

R. Ferro\*, A. Besostri\*, M.R. Giuca\*\*,  
R. Docimo\*\*\*, R. Gatto\*\*\*\*, G. Marzo\*\*\*\*

\*Surgery Department, Dental Unit, Cittadella Hospital,  
Health District No 15 "Alta Padovana" (Padua, Italy)

\*\*Department of Surgical Pathology, Unit of Paediatric Dentistry,  
University of Pisa, Italy

\*\*\*Department of Paediatric Dentistry,  
University of Rome "Tor Vergata", Italy

\*\*\*\*Department of Life, Health and Environmental Sciences  
University of L'Aquila, Italy

e-mail: roberto.ferro@ulss15.pd.it

## The Italian perspective on fluoride intake in children and adolescents

### ABSTRACT

**Aim** This paper represents the outcome of the meetings of the Committee composed by Pedodontists (SIOI – Italian Society of Paediatric Dentistry) and Paediatricians (FIMP – Italian Association of Paediatricians) with the aim to share an evidence-based common approach in caries prevention during childhood and adolescence. The most important topic was an update on fluoride administration methods in order to minimise the risk of fluorosis and maximise its caries-preventive effect.

**Conclusion** The conclusions of this work are exposed in a synoptic table (Table 1).

**Keywords** Adolescents; Children; Fluoride; Guidelines.

### Introduction

The prevalence of dental caries is drastically declining in industrialised countries with a remarkable increase of caries-free children. This decrease has been observed in Italy as well, through periodical and epidemiological surveys carried out in the last 30 years [Ferro et al., 2007a,b].

Data from the last 2011 survey (unpublished data) confirm that 3 out of 4 preschool children (3, 4, 5 years

of age) in the district pertaining to the AULSS 15 (Veneto region, Italy) are caries free and that the dmft index in this population (n=1070) is similar ( $0.85 \pm 2.20$ ) to the one recorded in other European countries [Health in Europe: Information and Data interface, 2011]. These trends have a common denominator: topical fluoride.

More than 70 years ago Trandley Dean [1942] demonstrated a lower caries prevalence in geographical areas of the USA where drinkable water contained high concentration of fluoride. Three years later (1945) the US National Health Service started the first successful experiment of artificial fluoridation of drinkable water in the area of Grand Rapids, Michigan [Arnold and Knutson, 1953]. For many years scientists linked the fluoride cariostatic action with a "pre-eruptive effect", supposing that fluoride was to be ingested during amelogenesis for caries to be prevented. However the most recent studies, following the caries decline in children and adolescents in industrialised countries that had started in the 70's [Kalsbeek et al., 1993] concluded that the caries-preventive effect of fluoride is almost exclusively posteruptive [Bibby et al., 1955; Fejerskov et al., 1981; Carlos, 1983; Wefel, 1990; Leverett, 1991; Zero, 1992; Ekstrand et al., 1994; Bratthall, 1996; Locker, 1999; Formon et al., 2000; Featherstone, 2000; Centers for Diseases Control [CDC], 2001; Aoba and Fejerskov, 2002; Zimmer et al. 2003; Warren and Levy, 2003; Fejerskov, 2004; Hellwig and Lennon, 2004; Marthaler, 2004, European Commission, 2005; Pizzo et al., 2007; Cheng et al., 2007].

### How Fluoride acts

During caries formation, fluoride minerals and organic acids move through the enamel diffusion channels located amongst rod-like structures made of crystals of apatite-like material (especially hydroxyapatite).

Human first formed enamel contains impurities such as carbonate and magnesium that make it more soluble in acid than pure hydroxyapatite. Acid conditions in the mouth cause surface crystals to dissolve and reform and the first to dissolve are the most soluble ones. When fluoride ions are present, the surface crystals will reform without impurities. Carbonate and magnesium are replaced by phosphate, fluoride and calcium making new crystals of hydroxyapatite, fluorohydroxiapatite and fluoroapatite. All of these forms of enamel apatite are more acid resistant than the original carbonated apatite.

All this dissolving and reforming process is called post-eruptive maturation and continues as long as the tooth is in the mouth and in contact with saliva. This phenomenon probably explains the clinical observation that the longer a tooth remains in the mouth, the more resistant it becomes to caries formation.

