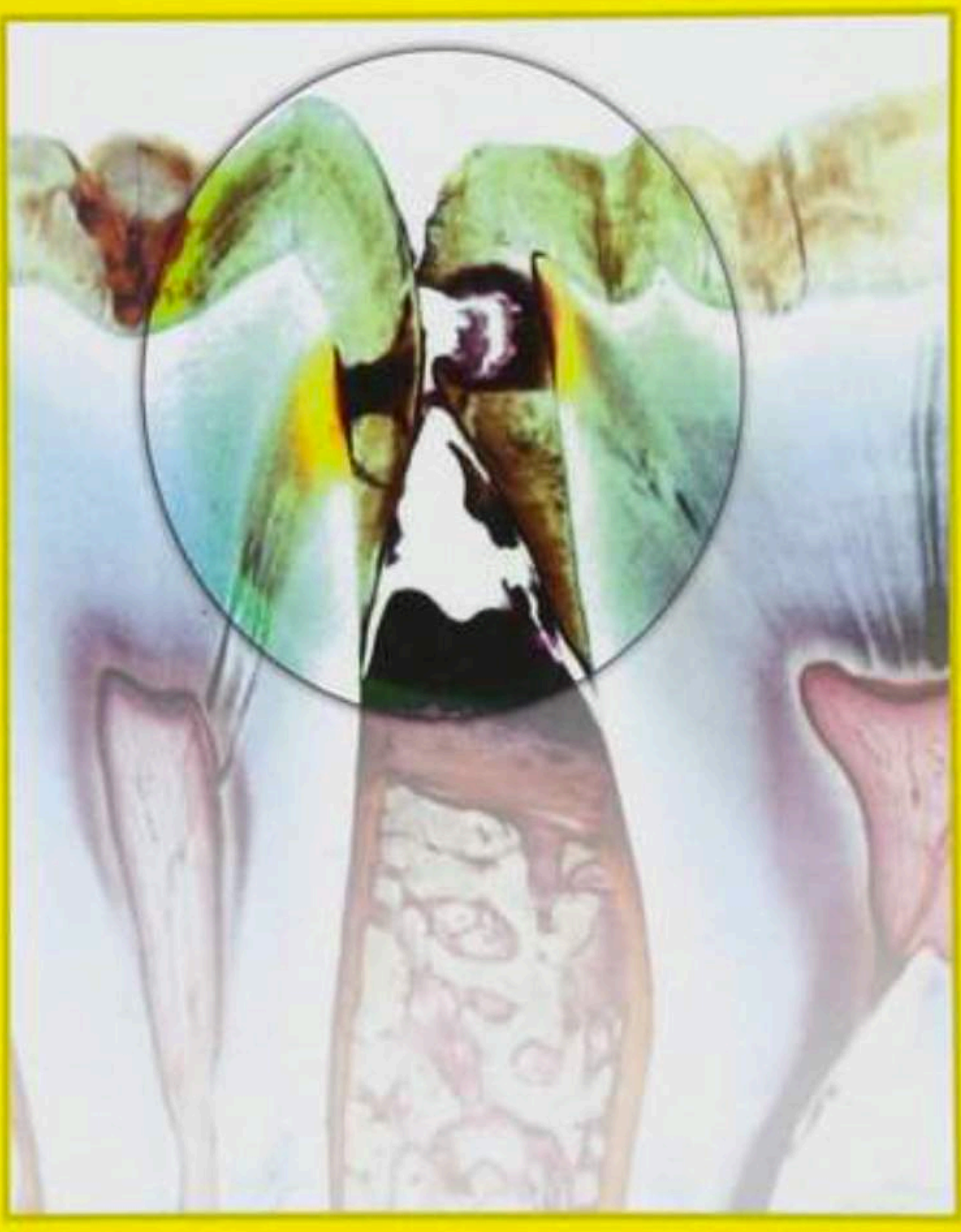
Dental Caries

The Disease and Its Clinical Management

Third Edition



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A Comparative Review of Marketing Authorization Decisions in Switzerland, the EU, and the USA

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Abstract

Background: In this study we compared Swissmedic's (SMC's) regulatory marketing authorization decisions to those of the US Food and Drug Administration (FDA) and European drug regulatory authorities (EU). We investigated the overall similarity of the regulatory decisions, approval, and postmarketing withdrawal rates in the 3 jurisdictions. In case regulatory decisions diverged, we analyzed the reasons for rejection of marketing authorization applications (MAAs). *Methods:* The study comprises 255 new molecular entity (NME) MAAs assessed by SMC by the EU and FDA between 2005 through 2014. Study parameters included the regulatory decision, postmarketing withdrawal rates, and the official reasons for rejection. *Results:* Regulatory decisions converged to a high degree among all 3 agencies (between 84% and 90%). SMC's average approval rate (84%) was slightly lower than those of the FDA (87%) and the EU (91%). Postmarketing withdrawal rates were generally low (4%-5%) but were 3 to 5 times higher when decisions among the drug regulatory authorities (DRAs) diverged. SMC's primary grounds for rejection were lack of efficacy (45%) and safety (40%). *Conclusions:* The 3 investigated DRAs adhere largely to the same scientific principles and regulatory guidelines; therefore, remaining disparities ought to be considered in a cultural, legal and public health priority context.

Keywords

Swissmedic, SMC, US FDA, EMA, MAA, regulatory decisions

Background

In order to fulfill its legal responsibilities and ensure the timely access of safe and efficacious innovative new medicinal products to the Swiss market, Swissmedic (SMC) is obliged to continuously optimize and streamline its drug evaluation processes. SMC actively fosters relationships with a number of foreign drug regulatory authorities (DRAs) and endeavors co-operation in form of agreements on information exchange such as Memorandum of Understanding (eg, with Health Canada, the Australian Therapeutic Goods Administration and the Singaporean Health Sciences Authority), Confidentiality Commitment (eg, with the US Food and Drug Administration [FDA]) and Exchanges of Letters (eg, with the EU).[1] The sharing of scientific information and views on the interpretation of marketing authorization data accelerates patients' access to innovative new medicinal products and saves resources due to reduced duplication of work. Although in recent years, many drug regulatory requirements have become increasingly harmonized on a global scale, divergence of regulatory decisions continues to be a matter of debate among patient organizations, the pharmaceutical industry, and regulators.

To this end, a comprehensive analysis of the degree of consensus on decisions among SMC, the EU, and FDA as well as the concerns substantiating rejections has been lacking. Our aim was thus to analyze marketing authorization applications (MAAs) containing new molecular entities (NMEs) with SMC decisions dating between 2005 and 2014 and to compare the review outcomes with the respective decisions of the FDA and those taken in the EU. Moreover, when decisions between SMC and either the EU or the FDA diverged, the main reasons associated with rejection were analyzed and categorized.

Methods

In order to compare the regulatory decisions on MAAs evaluated by SMC with those evaluated by the FDA and the

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Pathophysiology of Dental Caries

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Abstract

Carious lesion dynamics are dependent predominantly on the availability of fermentable sugars, other environmental conditions, bacteria, and host factors. Our current understanding of the microorganisms involved in the initiation and progression of caries is still rather incomplete. The most relevant acidogenic-aciduric bacterial species known to date are *Streptococcus mutans*, bifidobacteria, and lactobacilli. Whereas mutans streptococci are initiators, bifidobacteria and lactobacilli are more enhancers for progression. Boosters for microbial activity are specific environmental conditions, such as the presence of fermentable dietary sugars and the absence of oxygen. Based on these conditions, the necrotic and/or contaminated zone fulfils all criteria for disease progression and has to be removed. For those deep lesions where the pulp vitality is not affected, a selective removal of the contaminated leathery dentine should take place as this approach lowers the risk of regrowth of the few embedded microbial cells here. In repelling the microbial attack and repairing damage, the host has developed several ingenious strategies. A major resistance to carious lesion progression is mounted by the dentine-pulp tissues. The signalling molecules and growth factors released upon dentine demineralisation upregulate the odontoblast activity and act as sensor cells. After carious stimulation, odontoblasts initiate an inflammatory reaction by producing chemokines and synthesise a protective tertiary dentine. After the destruction of these cells, the pulp still has a high capacity to synthesise this tertiary dentine thanks to the presence of adult stem cells within the pulp. Also, in addition to the systemic regulation, the pulp which is located within inextensible the confines of the dentine walls has a well-developed local regulation of its inflammation, regeneration, and vascularisation. This local regulation is due to the activity of different pulp cell types, mainly the fibroblasts, which secrete soluble molecules that regulate all these processes.

