

## NL 1- BIOMARKERS OF EXPOSURE TO FLUORIDE

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Biological markers or biomarkers are defined as indicators that signal events in biological systems (human body) or samples. A biomarker is not used as diagnosis test, but as an indicator of a disease or biological alteration. The biomarkers are classified in three types: 1) exposure; 2) susceptibility and 3) biomarkers of effect. For biomarkers of fluoride the examples would be respectively: 1) plasma, bone, teeth, urine, saliva, dental plaque, plaque fluid, hair, nails; 2) genetic factors, acid-base disturbances, renal disturbances, bone growth and nutritional state; 3) reduction in the activity and severity of the dental caries, dental fluorosis and skeletal fluorosis. A biomarker of exposure is a substance of external origin or a metabolic derivate or the product of an interaction between a biological agent and molecules. The biomarker of susceptibility is an indicator that the individual is particularly sensitive to the effect of a substance and for the fluoride this can be a form of understanding the variation of individual dose-response for the same exhibition pattern to fluoride. The biomarkers of effect are the consequences of a previous exhibition: dental or skeletal fluorosis. In spite of the constant use of some biological materials as plasma and saliva in dental research, the use of these materials in pharmacokinetics models for biomarkers of exposure is still limited. One of the advantages in using biomarkers model is the possibility to simplify the collection, storage and analysis of samples. In spite of the fact that fluoride biomarkers are regarded as important auxiliaries in the evaluation of dental fluorosis risks, it is important to recognize that the biomarker model is in a developmental phase.

## NL 2- DENTAL FLUOROSIS: MECHANISMS

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Fluoride has a fundamental role in control of dental caries. According to the Centers for Disease Control of United States (CDC), the water fluoridation is one of the ten most important measures of Public Health in the 20<sup>th</sup> century. In Brazil, after the seventies, considering only the water fluoridation, this measure was responsible for the decrease of 50% in dental caries prevalence. This wide availability of fluoride is precisely related to the recent increase of dental fluorosis prevalence, which is an enamel alteration caused by an excessive exposition to fluoride. For a better comprehension of the several hypotheses that try to explain the dental fluorosis, we will briefly review the amelogenesis. In the formation of dental enamel, the amelogenins correspond to 90% of the enamel proteins. They suffer hydrolyses before being slowly removed from the matrix of enamel formation in the secretory stage. On the other hand, in transition/early maturation stage, they are intensely removed. Between the hypotheses that could explain the dental fluorosis causes are the reduction of free calcium (which is necessary to several enzymatic functions), the inhibition of proteases and the effects in the ameloblasts' functions, especially during the maturation stage. In this exposure, we will discuss these hypotheses and other ones based on a literature review.

## NL 3- MERCOSUR, FLUORIDE AND ORAL HEALTH

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Mercosur represents the fourth largest economic entity worldwide. The four countries member, Argentina, Brazil, Uruguay and Paraguay have experienced some progress in terms of market, but seems that the Dentistry does not have participation in the decisions about health, particularly the use of fluoride (F).

Thus, in the end of the last century there was tremendous change in the concept how F interferes with dental caries development. In the recent past it was considered that would be indispensable the ingestion of F during enamel formation for to have teeth caries resistant. Therefore, F was considered a micronutrient and when the water supply of a community was not fluoridated, the prescription of F supplements was mandatory or strongly recommended. Also, it was well know that the ingestion of F during the teeth formation was involved with dental fluorosis, a side-effect considered acceptable since the benefits of caries reduction was higher than the risks of fluorosis.

However, epidemiological data, from abroad since 1980 and from Brazil after the 90', suggested that would be not indispensable the ingestion of F and that there were strong evidences that main effect of F to reduce caries would be topic. Thus, water

fluoridation was considered to be an excellent systemic way for the local effect of F, and not a systemic method of F use. In this concept if the population regularly brushed the teeth using F-dentifrice, an impact in terms of public health should be found and in the present this has been observed even in Brazil. On the other hand, there is also risk of dental fluorosis since young children swallow part of the dentifrice during toothbrushing.

Furthermore, besides the ingestion of F from water supply and dentifrice, other sources of systemic exposure have been identified: drugs, mineral water, infant formula, chewing gum, tea and beverage, which could contribute for the risks of fluorosis. However, although in Brazil since the year 2002 there is initiative to control other ingestion of F, very few can be done since according to Mercosur F is considered a micronutrient and the daily recommended ingestion (DRI) is 4.0 mg. Additionally, it is not mandatory to show in the label of the product the contribution of F for the DRI.