Fluoride is stored in a plaque "reservoir" as calcium fluoride-like precipitates. Plaque fluid has higher fluoride levels than the saliva and like saliva it is also

supersaturated with calcium and phosphate. Fluoride accumulates in plaque from diet, fluoride toothpaste, fluoridated water, saliva and also from fluoride released from enamel during demineralisation. So, dental plaque acts as an intraoral reservoir for fluoride. When plaque becomes slightly acidic and before enamel starts to dissolve, fluoride ions are released from the calcium fluoride-like precipitates, thereby raising the amount of ionic fluoride in plaque fluid. This amount of fluoride works to inhibit bacterial growth, acid formation and enhance remineralisation.

The continuous use of daily low levels of fluoride is the key to fluoride effectiveness. Fluoride's incorporation into developing enamel is critical, but the continuing presence of fluoride ions at and in the enamel surface is the major factor in caries control [Buzalaf et al., 2011].

### *Toothpastes and other topical fluoride administration methods*

To work as a cariostatic agent fluoride must be in the right place (enamel-plaque interface), at the right time (during an acid attack) and in a sufficient amount (0.01-0.04 ppm) [CDC, 2001]. It is crucial to brush one's teeth twice a day with a fluoride toothpaste to achieve these conditions [Bloch-Zupan, 2001].

According to the directives of the European Union, the concentration of fluoride must not exceed 1,500 ppm [European Cosmetic Toiletry and Perfumery Association [COLIPA], 1995] and the most commonly used salts in toothpaste are: sodium fluoride, stannous fluoride, fluoridated amines and sodium monofluorophosphate.

Fluoride in toothpaste is effective [Marinho et al., 2003a] and harmless both for adults and children; an excessive intake can cause toxicity: acute (intoxication) or chronic (fluorosis).

Acute intoxication is very rare. As the toxic dose is 5mg/kg for a child of 10 kg it is 50 mg; this amount can be reached only after the ingestion of more than half a tube of a toothpaste (90 g) with a fluoride concentration of 1,000 ppm. Moreover scientific evidence recommends a careful parental control on the daily fluoride dose to be assumed by their children in the first three years of life in order to reduce the possibility of developing fluorotic lesions in the upper incisors [Bardsen, 1999; Hong et al., 2006a,b].

As children under 6 do not have a well-controlled swallowing reflex, toothpaste and fluoride are ingested: [Simard et al., 1991; Nacacche et al., 1992]; approximately 65% in 2-year-old children, 50% in 4-year-olds and about 343% in 5-year-olds [Benesty, 1999].

As the amount of ingested fluoride depends on the quantity of toothpaste, the most accredited international guidelines for the first years of life recommend a "smear" or a "pea-sized" to be applied on the toothbrush [American Academy of Pediatric Dentistry (AAPD), 2009, 2012; Australian Research Centre for Population

Oral Health, 2006; British Association for the Study of Community Dentistry (BASCD), 2009; British Society of Pediatric Dentistry, 2003; Canadian Dental Association, 2010; European Academy of Pediatric Dentistry, 2009; Irish Oral Dental Health Services Guideline Initiative, 2008; New Zealand Guidelines Group, 2009; Scottish Intercollegiate Guidelines Network, 2012; Scottish Dental Clinical Effectiveness Programme, 2010].

The minimum concentration of fluoride in toothpaste sufficient to prevent caries formation is 1,000 ppm [Ammari et al., 2003; Walsh et al., 2010]. Furthermore a recent RCT demonstrated that the preventive effect is maintained by an acidulated toothpaste (pH 4.5) with a fluoride concentration of 550 ppm [Vilhena et al., 2010].

Other than toothpastes, several methods of additional application of topical fluoride have been recognized as effective [American Dental Association, 2006; Marinho, 2003], including mouth rinses [Marinho, 2003b], gels [van Rijkorn, 1998; Marinho, 2002] and varnishes [Carvalho et al., 2010].

Mouth rinses have been used since the 1960s both in school health programs and individually; at schools, the average occurrence is one or two rinses per week and the most frequent formulation is sodium fluoride (230-900 ppm). A regular use of fluoride mouth rinses can reduce the formation of new carious lesions in children and adolescents [Marinho et al., 2003b].

Gels, which are used in professional and individual programmes (from the age of 7), contain high fluoride concentrations ( $\leq 12,000$  ppm); their efficacy have been widely demonstrated and the frequency of application can vary from 2 to 4 times per year, depending on the patient's age and risk level [Poulsen, 2009; American Dental Association, 2006].

Professional application of varnishes, with fluoride concentration between 7,000 and 56,300 ppm, are the most used products and they must be applied from 2 to 4 times per year; they are effective in both deciduous and permanent teeth [Marinho, 2002].

A combination of various methods to administer fluoride in a topical form, including daily usage of toothpastes, induces a slight decrease of carious lesions compared to using just toothpaste [Marinho, 2009].