Microbiology of Tooth Decay

Dentistry dates as far back as 5,000 BC when people in India, Egypt, Japan, and China thought dental caries were a result of a "tooth worm." The term "dental caries" first appeared in the literature around 1634 and is derived from the Latin word cariēs for decay and from ancient Irish ara-*chrinn*, it decays. The term was originally used simply to describe holes in the teeth with little

Appropriate uses of fluorides for children: guidelines from the Canadian Workshop on the Evaluation of Current Recommendations Concerning Fluorides

D. Christopher Clark, DDS, MPH

Objective: To prevent fluorosis caused by excessive fluoride ingestion by revising recommendations for fluoride intake by children.
Options: Limiting fluoride ingestion from fluoridated water, fluoride supplements and fluoride dentifrices.
Outcomes: Reduction in the prevalence of dental fluorosis and continued prevention of dental caries.
Evidence: Before the workshop, experts prepared comprehensive literature reviews of fluoride therapies, fluoride ingestion and the prevalence and causes of dental fluorosis. The papers, which were peer-reviewed, revised and circulated to the workshop participants, formed the basis of the workshop discussions.
Values: Recommendations to limit fluoride intake were vigorously debated before being adopted as the consensus opinion of the workshop group.
Benefits, harms and costs: Decrease in the prevalence of dental fluorosis with continuing preventive effects of fluoride use. The only significant cost would be in preparing new, low-concentration fluoride products for distribution.
Recommendations: Fluoride supplementation should be limited to children 3 years of age and older in areas where there is less than 0.3 ppm of fluoride in the water supply. Children in all areas should use only a "pea-sized" amount of fluoride dentifrice no more than twice daily under the supervision of an adult.
Validation: These recommendations are almost identical to changes to recommendations for the use of fluoride supplements recently proposed by a group of European countries.
Sponsors: The workshop was organized by Dr. D. Christopher Clark, of the University of British Columbia, and Drs. Hardy Limeback and Ralph C. Burgess, of the University of Toronto, and funded by Proctor and Gamble Inc., Toronto, the Medical Research Council of Canada and Health Canada (formerly the Department of National Health and Welfare). The recommendations were formally adopted by the Canadian Dental Association in April 1993.

Objectif : Prévenir la fluorose causée par une ingestion excessive de fluorure en révisant les recommandations relatives à l'absorption de fluorure par les enfants.
Options : Limiter l'ingestion de fluorure contenu dans l'eau fluorée, les suppléments de fluorure et les dentifrices au fluorure.
Résultats : Réduction de la prévalence de la fluorose dentaire et maintien de la prévention des caries dentaires.

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Adapted with permission from an article in the Journal of the Canadian Dental Association *(1993; 59: 272–279).*

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← For prescribing information see page 1839

The impact of dietary and lifestyle factors on the risk of dental caries among young children in Qatar

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Aim

The aim of the current study was to investigate the relationship between dietary intake, type of feeding during infancy, other lifestyle and sociodemographic factors, and dental caries.

Design

A cross-sectional study.

Setting

The study was carried out on children younger than 16 years of age who visited Primary Health Care Centers. The study was carried out over a period from October 2010 to June 2011 in Qatar.

Participants

A random sample of 1752 children aged 6–15 years old who visited the Primary Health Care Centers was approached, and parents of 1284 children provided their consent and fulfilled the inclusion criteria (corresponding to a response rate of 73%).

Methods

The study was based on a questionnaire that included variables such as sociodemographic information, lifestyle, family history, and feeding patterns during infancy, information on oral hygiene practices, and clinical examination. The status of dental caries was recorded on the basis of the WHO criteria.

Results

The prevalence of dental caries [decayed, missed, or filled tooth (DMFT)] in the permanent dentition among children was 73% [95% confidence interval (CI): 71–75%], with a mean DMFT value of 4.5 (SD: 4.2). The numbers of children consuming sea food, cod liver oil, and vitamin-D-fortified milk less than once a week were significantly higher in the dental caries group compared with those without caries (11.7 vs. 8.3%; $P=0.05$, 92.4 vs. 87.5%; $P=0.005$, and 10.6 vs. 6.3%; $P=0.011$, respectively). Multivariable logistic regression analysis showed that being female [adjusted odds ratio (OR): 1.41; 95% CI: 1.07–1.84], having a BMI greater than the 95th percentile versus less than the 85th percentile (adjusted OR: 2.12; 95% CI: 1.17–3.84), a monthly household income of at least 10 000 QAR (adjusted OR: 2.61; 95% CI: 1.69–4.02), consumption of cod liver oil less than once a week (adjusted OR: 2.13; 95% CI: 1.35–3.37), 1-year increase in age (adjusted OR: 1.05; 95% CI: 1.01–1.11), being formula fed during infancy (adjusted OR: 2.27; 95% CI: 1.59–3.21), and frequency of tooth brushing once a day or less (adjusted OR: 1.36; 95% CI: 1.01–1.83) were associated independently with the risk of dental caries among children in Qatar.

Conclusion and recommendations

Being female, overweight or obese, and monthly household income higher than US$2747 (≥10 000 QAR) were independent risk factors for dental caries. However, consumption of cod liver oil (at least once a week) and frequency of tooth brushing (more than once a day) were protective against dental caries. Health awareness and education on frequent tooth brushing, adequate nutrition, and obesity prevention should be promoted to avoid dental caries among children.

Keywords:

dental caries, diet, lifestyle, nutrition, prevalence, risk factors, vitamin D

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REPORTS OF COUNCILS AND BUREAUS

The current status of topical fluorides in preventive dentistry

Council on Dental Therapeutics

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Hundreds of clinical studies conducted during the past 25 years have evaluated the use of topical fluorides in protecting the enamel surface of teeth from caries attack. These investigations have led to the development of the various topical fluoride procedures that are available today. This paper summarizes current knowledge on the subject by reviewing pertinent studies and by pinpointing the conclusions they support. The material covered in the paper should be helpful to dental personnel and dental health agencies in their promotional efforts in preventive dentistry and in developing and managing the increasing number of comprehensive dental programs for children.

Topical fluoride solutions

■ *Sodium fluoride:* The recommended treatment technic for the application of a solution of sodium fluoride begins with cleaning the clinical crowns of the teeth, with use of a standard prophylaxis paste in a motor-driven rubber cup.[1] After the prophylaxis, an upper and opposing lower quadrant (half the mouth at a time) are isolated with cotton rolls held in appropriate holders and the teeth are dried thoroughly with a stream of compressed air. A 2% sodium fluoride solution is applied to the teeth with cotton applicators so that all surfaces are made visibly wet. The solution is permitted to dry for about three minutes. Second, third, and fourth applications, not preceded by prophylaxes, are given at intervals of approximately one week. As with all topically applied fluoride agents, caries inhibition presumably begins as soon as treatment is completed. The series of treatments is recommended at ages 3, 7, 11, and 13.[2] These ages were selected so that fluoride is applied shortly after the eruption of groups of teeth, thus minimizing the time that teeth are at risk from caries attack before treatment. The ages should be varied, if possible, with each child's individual pattern of tooth eruption.

The procedure for the application of sodium fluoride was developed by Knutson and co-workers[3-8] who tested different fluoride solutions, concentrations, and frequencies of application in a series of large-scale studies involving thousands of schoolchildren. In summary, results of these early studies indicated that: a minimum of four applications with a 2% sodium fluoride solution appears to give the maximum effect—a reduction of about 40% in new carious teeth; increasing the interval between individual applications in the series from about one week to three to six months decreases the effectiveness of treatment; and omission of a prophylaxis preceding the series of treatments reduces the benefits by about half.

Studies conducted throughout the world by other investigators[9-14] have confirmed the caries-preventive properties of topically applied sodium fluoride. A variety of technics of application have been tested but the procedure developed by the Public Health Service has been the most widely used and it appears to be the most reliable. A review of the literature reveals an impressive number of studies that have essentially duplicated the results obtained by Knutson and his co-workers. In spite of some variation, 30% to 40% reductions in dental caries incidence in the permanent teeth of children living in an area with insufficient levels of fluoride in the water supply have been reported quite consistently.[15-18]

Certain aspects of the potential usefulness of topically applied sodium fluoride need further investigation. More long-term studies must be done to determine precisely how long after treatment sodium fluoride continues to exert a beneficial effect; results of some investigations suggest that a falloff in effectiveness may occur in less than three years,[15,19,20] yet there is little evidence

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Global goals for oral health 2020

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How to use this document

It is anticipated that dentists and other health planners in many different circumstances will use this document for guidance when developing their plans for oral health. We recognise that no document can provide an exact blue print for each and every set of circumstances where oral health plans are to be developed. What is presented here is a range of possible areas that need to be taken into consideration when plans are being developed. It also provides a useful checklist against which existing plans might be examined to determine if there are any possible gaps.

Fundamental to the success of any plan is a clear understanding of what resources are already available or might become available once the plan has been adopted officially. Initially it may not be necessary to have a detailed inventory of all resources available, a simple analysis like the completion of the questionnaire in Annexure B will give a quick guide as to the level of resources available to you. This, combined with a prioritised list of the oral health problems of the community or population you are planning for, will help you identify those types of interventions that are likely to be most appropriate and sustainable under the prevailing circumstances.