On the other hand, my concern is not only to guarantee the safety use of F but also to preserve its benefit reducing caries. However, according to Mercosur the maximum F concentration in dentifrice is 0.15% (1500 ppm) but in terms of total not soluble F. This means that is possible to sell a dentifrice in the Mercosur countries' containing 100% of insoluble F, so inactive against caries.

In conclusion: (1) It seems that the Dentistry was not represented in the decisions about the Mercosur; (2) If was we were not well represented and (3) something should be done.

## NL 4- SOURCES OF FLUORIDE INTAKE

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In the last years, due to the use of fluorides, there has been a reduction in the prevalence of dental caries, simultaneously with an increase in the prevalence of dental fluorosis, both in EME countries and non-EME countries. This increase in the prevalence of dental fluorosis is attributed to the excessive fluoride intake from all sources during the critical period of tooth formation.

There are many sources of fluoride available. Artificial fluoridation of public water supply is recognized among the ten best public preventive health measures in the last years, and does not contribute excessively to total fluoride intake, when well controlled. However, when fluoridated water is used to reconstitute foods and drinks, mainly infant formulas, as well as in food industries, it can contribute significantly to total fluoride intake. Regarding bottled water, most of them have low fluoride levels, but some brands have high fluoride levels, not adequately shown on their labels, which impairs the access of the general population to this information.

Another important source of fluoride intake is the fluoridated dentifrice. Fluoride ingestion from dentifrice ranges from 0 to 100% of the amount placed onto the toothbrush, and is inversely related to the age of the child. To minimize this ingestion, two measures have been recommended: to reduce the amount of dentifrice placed onto the toothbrush and/or to reduce the amount of fluoride incorporated in the dentifrices. In the case of reducing the amount of dentifrice placed onto the toothbrush, it must be considered that in most families, parents work and people who take care of the children may not follow the instructions given regarding the dosage of the dentifrice. By other hand, there is still controversy about the therapeutic efficacy of low fluoride dentifrices.

Infant formulas also have been reported among the sources of fluoride intake, especially soy-based formulas, since soy extract has higher fluoride levels. There are three kinds of infant formulas: ready-to-drink, powdered and concentrated liquid formulas. Ready-to-drink formulas usually do not provide large amounts of fluoride. However, formulas which have to be reconstituted can provide fluoride levels that can exceed the upper limit recommended, especially when reconstituted with fluoridated water.

Some market-basket studies done in Brazil have shown high fluoride levels in many industrialized foods and drinks, as well as in medicines chronically used by children. These sources could contribute significantly to their total daily fluoride intake. However, this information is not available on the product's labels. Thus it would be important the promulgation of a law concerning the maximum fluoride levels allowed in infant foods, drinks and medicines, as well as obliging the manufacturers to include the fluoride concentrations on the products' labels.

## NL 5- DENTAL FLUOROSIS AND PUBLIC HEALTH

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Among the preventive methods used in Public Health are those adjusted to population strategies, due to their impact on the population health levels. Dental caries prevalence has been declining all over the world, as well as in Brazil. This decline is largely attributed to the use of fluoride through public water supply and dentifrices (measures involving populations). The importance of public water fluoridation for the reduction on the dental caries levels is high, mainly when we consider that the impact of this measure is higher when social economic conditions are lower and the population does not have access to other preventive measures. Studies have been demonstrating that fluoridated water contributes to the reduction of the effects of social inequalities on caries experience.

However, despite the benefits on caries reduction and the risk for dental fluorosis are connected, in Public Health a low prevalence of mild forms of dental fluorosis is considered acceptable in relation to the significant protection caused by the ingestion of optimally fluoridated water. With the increase in the methods for the constant utilization of fluoride, mainly fluoridated dentifrices, clinical and public health professionals have focused their attention on a possible increase in the prevalence of dental fluorosis in the population. This has prompted to discussions regarding the necessity of control of fluoride levels, including the suspension of public water fluoridation. Thus, an important question becomes relevant: should dental fluorosis be considered a public health problem?

In this sense, we propose to analyze dental fluorosis in the light of the necessary conditions for that a disease is considered as a public health problem, as well as to establish its priority degree when compared to other diseases: a) the prevalence of the problem in a population; b) its seriousness, represented by the destructive effects on the individual or the community; c) the perception of the problem by the population, focusing on its impact on life quality; d) the susceptibility or availability of efficient methods for its control or prevention.