Elwood [2008] classified the different methods of fluoride administration as follows.

- *Self-applied methods*, used at home: toothpastes, mouth rinses, gels (topical fluoride), tablets, drops and lozenges (topical + systemic fluoride).
- *Professional methods*, delivered by healthcare professionals: gels, varnishes (topical fluoride).
- *Community methods*, introduced on a population basis: water, milk and salt fluoridation (systemic fluoride). Fluoridation of drinkable water has never been done in Italy and, generally, with the only exception of some areas in Campania region, fluoride content in water is low. The evaluation

AGE	ALL	HIGH-RISK INDIVIDUALS
0-3 years	<ul style="list-style-type: none"> <li>» Daily oral hygiene provided or supervised by parents/tutors</li> <li>» "Smear-size" amount of toothpaste with a fluoride concentration of 1,000 ppm</li> <li>» Tooth-brushing twice a day since eruption of first primary tooth</li> <li>» Check the daily frequency and intake of sugared foods and beverages, particularly at night-time</li> <li>» "sugar-free" drugs if possible</li> </ul>	<ul style="list-style-type: none"> <li>» systemic fluoride (drops, tablets)</li> </ul>
3-6 years	<ul style="list-style-type: none"> <li>» regular dental check-ups</li> <li>» tooth-brushing supervised by parents/tutors</li> <li>» "pea-size" amount of toothpaste with a fluoride concentration of 1,000 ppm</li> <li>» Check the daily frequency and intake of sugary foods and beverages, particularly at night-time</li> <li>» "sugar-free" drugs if possible</li> </ul>	<ul style="list-style-type: none"> <li>» fluoride varnishes</li> </ul>
> 7 years	<ul style="list-style-type: none"> <li>» regular dental check-ups</li> <li>» dental floss ( from 14 years)</li> <li>» "pea-size" amount of toothpaste with a fluoride concentration of 1,000 ppm</li> </ul>	<ul style="list-style-type: none"> <li>» dental sealants</li> <li>» fluoride varnishes</li> <li>» fluoride gels (also self applied)</li> <li>» fluoride rinses</li> </ul>

TABLE 1 Caries prevention in children and adolescents.

- » Ammari et al. 2003.
- » American Academy of Paediatric Dentistry: Guideline on caries risk assessment and management for infants, children and adolescents. 2011.
- » American Dental Association: Dietary fluoride supplements: evidence-based clinical recommendations. 2010.
- » American Dental Association: Non fluoride caries preventive agents: evidence-based clinical recommendations, 2011.
- » British Association for the Study of Community Dentistry: Delivering better oral health. An evidence-based toolkit for prevention, 2009.
- » Scottish Dental Clinical Effectiveness Programme 2010: Drug prescribing for Dentistry, 2010
- » Scottish Intercollegiate Guidelines Network, 2005.

of fluoride ingestion through water is even more difficult due to the widespread habit of drinking bottled water with different ion concentrations. The same problem occurs with infant formula, as it is actually the concentration of fluoride in the water used in its production that affects the daily dose. The addition of sodium fluoride or calcium fluoride to salt (250 mg/kg) has given the same results of consumption of artificially fluoridated water [Gillespie and Roviralta, 1985]. Just like fluoridated water, also fluoridated salt represents an effective and low-cost method, with the advantage of being used individually and voluntarily, escaping from any ideological or political opposition.

### High-risk subjects and fluoride

Additional fluoride therapy (systemic and topical) should be targeted towards individuals at high caries risk, i.e. those with carious lesions or their consequences (conservative restoration).

Fluoride supplements in drops or tablet form are to be swallowed to be effective and are indicated exclusively in high-risk subjects or when an adequate amount cannot be ensured in any other way [Ismail, 2008; Rozier et al., 2010; Tubert-Jeannin et al., 2011].

In pregnant women administration of fluoride tablets has been demonstrated not to be effective in preventing the formation of carious lesion in their offspring [Leverett, 1997; Sa Roriz Fonteles, 2005].

Table 1 summarises the scientific evidence on caries prevention for childhood and adolescence based both on the literature and the most accredited international guidelines as provided in 2013 by the joined Committee composed by SIOI (the Italian Society of Pediatric Dentistry) and FIMP (Italian Association of Paediatricians).