Background

The FDI and the WHO established the first Global Oral Health Goals jointly in 1981 to be achieved by the year 2000. A review of these goals, carried out just prior to the end of this period, established that they had been useful and, for many populations, had been achieved or exceeded. However, for a significant proportion of the world's population, they remained only a remote aspiration. Nonetheless, the Oral Health Goals had stimulated awareness of the importance of oral health amongst national and local governments and acted as a catalyst for securing resources for oral health in general. Therefore, even though not all countries had achieved the goals, they provided a key focus for the effort.

Recently, the FDI, WHO and IADR have embarked on the activity of preparing goals for the new millennium, for the year 2020, and these are presented here. They were developed by a Working Group including representatives of the FDI, WHO and IADR from different regions of the world (see Annexure A for the Group's membership).

The drafts of this document were circulated to all National Dental Association members (NDAs) of the FDI and placed on the global Dental Public Health list server for comment. All WHO Collaborating Centres in Oral Health (WHOCC) and the IADR were also consulted. Responses received from NDAs, IADR, WHOCC as well as from individuals have subsequently been incorporated in this document.

Aims

This document, which contains proposals for new Global Oral Health Goals, Objectives and Targets of increasing detail and complexity, aims to provide a framework for health policy makers at different levels – regional, national and local. The goals and targets are not intended to be prescriptive. By being focused broadly on the global level, it is hoped that it will encourage local action in the spirit of the United Nations Development Programme's report: '*Think globally act locally*'. Thus, the document will provide an instrument for local and national health care planners to specify realistic goals and standards for oral health to be achieved by the year 2020.

The process of formulating a regional, national or local oral health strategy necessitates many stages. This document provides the first step in that process by guiding health planners to evaluate the current situation of oral health and

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Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015

*GBD 2015 Disease and Injury Incidence and Prevalence Collaborators**

Background Non-fatal outcomes of disease and injury increasingly detract from the ability of the world's population to live in full health, a trend largely attributable to an epidemiological transition in many countries from causes affecting children, to non-communicable diseases (NCDs) more common in adults. For the Global Burden of Diseases, Injuries, and Risk Factors Study 2015 (GBD 2015), we estimated the incidence, prevalence, and years lived with disability for diseases and injuries at the global, regional, and national scale over the period of 1990 to 2015.

Methods We estimated incidence and prevalence by age, sex, cause, year, and geography with a wide range of updated and standardised analytical procedures. Improvements from GBD 2013 included the addition of new data sources, updates to literature reviews for 85 causes, and the identification and inclusion of additional studies published up to November, 2015, to expand the database used for estimation of non-fatal outcomes to 60 900 unique data sources. Prevalence and incidence by cause and sequelae were determined with DisMod-MR 2.1, an improved version of the DisMod-MR Bayesian meta-regression tool first developed for GBD 2010 and GBD 2013. For some causes, we used alternative modelling strategies where the complexity of the disease was not suited to DisMod-MR 2.1 or where incidence and prevalence needed to be determined from other data. For GBD 2015 we created a summary indicator that combines measures of income per capita, educational attainment, and fertility (the Socio-demographic Index [SDI]) and used it to compare observed patterns of health loss to the expected pattern for countries or locations with similar SDI scores.

Findings We generated 9·3 billion estimates from the various combinations of prevalence, incidence, and YLDs for causes, sequelae, and impairments by age, sex, geography, and year. In 2015, two causes had acute incidences in excess of 1 billion: upper respiratory infections (17·2 billion, 95% uncertainty interval [UI] 15·4–19·2 billion) and diarrhoeal diseases (2·39 billion, 2·30–2·50 billion). Eight causes of chronic disease and injury each affected more than 10% of the world's population in 2015: permanent caries, tension-type headache, iron-deficiency anaemia, age-related and other hearing loss, migraine, genital herpes, refraction and accommodation disorders, and ascariasis. The impairment that affected the greatest number of people in 2015 was anaemia, with 2·36 billion (2·35–2·37 billion) individuals affected. The second and third leading impairments by number of individuals affected were hearing loss and vision loss, respectively. Between 2005 and 2015, there was little change in the leading causes of years lived with disability (YLDs) on a global basis. NCDs accounted for 18 of the leading 20 causes of age-standardised YLDs on a global scale. Where rates were decreasing, the rate of decrease for YLDs was slower than that of years of life lost (YLLs) for nearly every cause included in our analysis. For low SDI geographies, Group 1 causes typically accounted for 20–30% of total disability, largely attributable to nutritional deficiencies, malaria, neglected tropical diseases, HIV/AIDS, and tuberculosis. Lower back and neck pain was the leading global cause of disability in 2015 in most countries. The leading cause was sense organ disorders in 22 countries in Asia and Africa and one in central Latin America; diabetes in four countries in Oceania; HIV/AIDS in three southern sub-Saharan African countries; collective violence and legal intervention in two north African and Middle Eastern countries; iron-deficiency anaemia in Somalia and Venezuela; depression in Uganda; onchoceriasis in Liberia; and other neglected tropical diseases in the Democratic Republic of the Congo.

Interpretation Ageing of the world's population is increasing the number of people living with sequelae of diseases and injuries. Shifts in the epidemiological profile driven by socioeconomic change also contribute to the continued increase in years lived with disability (YLDs) as well as the rate of increase in YLDs. Despite limitations imposed by gaps in data availability and the variable quality of the data available, the standardised and comprehensive approach of the GBD study provides opportunities to examine broad trends, compare those trends between countries or subnational geographies, benchmark against locations at similar stages of development, and gauge the strength or weakness of the estimates available.

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See **Editorial** page 1447

See **Comment** pages 1448 and 1450

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Fluoride Varnish in the Prevention of Dental Caries in Children and Adolescents: A Systematic Review

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ABSTRACT

Objective: To develop a scientifically current and evidence-based protocol for the use of fluoride varnish for the prevention of dental caries among high-risk children and adolescents.

Methods: Previous systematic reviews on this topic were used as the basis for the current review. Ovid MEDLINE, CINAHL and several other relevant bibliographic databases were searched for English-language articles, with human subjects, published from 2000 to 2007.

Results: A total of 105 articles were identified by the literature search; relevance was determined by examining the title, abstract and body of the article. Seven original research studies met the inclusion criteria. These articles were read and scored independently by 2 reviewers, and evidence was extracted for systematic review.

Recommendations: The following recommendations were developed on the basis of the evidence:

1. For high-risk populations (e.g., people with low socioeconomic status, new immigrants and refugees, First Nations and Inuit children and adolescents), fluoride varnish should be applied twice a year, unless the individual has no risk of caries, as indicated by past and current caries history. This schedule of application would permit sealants to be checked biannually to ensure retention.
2. Single-dose packages of fluoride varnish should be used for children; the varnish in such packages should be stirred vigorously before application, to ensure that any precipitated fluoride is redissolved.
3. There is good evidence of the complementary efficacy of preventive strategies such as sealants and varnish, as well as toothbrushing and nutritional counselling; oral health care programs should therefore include as many complementary strategies as possible.

For citation purposes, the electronic version is the definitive version of this article: www.cda-adc.ca/jcda/vol-74/issue-1/73.html

First developed and marketed in the 1960s in the form of sodium fluoride (Duraphat, Colgate, New York, N.Y.) and in the 1970s in the form of silane fluoride (Fluor Protector, Ivoclar Vivadent, Lichtenstein, Germany), fluoride varnishes prolong contact between fluoride and enamel. The effectiveness, ease of application and relative safety of these products offer significant advantages over other topical fluoride treatments, such as gels and rinses.[1–3] The general method of application is shown in **Fig. 1**.

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ORIGINAL ARTICLE
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Effect of organic versus inorganic fluoride on enamel microhardness: An *in vitro* study

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Abstract

Introduction: Dental caries is one of the most prevalent infectious diseases affecting the human dentition. Fluorides are effective anti-carious agents and have been widely used for caries prevention in the form of systemic and topical fluorides. Neutral sodium fluoride (NaF) is commonly used as a topical fluoride agent. A special category of topical fluorides are organic fluorides in the form of amine fluorides (AmF). Researchers have reported that AmF is superior to inorganic fluorides in improving the caries resistance of enamel due to the significant anti-enzyme effect of the organic fragment. **Aim:** The aim of the present study was to compare the enamel surface micro hardness after topical application of NaF and AmF solutions. **Materials and Methods:** Twenty fresh samples of sound human enamel were treated with demineralizing solution for 72 h and divided into Group A (treated with NaF) and Group B (treated with AmF) solutions for 3 min twice daily for 7 days. In between treatment, the samples were stored in artificial saliva. The enamel surface hardness was measured with Vickers hardness test at baseline, post-demineralization and post-treatment with two different fluoride solutions (NaF and AmF) and a comparative analysis was made. **Results:** The increase in mean micro hardness of human enamel after treatment with AmF application was found to be statistically significant ($P < 0.01$) when compared to the mean micro hardness after treatment with NaF. **Conclusion:** Fluoride enhances the remineralization process by accelerating the growth of enamel crystals that have been demineralized. It can be concluded from the present study that AmF compounds result in a marked increase in enamel micro hardness when compared to NaF.

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Available from: https://www.jcd.org.in/text.asp?2013/16/3/203/111314

Full Text

Introduction

Dental caries is the most prevalent chronic infectious disease affecting the human dentition. It is currently recognized as a dynamic process since periods of demineralization alternate with periods of remineralization through the action of calcium, fluoride, and phosphorous present in the saliva. [1] It is, therefore, viewed as a biofilm induced disease cause by an imbalance in physiologic equilibrium between tooth mineral and biofilm fluid. [1]

The surgical approach to managing dental caries was developed a century ago as at that time there was no other valid alternative. Presently, advances in the field of caries research have led to improved understanding of the disease process. Now, early detection of initial carious lesions and emphasis on preventive measures holds the key to controlling dental caries. [2]

The discovery of the anti-cariogenic properties of fluorides is one of the most important landmarks in the history of dentistry. [3] Fluoride is the most commonly used remineralizing agent. The cariostatic effect of fluoride is primarily due to its ability to decrease the rate of demineralization by forming fluorhydroxyapatite and enhancing the remineralization of incipient carious lesions. [4]

Fluoride incorporated into the enamel mineral during tooth development has little effect on the caries process. It is the fluoride that is incorporated post-eruptively during the caries challenge that plays an important role in caries prevention. The most effective caries preventive fluoride regimen is provided by the daily application of topical fluoride in the form of dentifrices and mouth-rinses. [5]

The various types of topical fluorides used in dentistry are: Sodium fluoride (NaF), sodium mono-fluorophosphate, stannous fluorides and acidulated phosphate fluoride. All these fluorides are inorganic in nature and are available in the form of solutions, varnishes, foam, gels, dentifrices, etc. [3] Bioavailability of fluoride is an important factor in caries prevention. This depends on the solubility of the fluoride containing compound and its adhesion to the tooth surface. [6],[7]

In 1957, Muhleman et al. found that organic fluoride like amino fluoride compounds were superior to inorganic fluorides in reducing the solubility of the enamel. [8] Subsequently, products containing amine fluorides (AmFs) were introduced and have gained popularity in Scandinavian countries. Research has demonstrated that AmF produces the most powerful enrichment of fluoride in enamel. [9],[10] AmF has greater anti-cariogenic property for two reasons: (a) Presence of fluoride, (b) the amine (organic) component has an antiplaque effect inhibiting bacterial adhesion and tensioactive property which allows accumulation of fluoride close to the tooth surface providing a sustained fluoride release. [9],[11] Recently, AmF containing dentifrices and mouth-rinses have been introduced in India.

Hence, the aim of the present in vitro study was to compare the micro hardness of demineralized enamel after topical application of NaF and AmF solutions.

Materials and Methods

Twenty intact and non-carious sound human premolars extracted from patients of age group 14-20 years for orthodontic purpose were collected and disinfected according to Occupational Safety and Health Administration (OSHA) recommendations. The teeth were decoronated at cement-enamel junction and sectioned mesio-distally into two halves using a high speed diamond disc. The resultant 40 samples were randomly divided into 2 groups-Group A (n = 20 samples) and Group B (n = 20 samples). The samples were mounted in cylindrical molds filled with self-cure acrylic resin and polished. A Vickers micro hardness (ZWIK/ROELL indentec, Japan) indenter (Vicker's Hardness (VH) indenter) was used to evaluate the baseline micro hardness under 100 g loads applied for 15 s at 5 different points each 1 mm apart and the mean was measured. Samples were stored in glass tubes

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INVITED REVIEW

Guidelines on the use of fluoride for caries prevention in children: an updated EAPD policy document

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Abstract

Aim To update the exisitng European Academy of Paediatric Dentistry (EAPD) 2009 fluoride guidelines.

Methods Experts met in Athens, Greece duirng November 2018 for the following groups: I Fluoride toothpastes, II Fluoride gels, rinses and varnishes, III Fluoridated milk, fluoridated salt, tablets/lozenges and drops, IV Water fluoridation. Systematic reviews and meta-analyses were reviewed and discussed for each of the groups. The GRADE system was used to assess the quality of evidence which was judged as HIGH, MODERATE, LOW or VERY LOW based on the assessment of eight criteria which can influence the confidence of the results. Following the quality assessment, GRADE was then used to indicate the strength of recommendation for each fluoride agent as STRONG or WEAK/CONDITIONAL.

Results Parents must be strongly advised to apply an age-related amount of toothpaste and assist/supervise tooth brushing until at least 7 years of age. The EAPD strongly endorses the daily use of fluoride as a major part of any comprehensive programme for the prevention and control of dental caries in children. Regardless of the type of programme, community or individually based, the use of fluoride must be balanced between the estimation of caries-risk and the possible risks of adverse effects of the fluorides. Fluoride use is considered safe when the manufacturer's instructions are followed. Preventive programmes should be re-evaluated at regular intervals and adapted to a patient's or population's needs and risks.

Conclusions For the majority of European Countries, the EAPD recommends the appropriate use of fluoride toothpaste in conjunction with good oral hygiene to be the basic fluoride regimen.

Keywords Fluoride · Caries · Child

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Background considerations

The European Academy of Paediatric Dentistry (EAPD), in collaboration with the Hellenic Division of EAPD, organised a workshop in Athens, Greece (June 1997), aimed at drawing up guidelines for future use of fluorides among European children. The first draft of these guidelines was published in the EAPD newsletter, and members were invited to make comments and suggestions. The revised first draft was then presented at the biannual EAPD Congress in Sardinia (1998), where it was discussed in great detail, so that the members' viewpoints were taken into consideration. The major concepts of the proposed guidelines were approved, and a working group, consisting of the authors of the original paper, were authorised to finalise and publish the recommendations (Oulis et al. 2000). In November 2008, the EAPD organised another workshop, again in Athens, Greece, to update the original fluoride guidelines (Toumba et al. 2009). These updated fluoride guidelines employed the

20 Variations in the Anatomy of the Teeth

Yasuhiko Kamura

20.1 Introduction

For the success of dental therapy, knowledge of tooth anatomy cannot be ignored. It is essential to know the normal configurations of the teeth and their variations. There are numerous variations in the internal anatomy of teeth due to developmental anomalies, hereditary factors, trauma, etc.

20.1.1 Variations in Development

1. Amelogenesis Imperfecta

   Amelogenesis imperfecta (AI) comprises a group of hereditary disorders of dental enamel. The reported incidences range between 43:10,000 in Turkey (Altug-Atac and Erdem 2007), 14:10,000 in Sweden (Bäckman and Holm 1986), 10:10,000 in Argentina (Sedano 1975), and 1.25:10,000 in Israel (Chosack et al. 1979). The structure and clinical appearance of the enamel are affected in both primary and permanent dentition, and there is hypomineralization and/or hypoplasia with discoloration, sensitivity, and fragility. The main aim of treatment should be early diagnosis, pain management, prevention, stabilization, restoration of defects, and regular maintenance (Fig. 20.1).
2. Enamel Pearl

   Ectopic globules of enamel, or so-called enamel (enamelous) pearls, droplets, globules, nodules, knots, or exostoses, are a developmental anomaly of teeth (Moskow and Canut 1990). They can be either internal or external, the former being more common on the root surface. Internal ectopic globules are

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The current status of topical fluorides in preventive dentistry

Council on Dental Therapeutics

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Hundreds of clinical studies conducted during the past 25 years have evaluated the use of topical fluorides in protecting the enamel surface of teeth from caries attack. These investigations have led to the development of the various topical fluoride procedures that are available today. This paper summarizes current knowledge on the subject by reviewing pertinent studies and by pinpointing the conclusions they support. The material covered in the paper should be helpful to dental personnel and dental health agencies in their promotional efforts in preventive dentistry and in developing and managing the increasing number of comprehensive dental programs for children.

Topical fluoride solutions

■ *Sodium fluoride:* The recommended treatment technic for the application of a solution of sodium fluoride begins with cleaning the clinical crowns of the teeth, with use of a standard prophylaxis paste in a motor-driven rubber cup.[1] After the prophylaxis, an upper and opposing lower quadrant (half the mouth at a time) are isolated with cotton rolls held in appropriate holders and the teeth are dried thoroughly with a stream of compressed air. A 2% sodium fluoride solution is applied to the teeth with cotton applicators so that all surfaces are made visibly wet. The solution is permitted to dry for about three minutes. Second, third, and fourth applications, not preceded by prophylaxes, are given at intervals of approximately one week. As with all topically applied fluoride agents, caries inhibition presumably begins as soon as treatment is completed. The series of treatments is recommended at ages 3, 7, 11, and 13.[2] These ages were selected so that fluoride is applied shortly after the eruption of groups of teeth, thus minimizing the time that teeth are at risk from caries attack before treatment. The ages should be varied, if possible, with each child's individual pattern of tooth eruption.

The procedure for the application of sodium fluoride was developed by Knutson and co-workers[3-8] who tested different fluoride solutions, concentrations, and frequencies of application in a series of large-scale studies involving thousands of schoolchildren. In summary, results of these early studies indicated that: a minimum of four applications with a 2% sodium fluoride solution appears to give the maximum effect—a reduction of about 40% in new carious teeth; increasing the interval between individual applications in the series from about one week to three to six months decreases the effectiveness of treatment; and omission of a prophylaxis preceding the series of treatments reduces the benefits by about half.

Studies conducted throughout the world by other investigators[9-14] have confirmed the caries-preventive properties of topically applied sodium fluoride. A variety of technics of application have been tested but the procedure developed by the Public Health Service has been the most widely used and it appears to be the most reliable. A review of the literature reveals an impressive number of studies that have essentially duplicated the results obtained by Knutson and his co-workers. In spite of some variation, 30% to 40% reductions in dental caries incidence in the permanent teeth of children living in an area with insufficient levels of fluoride in the water supply have been reported quite consistently.[15-18]

Certain aspects of the potential usefulness of topically applied sodium fluoride need further investigation. More long-term studies must be done to determine precisely how long after treatment sodium fluoride continues to exert a beneficial effect; results of some investigations suggest that a falloff in effectiveness may occur in less than three years,[15,19,20] yet there is little evidence

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Global goals for oral health 2020

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Houston, USA, Leader of FDI Joint Working Group
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World Health Organisation, Geneva, Switzerland
John Clarkson
International Association for Dental Research, Alexandria, USA
Newell Johnson
FDI Science Commission, Ferney-Voltaire, France

How to use this document

It is anticipated that dentists and other health planners in many different circumstances will use this document for guidance when developing their plans for oral health. We recognise that no document can provide an exact blue print for each and every set of circumstances where oral health plans are to be developed. What is presented here is a range of possible areas that need to be taken into consideration when plans are being developed. It also provides a useful checklist against which existing plans might be examined to determine if there are any possible gaps.

Fundamental to the success of any plan is a clear understanding of what resources are already available or might become available once the plan has been adopted officially. Initially it may not be necessary to have a detailed inventory of all resources available, a simple analysis like the completion of the questionnaire in Annexure B will give a quick guide as to the level of resources available to you. This, combined with a prioritised list of the oral health problems of the community or population you are planning for, will help you identify those types of interventions that are likely to be most appropriate and sustainable under the prevailing circumstances.

Background

The FDI and the WHO established the first Global Oral Health Goals jointly in 1981 to be achieved by the year 2000. A review of these goals, carried out just prior to the end of this period, established that they had been useful and, for many populations, had been achieved or exceeded. However, for a significant proportion of the world's population, they remained only a remote aspiration. Nonetheless, the Oral Health Goals had stimulated awareness of the importance of oral health amongst national and local governments and acted as a catalyst for securing resources for oral health in general. Therefore, even though not all countries had achieved the goals, they provided a key focus for the effort.

Recently, the FDI, WHO and IADR have embarked on the activity of preparing goals for the new millennium, for the year 2020, and these are presented here. They were developed by a Working Group including representatives of the FDI, WHO and IADR from different regions of the world (see Annexure A for the Group's membership).

The drafts of this document were circulated to all National Dental Association members (NDAs) of the FDI and placed on the global Dental Public Health list server for comment. All WHO Collaborating Centres in Oral Health (WHOCC) and the IADR were also consulted. Responses received from NDAs, IADR, WHOCC as well as from individuals have subsequently been incorporated in this document.

Aims

This document, which contains proposals for new Global Oral Health Goals, Objectives and Targets of increasing detail and complexity, aims to provide a framework for health policy makers at different levels – regional, national and local. The goals and targets are not intended to be prescriptive. By being focused broadly on the global level, it is hoped that it will encourage local action in the spirit of the United Nations Development Programme's report: '*Think globally act locally*'. Thus, the document will provide an instrument for local and national health care planners to specify realistic goals and standards for oral health to be achieved by the year 2020.

The process of formulating a regional, national or local oral health strategy necessitates many stages. This document provides the first step in that process by guiding health planners to evaluate the current situation of oral health and

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Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015

*GBD 2015 Disease and Injury Incidence and Prevalence Collaborators**

Background Non-fatal outcomes of disease and injury increasingly detract from the ability of the world's population to live in full health, a trend largely attributable to an epidemiological transition in many countries from causes affecting children, to non-communicable diseases (NCDs) more common in adults. For the Global Burden of Diseases, Injuries, and Risk Factors Study 2015 (GBD 2015), we estimated the incidence, prevalence, and years lived with disability for diseases and injuries at the global, regional, and national scale over the period of 1990 to 2015.

Methods We estimated incidence and prevalence by age, sex, cause, year, and geography with a wide range of updated and standardised analytical procedures. Improvements from GBD 2013 included the addition of new data sources, updates to literature reviews for 85 causes, and the identification and inclusion of additional studies published up to November, 2015, to expand the database used for estimation of non-fatal outcomes to 60 900 unique data sources. Prevalence and incidence by cause and sequelae were determined with DisMod-MR 2.1, an improved version of the DisMod-MR Bayesian meta-regression tool first developed for GBD 2010 and GBD 2013. For some causes, we used alternative modelling strategies where the complexity of the disease was not suited to DisMod-MR 2.1 or where incidence and prevalence needed to be determined from other data. For GBD 2015 we created a summary indicator that combines measures of income per capita, educational attainment, and fertility (the Socio-demographic Index [SDI]) and used it to compare observed patterns of health loss to the expected pattern for countries or locations with similar SDI scores.

Findings We generated 9·3 billion estimates from the various combinations of prevalence, incidence, and YLDs for causes, sequelae, and impairments by age, sex, geography, and year. In 2015, two causes had acute incidences in excess of 1 billion: upper respiratory infections (17·2 billion, 95% uncertainty interval [UI] 15·4–19·2 billion) and diarrhoeal diseases (2·39 billion, 2·30–2·50 billion). Eight causes of chronic disease and injury each affected more than 10% of the world's population in 2015: permanent caries, tension-type headache, iron-deficiency anaemia, age-related and other hearing loss, migraine, genital herpes, refraction and accommodation disorders, and ascariasis. The impairment that affected the greatest number of people in 2015 was anaemia, with 2·36 billion (2·35–2·37 billion) individuals affected. The second and third leading impairments by number of individuals affected were hearing loss and vision loss, respectively. Between 2005 and 2015, there was little change in the leading causes of years lived with disability (YLDs) on a global basis. NCDs accounted for 18 of the leading 20 causes of age-standardised YLDs on a global scale. Where rates were decreasing, the rate of decrease for YLDs was slower than that of years of life lost (YLLs) for nearly every cause included in our analysis. For low SDI geographies, Group 1 causes typically accounted for 20–30% of total disability, largely attributable to nutritional deficiencies, malaria, neglected tropical diseases, HIV/AIDS, and tuberculosis. Lower back and neck pain was the leading global cause of disability in 2015 in most countries. The leading cause was sense organ disorders in 22 countries in Asia and Africa and one in central Latin America; diabetes in four countries in Oceania; HIV/AIDS in three southern sub-Saharan African countries; collective violence and legal intervention in two north African and Middle Eastern countries; iron-deficiency anaemia in Somalia and Venezuela; depression in Uganda; onchoceriasis in Liberia; and other neglected tropical diseases in the Democratic Republic of the Congo.

Interpretation Ageing of the world's population is increasing the number of people living with sequelae of diseases and injuries. Shifts in the epidemiological profile driven by socioeconomic change also contribute to the continued increase in years lived with disability (YLDs) as well as the rate of increase in YLDs. Despite limitations imposed by gaps in data availability and the variable quality of the data available, the standardised and comprehensive approach of the GBD study provides opportunities to examine broad trends, compare those trends between countries or subnational geographies, benchmark against locations at similar stages of development, and gauge the strength or weakness of the estimates available.

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See Editorial page 1447

See Comment pages 1448 and 1450

*Collaborators listed at the end of the Article

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Fluoride Varnish in the Prevention of Dental Caries in Children and Adolescents: A Systematic Review

Amir Azarpazhooh, *DDS, MSc;* **Patricia A. Main,** *BDS, DDS, DDPH, MSc, FRCD(C)*

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ABSTRACT

Objective: To develop a scientifically current and evidence-based protocol for the use of fluoride varnish for the prevention of dental caries among high-risk children and adolescents.

Methods: Previous systematic reviews on this topic were used as the basis for the current review. Ovid MEDLINE, CINAHL and several other relevant bibliographic databases were searched for English-language articles, with human subjects, published from 2000 to 2007.

Results: A total of 105 articles were identified by the literature search; relevance was determined by examining the title, abstract and body of the article. Seven original research studies met the inclusion criteria. These articles were read and scored independently by 2 reviewers, and evidence was extracted for systematic review.

Recommendations: The following recommendations were developed on the basis of the evidence:

1. For high-risk populations (e.g., people with low socioeconomic status, new immigrants and refugees, First Nations and Inuit children and adolescents), fluoride varnish should be applied twice a year, unless the individual has no risk of caries, as indicated by past and current caries history. This schedule of application would permit sealants to be checked biannually to ensure retention.
2. Single-dose packages of fluoride varnish should be used for children; the varnish in such packages should be stirred vigorously before application, to ensure that any precipitated fluoride is redissolved.
3. There is good evidence of the complementary efficacy of preventive strategies such as sealants and varnish, as well as toothbrushing and nutritional counselling; oral health care programs should therefore include as many complementary strategies as possible.

For citation purposes, the electronic version is the definitive version of this article: www.cda-adc.ca/jcda/vol-74/issue-1/73.html

First developed and marketed in the 1960s in the form of sodium fluoride (Duraphat, Colgate, New York, N.Y.) and in the 1970s in the form of silane fluoride (Fluor Protector, Ivoclar Vivadent, Lichtenstein, Germany), fluoride varnishes prolong contact between fluoride and enamel. The effectiveness, ease of application and relative safety of these products offer significant advantages over other topical fluoride treatments, such as gels and rinses.[1–3] The general method of application is shown in **Fig. 1.**

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ORIGINAL ARTICLE
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Effect of organic versus inorganic fluoride on enamel microhardness: An *in vitro* study

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Abstract

Introduction: Dental caries is one of the most prevalent infectious diseases affecting the human dentition. Fluorides are effective anti-carious agents and have been widely used for caries prevention in the form of systemic and topical fluorides. Neutral sodium fluoride (NaF) is commonly used as a topical fluoride agent. A special category of topical fluorides are organic fluorides in the form of amine fluorides (AmF). Researchers have reported that AmF is superior to inorganic fluorides in improving the caries resistance of enamel due to the significant anti-enzyme effect of the organic fragment. **Aim:** The aim of the present study was to compare the enamel surface micro hardness after topical application of NaF and AmF solutions. **Materials and Methods:** Twenty fresh samples of sound human enamel were treated with demineralizing solution for 72 h and divided into Group A (treated with NaF) and Group B (treated with AmF) solutions for 3 min twice daily for 7 days. In between treatment, the samples were stored in artificial saliva. The enamel surface hardness was measured with Vickers hardness test at baseline, post-demineralization and post-treatment with two different fluoride solutions (NaF and AmF) and a comparative analysis was made. **Results:** The increase in mean micro hardness of human enamel after treatment with AmF application was found to be statistically significant ($P < 0.01$) when compared to the mean micro hardness after treatment with NaF. **Conclusion:** Fluoride enhances the remineralization process by accelerating the growth of enamel crystals that have been demineralized. It can be concluded from the present study that AmF compounds result in a marked increase in enamel micro hardness when compared to NaF.

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Full Text

Introduction

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The surgical approach to managing dental caries was developed a century ago as at that time there was no other valid alternative. Presently, advances in the field of caries research have led to improved understanding of the disease process. Now, early detection of initial carious lesions and emphasis on preventive measures holds the key to controlling dental caries. [2]

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Hence, the aim of the present in vitro study was to compare the micro hardness of demineralized enamel after topical application of NaF and AmF solutions.

Materials and Methods

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REVIEW / SYNTHÈSE

Antimicrobial actions of fluoride for oral bacteria

Robert E. Marquis

Abstract: Fluoride is widely used as a highly effective anticaries agent. Although it is felt that its anticaries action is related mainly to effects on mineral phases of teeth and on the process of remineralization, fluoride also has important effects on the bacteria of dental plaque, which are responsible for the acidification of plaque that results in demineralization. The results of recent studies have shown that fluoride can affect bacterial metabolism through a set of actions with fundamentally different mechanisms. It can act directly as an enzyme inhibitor, for example for the glycolytic enzyme enolase, which is inhibited in a quasi-irreversible manner. Direct action seems also to occur in inhibition of heme-based peroxidases with binding of fluoride to heme. The flavin-based peroxidases of many oral bacteria are insensitive to fluoride. Another mode of action involves formation of metal–fluoride complexes, most commonly AlF_4^-. These complexes are responsible for fluoride inhibition of proton-translocating F-ATPases and are thought to act by mimicking phosphate to form complexes with ADP at reaction centers of the enzymes. However, the actions of fluoride that are most pertinent to reducing the cariogenicity of dental plaque are those related to its weak-acid character. Fluoride acts to enhance membrane permeabilities to protons and compromises the functioning of F-ATPases in exporting protons, thereby inducing cytoplasmic acidification and acid inhibition of glycolytic enzymes. Basically, fluoride acts to reduce the acid tolerance of the bacteria. It is most effective at acid pH values. In the acidic conditions of cariogenic plaque, fluoride at levels as low as 0.1 mM can cause complete arrest of glycolysis by intact cells of *Streptococcus mutans*. Overall, the anticaries actions of fluoride appear to be complex, involving effects both on bacteria and on mineral phases. The antibacterial actions of fluoride appear themselves to be complex but to be dominated by weak-acid effects.

Key words: fluoride, oral bacteria, dental caries, glycolysis.

Résumé : Le fluor est largement utilisé à cause de sa haute efficacité contre la carie dentaire. Même si la tendance est de croire que cette propriété soit surtout reliée aux effets sur les phases minérales des dents et sur le processus de reminéralisation, le fluor a aussi un effet important sur les bactéries de la plaque dentaire responsables de l'acidification de la plaque qui cause la déminéralisation. Des travaux récents ont montré que le fluor pouvait affecter le métabolisme bactérien de plusieurs façons et selon des mécanismes fondamentalement différents. Il peut agir comme un inhibiteur enzymatique, par exemple sur l'énolase (une enzyme de glycolyse), qui se retrouvera inhibée de manière quasi irréversible. Les peroxydases ayant un constituant hème sont aussi directement inhibées par la liaison du fluor avec l'hème. Par contre, les peroxydases ayant un constituant flavine présentes chez plusieurs bactéries orales demeurent insensibles au fluor. Un autre mode d'action implique la formation de complexes métal–fluor dont Alf_4^- qui est le plus commun. Ces complexes sont responsables de l'inhibition des F-ATPases translocatrices de protons et sembleraient agir en déviant le phosphate qui forme des complexes avec l'ATP aux sites de réaction de ces enzymes. D'autre part les actions du fluor qui sont les plus pertinentes pour réduire les caries de la plaque dentaire sont celles reliées à son caractère d'acide faible. Le fluor augmente la perméabilité membranaire aux protons et compromet le fonctionnement des F-ATPases en expulsant les protons, ce qui a pour effet de provoquer l'acidification cytoplasmique et l'inhibition acide des enzymes de la glycolyse. Fondamentalement, l'action du fluor est de diminuer l'acidotolérance des bactéries. De fluor a un maximum d'efficacité aux valeurs acides de pH. Dans les conditions acides qui permettent la progression de la carie au niveau de la plaque, la présence de fluor à des concentrations aussi faibles que 0.1 mM pourra arrêter complètement la glycolyse efectuée

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Fluoride toothpastes for preventing dental caries in children and adolescents (Review)

Marinho VCC, Higgins JPT, Logan S, Sheiham A

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Systematic Review of Controlled Trials on the Effectiveness of Fluoride Gels for the Prevention of Dental Caries in Children

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Abstract: Fluoride gels have been widely used since the 1970s. The aim of this review was to assess the effectiveness and safety of fluoride gels in the prevention of dental caries in children and to examine factors potentially modifying their effectiveness. Relevant randomized or quasi-randomized trials were identified without language restrictions by searching multiple databases, reference lists of articles, and journals and by contacting selected authors and manufacturers. Trials with blind outcome assessment comparing fluoride gel with placebo or no treatment for at least one year and involving children under seventeen years of age were selected. Inclusion decisions, quality assessment, and data extraction were duplicated in a random sample of one third of studies, and consensus was achieved by discussion or a third party. Random effects meta-analyses were performed where data could be pooled. Potential sources of heterogeneity were examined in random effects meta-regression analyses. The main outcome was caries increment measured by the change in decayed, missing, and filled permanent tooth surfaces (D(M)FS). The primary measure of effect was the prevented fraction (PF) that is the difference in mean caries increment between the treatment and control groups expressed as a percentage of the mean increment in the control group. Potential adverse effects and unacceptability of treatment were also recorded. Twenty-five studies were included, involving 7,747 children. For the twenty-three that contributed data for meta-analysis, the D(M)FS pooled prevented fraction estimate was 28 percent (95 percent CI, 19 percent to 37 percent; $p<0.0001$). There was clear heterogeneity, confirmed statistically ($p<0.0001$). The effect of fluoride gel varied according to type of control group used, with D(M)FS PF on average being 19 percent (95 percent CI, 5 percent to 33 percent; $p<0.009$) higher in non-placebo controlled trials. Only two trials reported on adverse events. There is clear evidence of a caries-inhibiting effect of fluoride gel. The best estimate of the magnitude of this effect, based on the fourteen placebo-controlled trials, is a 21 percent reduction (95 percent CI, 14 to 28 percent) in D(M)FS. This corresponds to an NNT of two (95 percent CI, 1 to 3) to avoid one D(M)FS in a population with a caries increment of 2.2 D(M)FS/year, or an NNT of twenty-four (95 percent CI, 18 to 36) based on an increment of 0.2 D(M)FS/year. However, further work is needed to identify and quantify potential harmful effects of fluoride gels.

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Key words: dental caries, caries prevention, fluoride gel, fluoride, topical application, meta-analysis, systematic review

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Topically applied fluoride gels have been widely used in dental surgeries and prevention programs in schools in many countries during recent decades. However, with the widespread use of fluoride, especially in the form of toothpaste, and the low caries severity and prevalence in many countries, questions have been raised about their cost-effectiveness and the possibility of overexposure to fluoride, particularly because of the high concentration of fluoride in some gels. The aim of this systematic review was to assess the effectiveness and safety of fluoride gels in the prevention of dental caries in children and to examine formally the main factors that may influence their effectiveness including initial level of caries severity, background exposure to other fluoride sources, methods of application, and fluoride concentration.

Fluoride gels can be professionally or self-applied under supervision, at a frequency from once to several times a year. Various fluoride compounds, concentrations, and methods of gel application have been used, with or without prior dental prophylaxis.

Use of Professionally Administered Topical Fluorides in Asia

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ABSTRACT

Professionally applied topical fluoride varnish, gel, and solution have been shown to be effective in preventing and in arresting dental caries. Their use in different countries in Asia varies greatly and may not correlate with the dental caries situation of the populations in the countries. In the higher-income countries, use of fluoride varnish and gel is common among dental professionals. In contrast, the use of professionally administered topical fluorides is not common in the lower-income countries. Fluoride varnish, being easy to apply and safe, has been the preferred agent for the prevention of early childhood caries, which is prevalent in many developing countries in Asia. The relatively high cost of professionally administered fluoride agents and the shortage of a dental workforce, especially in lower income countries, have hampered the widespread adoption of these effective caries prevention methods in the private and public dental services. Government health policies should be pursued to lower the cost of treatment, either through incentives for local production and/or elimination of taxes and tariffs on imported fluoride products.

The use of fluorides, both systemic and topical, has been advocated by the World Health Organization as an appropriate means to prevent dental caries worldwide (Petersen and Lennon, 2004; Petersen *et al*., 2008). Topical fluoride agents can be either self-applied, *e.g.,* toothpaste and mouthrinse, or professionally administered, *e.g*., varnish and gel. A Cochrane systematic review found that the use of topical fluorides could reduce dental caries by, on average, 26% (Marinho *et al*., 2003a). There is no clear clinical evidence that any one of the topical fluorides is more effective than the others in preventing dental caries in children and adolescents (Marinho *et al*., 2004a). Despite this, when topical fluorides are used in addition to fluoride toothpaste, there is a modest reduction in caries of around 10% compared with that achieved with toothpaste use alone (Marinho *et al*., 2004b). The recommended use of professionally administered topical fluoride and the frequency of application depend on the assessed dental caries risk of the individual or population—*i.e.*, higher frequency of application for people with higher caries risk, longer time interval for people with moderate risk—and the use is not necessary in people with low risk (ADA Council on Scientific Affairs, 2006; Chu *et al*., 2010).

In Asia, large differences in the economic development of the various countries and also in the health status of their populations can be observed (World Bank, 2011; World Health Organization, 2011). Similarly, great diversities exist regarding the dental caries situation of children and adults, with countries being classified as high level, such as the Philippines, through moderate level, such as South Korea, to low level, such as India, and to very low level, such as China (Petersen, 2003). Asian countries also vary in their approaches to control caries, at either the individual or the population level.

The aim of this paper is to describe the current situation of the use of professionally administered topical fluorides in various Asian countries, discussing the barriers and perspectives for their implementation as an effective caries preventive approach. A description of the use of self-applied topical fluorides in Asia can be found in a paper by Zero *et al.* (2012).

PROFESSIONALLY APPLIED FLUORIDES

Fluoride Gel/Foam

Different fluoride compounds have been used in fluoride gels for years. Sodium fluoride can be used in a neutral pH environment or can be acidulated and buffered with a phosphate to form acidulated phosphate fluoride (APF). Clinical use of APF was developed in the 1960s, and the concentration commonly used in fluoride gel today is 1.23% (Newbrun, 2011). In the application, a sufficient amount of gel to cover the teeth in a dental arch is dispensed into a disposable tray and inserted into the mouth. The recommended application time is 4 min, and the patient should expectorate the gel afterward (Hawkins *et al*., 2003).

A Cochrane systematic review of fluoride gel found good evidence to support its dental caries-preventive effect (Marinho

Key Words

dental caries, fluoride, Asian, preventive dentistry, dentists, dental health services.

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Topical Fluorides

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STUDIES ON DENTAL CARIES

X. A Procedure for the Recording and Statistical Processing of Dental Examination Findings

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INTRODUCTION

In 1936, the authors undertook to plan a study of the way dental caries attacks complete population groups such as found in typical urban communities in the United States. The execution of this investigation was visualized in terms of several steps: Actual observations on the condition of the teeth of a large number of persons; translation of these direct observations into written records; summarization and tabulation of the recorded findings; and finally, interpretation of the data as a whole. Although it is clear that all these steps are interrelated, it is apparent that each is an entity in itself having individual provinces and problems. The second and third steps are closely related and together represent what might be designated the "statistical engineering" aspects of the study. The present paper deals with this province. It is concerned largely with a description of a particular record form and the machine processing methods developed for the analysis of dental observations recorded on this form.

THE EXAMINATION AND RECORDING PROCEDURE

Preliminary considerations: Methods for recording observations on biological material may be simple or complex depending on the variables under study and on the particular objectives of the investigation. Dental caries, a condition from which few individuals of the United States are free, is exceedingly variable in the way it attacks different persons. In addition, the several morphological types of teeth and coronal surfaces in both the deciduous and permanent dentitions have different caries susceptibilities. Furthermore, the evidence of caries may be manifested in a variety of ways: As teeth

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Time Trends in Caries Experience of 6- and 12-Year-Old Children of Different Socioeconomic Status in The Hague

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Key Words
Caries experience
Epidemiology
Socioeconomic status

Abstract

The caries experience among 6- and 12-year-old children in the The Netherlands from the mid seventies showed a continued decreasing trend. A halt in the decline of caries experience of the primary dentition of 6-year-olds occurred after 1983, whereas among 12-year-old children the decrease in mean DMFS values continued in the period 1980–1989. The 1996 survey in The Hague showed that the decline in caries in 12-year-old native children of low socioeconomic status (SES) has come to an end (average DMFT of 1.1). However, in medium- and high-SES groups, the percentages of caries-free children have continued to rise. Of the medium-SES 6- and 12-year-old children, 79 and 89% were caries-free, respectively; in the high-SES children the respective figures were 84 and 86%. A DMFT of 0.3 in 12-year-olds of medium and high SES was found, the general value was 0.7 and 74% with zero caries experience.

In The Netherlands the decrease of caries experience in schoolchildren was first noticed in the mid seventies [Kalsbeek, 1982]. From results of a meta-analysis on all known epidemiological caries studies performed between 1980 and 1989, it appeared that after 1983 a halt in the decline of caries experience among 6-year-olds occurred, whereas among 12-year-olds, the decrease in mean DMFS scores continued in the period 1980–1989 [Truin et al, 1993]. The 1993 survey in The Hague illustrated a further improvement of dental health among 12-year-olds by a significant increase in percentages of caries-free children between 1989 and 1993 [Truin et al., 1994]. In some low caries prevalence countries, the caries prevalence of the permanent teeth seems to bottom out in children at this age [Marthaler et al., 1996]. In 1993 the average DMFT of 0.8 in the 12-year-old group of native children in The Hague was extremely low compared to other European countries [Marthaler et al., 1996]. An interesting question was if that level of caries in permanent teeth in 12-year-olds would tend to stabilize, or would change; a second question was whether the same pattern would be seen in children of different socioeconomic status (SES), and a third question was if the caries activity in the deciduous dentition of 6-year-old children had changed since the last survey.

In January 1996, the cross-sectional study in The Hague was repeated and the results of the examinations are described and compared to findings of earlier years in the present article.

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Henri Moissan: Winner of the Nobel Prize for Chemistry 1906

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Keywords:
electrochemistry · fluorine · high-temperature chemistry · history of science

On December 10, 1906, Henri Moissan (1852–1907) became the first French chemist to be awarded the Nobel Prize. At the award ceremony in Stockholm, the President of the Royal Swedish Academy of Sciences, P. Klason, described the two essential aspects of this great scientist's work in the following terms, saying the prize had been awarded to Moissan, "*for having isolated and investigated the chemical element fluorine and for having introduced the electric furnace into the service of science—exploits whereby he has opened up new fields for scientific research and industrial activity*".[1] Indeed, Moissan had isolated fluorine twenty years earlier during a historic experiment; he also paved the way for high-temperature synthesis.

Figure 1. Henri Moissan (1852–1907).

The Early Years

Henri Moissan was born in Paris in 1852 but spent much of his teenage years and his early professional life in Meaux, where he was an apprentice clockmaker (Figure 1). In 1870 war against Prussia obliged his family to return to Paris, and he joined the army for a year before enrolling at the Ecole Supérieure de Pharmacie de Paris. Henri Moissan was divided for many years between his two loves, pharmacy and experimental chemistry, and enrolled first in 1872 at the Ecole de Chimie Expérimentale, headed by Edmond Frémy at the Muséum, before joining P. P. Dehérain's research group, also at the Muséum, where he carried out research into vegetable physiology, the absorption of oxygen, and the emission of carbon dioxide in plants kept in obscurity. He was appointed a senior chemist in 1879. An account of his research during this period into the chemistry of pyrophoric iron and metal oxides of the iron family can be found in the doctoral thesis he wrote in 1880. At the same time, he climbed the hierarchical ladder at the Ecole Supérieure de Pharmacie de Paris. In 1880 he was appointed Maître de Conférences and Chef de Travaux Pratiques, before becoming Professeur Agrégé in 1882 with a thesis entitled "*Série du Cyanogène*" (The Cyanogen Series).[2,3]

It was only in 1884 that Moissan began to concentrate solely on isolating fluorine, a halogen discovered in the early years of the 19th century thanks to the work of A. M. Ampère in France and H. Davy in England (see inset).[4–7] Yet the gas had never been isolated because of its violent reactivity.

1886: A Great Year for Fluorine

Several generations of chemists had tried in vain to isolate fluorine, notably by electrolyzing phosphorus and arsenic fluorides, but Moissan was determined to find a way. His genius lay in the idea of turning the bath into a conductor by adding a molten potassium fluoride salt, KHF_2. (Pure hydrogen fluoride, HF, could not suffice as its capacity as an electric conductor was too weak.) Moissan devised a platinum electrolyzer and lowered the reaction temperature of the electrolytic solution of HF + KHF_2 to limit corrosion. The platinum electrolyzer was U-shaped and stopped with fluorite (CaF_2) stoppers (Figure 2). The cathode and the anode were made of irridated platinum to provide better resistance to the fluorine. The traces of hydrogen fluoride were condensed at the end of the apparatus in a low-temperature trap and also by sodium fluoride. On June 28, 1886, a gaseous product was identified at the anode of the electrolyzer: Fluorine (F_2) had been successfully isolated, thus resolving one of the most difficult challenges in the realm of inorganic chemistry (Figure 3).[8] The yellow-green gas obtained was highly toxic and proved to be a

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Chapter 1

Epidemiology of Dental Caries

JAY D. SHULMAN AND DAVID P. CAPPELLI

CARIES EPIDEMIOLOGY

THE SCIENCE OF CARIES

TYPES OF CARIES

POPULATION-BASED MEASURES OF CARIES

- **Coronal Caries**
- **Early Childhood Caries**
- **Root Caries**
- **Definitions of Risk**
- **Geographic Variation**
- **Secular Trends**
- **Sociodemographic Factors**
  - Age
  - Gender
  - Race and Ethnicity
  - Income
  - Concentration of Caries
  - Life Course
- ***Healthy People 2010***

SUMMARY

LEARNING OBJECTIVES

Upon completion of this chapter, the learner will be able to:

- Explain the biological process of caries development
- Describe etiological factors associated with caries
- Examine population-based measures of dental caries
- Discuss trends in caries prevalence
- Outline the *Healthy People 2010* caries objectives

KEY TERMS

Caries balance
Confidence limits
Decayed, Missing, Filled (DMF)
Demineralization
Dental caries
Enamel caries
Early childhood caries
National Health and Nutrition Examination Survey (NHANES)
Remineralization

Dental caries remains the most prevalent chronic childhood disease and is five times more prevalent than asthma.[1] This chapter provides foundational knowledge about the prevalence and trends of dental caries in the population, and explores population-based measurement systems. Dental caries is described as a disease process and the causal profile of the disease is outlined. Surveillance methods and disease trends in the U.S. population for both children and adults are described by using data from several national surveys. The **National Health and Nutrition Examination Survey** (NHANES) series comprises NHANES I (1971 to 1974),[2] NHANES III (1988 to 1994),[3] and NHANES (1999 to present).[4]

CARIES EPIDEMIOLOGY

Dental caries is a diet-dependent, transmissible, microbiologically mediated disease.[6] Similar to periodontal disease, it follows both an infectious and chronic disease model. The microorganisms that cause dental caries are transmitted vertically from mother to child soon after tooth eruption.[7] Studies indicate that the greater the delay in transmission, the lesser the caries burden through life.[7] Once caries is established, prevention focuses on the mitigation of risk factors that contribute to disease. Dental caries is caused by the interrelationship of multiple factors over time (Figure 1-1). These factors were described by Keyes in the 1960s using a Venn diagram (see Figure 4-1) of intersecting causal circles.[8] Modifications of this model appear in the literature, but all have their basis in the original Venn diagram. The cause of dental caries is related to a number of factors that are categorized into

The Role of Fluoride in the Prevention of Tooth Decay

Howard Pollick, BDS, MPH

KEYWORDS

• Dental caries • Dental decay • Oral health • Fluorides • Primary prevention
• Secondary prevention • Children

KEY POINTS

- Fluoride is the key to prevention of tooth decay.
- There are multiple fluoride modalities.
- Effectiveness and safety of fluoride depend on dose and concentration.
- Individual level fluoride use occurs at home and with professional application.
- Community level prevention occurs through fluoridation of water or salt.

INTRODUCTION

Dental Caries (Tooth Decay) in Children

Early childhood caries (ECC) is defined as the presence of one or more decayed (non-cavitated or cavitated lesions), missing (due to caries), or filled tooth surfaces in any primary tooth in a child younger than 6 years.[1] For children older than 6 years, there is no special category or definition of dental caries (see separate section/chapter on Dental Caries).

Fluoride is the Key to Prevention of Tooth Decay

Fluoride works to reduce the prevalence and severity of dental caries that requires restorative dental care, in preeruptive, posteruptive, systemic, and topical situations.

There are multiple mechanisms by which fluoride works:[2]

- Through reducing demineralization of enamel in the presence of acids produced by cariogenic bacteria in dental plaque breaking down fermentable carbohydrates,
- Through remineralization of early enamel caries, and
- Through inhibition of bacterial activity in dental plaque.

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COMMUNITY DENTISTRY AND ORAL EPIDEMIOLOGY

The World Oral Health Report 2003: continuous improvement of oral health in the 21st century – the approach of the WHO Global Oral Health Programme

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Abstract – Chronic diseases and injuries are the leading health problems in all but a few parts of the world. The rapidly changing disease patterns throughout the world are closely linked to changing lifestyles, which include diets rich in sugars, widespread use of tobacco, and increased consumption of alcohol. In addition to socio-environmental determinants, oral disease is highly related to these lifestyle factors, which are risks to most chronic diseases as well as protective factors such as appropriate exposure to fluoride and good oral hygiene. Oral diseases qualify as major public health problems owing to their high prevalence and incidence in all regions of the world, and as for all diseases, the greatest burden of oral diseases is on disadvantaged and socially marginalized populations. The severe impact in terms of pain and suffering, impairment of function and effect on quality of life must also be considered. Traditional treatment of oral diseases is extremely costly in several industrialized countries, and not feasible in most low-income and middle-income countries. The WHO Global Strategy for Prevention and Control of Noncommunicable Diseases, added to the common risk factor approach is a new strategy for managing prevention and control of oral diseases. The WHO Oral Health Programme has also strengthened its work for improved oral health globally through links with other technical programmes within the Department for Noncommunicable Disease Prevention and Health Promotion. The current oral health situation and development trends at global level are described and WHO strategies and approaches for better oral health in the 21st century are outlined.

Key words: common risk factors; disease prevention; health policy; health promotion; oral health; WHO

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The *World Health Report 2002* outlined the extent of disease, disability and death in the world today that can be attributed to a number of the most important risks to human health (1). This is of great interest in itself but, more importantly, the report also indicated how much of this burden could be avoided in the next couple of decades if the same risk factors were reduced from now onwards. The report identified a number of cost-effective interventions to counter some of these risk factors. Intervention is defined broadly as 'any health action – any promotive, preventive, curative, or rehabilitative activity where the primary intent is to improve health'. Apart from the obvious health

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World Health Organization

The World Oral Health Report 2003

Continuous improvement of oral health in the 21st century – the approach of the WHO Global Oral Health Programme