## References

- » American Academy of Pediatric Dentistry (AAPD). Council on Clinical Affairs. Guideline on perinatal oral health care. Reference Manual, 2009:90-94.
- » American Academy of Paediatric Dentistry: Guideline on fluoride therapy. Reference Manual V34/no 6 2012/2013 (revised 2012) a:162-163.
- » American Academy of Paediatric Dentistry-Council on Clinical Affairs: Guideline on infant oral health care. Reference Manual V34/no 6 2012/2013 (revised 2012)b:132-136.
- » American Dental Association Council on Clinical Affairs: Professionally applied topical fluoride: evidence-based clinical recommendations. J Am Dent Assoc 2006; 137:1151- 1159.
- » Ammari AB, Bloch-Zupan A, Ashley PF: Systematic review of studies comparing 600 ppm fluoride or less with high fluoride toothpastes of 1.000 ppm or above. Caries Res, 2003; 37(2): 85-92.
- » Aoba T, Fejerskov O: Dental fluorosis: chemistry and biology. Critical reviews in oral biology and medicine, 2002;13(2):155-170.
- » Arnold FA, Knutson JW: Effect of fluoridated public water supplies on dental caries prevalence. Results of the seventh year of study at Gran Rapids-Muskegon. Mich Publ Health Rep, 1953;68:141-148.
- » Australian Research Centre for Population Oral Health: The use of fluorides in Australia: guidelines. Austr Dent J 2006; 51:195-199.
- » Bardsen A, Klock KS, Bjorvatn K: Dental fluorosis among persons exposed to high- and low-fluoride drinking water in western Norway. Community Dent Oral Epidemiol, 1999;27(4):259-267.
- » Benesty P, Fortier JP, Aldin P: Interets et risqué des dentrifrices fluores chez le jeune enfant. Le Chirurgien Dentiste de France, 1999;931:41-47.
- » Bibby BG, Wilkins E, Witol E: A Preliminary study of the effects of fluoride lozenges and pills on dental caries. Oral Surg Oral Med Oral Pathol, 1955;8:213-216.
- » Bloch-Zupan A: Is the fluoride concentration limit of 1,500 ppm in cosmetics (EU guideline) still up-to-date? Caries Res, 2001;35(suppl1):22-25.
- » Bratthall D, Petersson GH, Sundberg H: Reasons for the caries decline: what do the experts believe? Eur J Oral Sci, 1996;104:416-422.
- » British Association for the Study of Community Dentistry (BASCD): Delivering better oral health. An evidence-based toolkit for prevention. 2nd edition. April 2009.
- » British Society of Paediatric Dentistry: A policy document on oral health care in preschool children. Int J Paediatr Dent 2003; 13:279-285.
- » Buzalaf MAR, Pessan JP, Honorio HM, ten Cate JM: Mechanisms of action of fluoride for caries control. Fluoride and the oral environment. Monographs in Oral Science vol.22- MAR Buzalaf Ed - Karger, 2011.
- » Canadian Dental Association position on: Use of fluorides in caries prevention. Revised April 2010-website last accessed September 25th 2013.
- » Carlos JP: Comments on fluoride. J Pedodontics Winter, 1983;135-136.
- » \*Carvalho DM, Salazar M, Oliveira BH, Coutinho ES: Fluoride varnishes and

- decrease in caries incidence in preschool children: a systematic review. *Revista Brasileira de Epidemiologia*, 2010;13(1): 139-149.
- › Centers for Diseases Control: Recommendations for using fluoride to prevent and control dental caries in the United States. *MMWR* 2001;50: 1-42.
  - › Cheng KK, Chalmers I, Sheldon TA: Adding fluoride to water supplies. *Br Med J*,2007;335(7622):699-702.
  - › Dean HT, Arnold FA jr, Evolve E: Domestic water and dental caries V. Additional studies of the relation of fluoride domestic waters to dental caries experience in 4425 white children aged 12-14 years of 13 cities in 4 states. *Publ Health Rep*, 1942;57:1155-1179.
  - › Ekstrand J, Formon SJ, Ziegler EE, Nelson SE: Fluoride pharmacokinetics in infancy. *Pediatr Res*, 1994;35:157-163.
  - › Elwood RP, Fejerskov O, Cury JA, Carlkson B . Fluoride in caries control; in Fejerskov O, Kidd EAM (eds): *Dental caries: The disease and its clinical management*, ed 2. Oxford, Blackwell & Munksgaard,2008;287-323.
  - › European Academy of Paediatric Dentistry: Guidelines on the use of fluoride in children: an EAPD policy document. *Eur Arch Paediatr Dent* 2009; 10(3):129-135.
  - › European Commission - General Scientific Committee on Consumer Products: The safety of fluorine compounds in oral hygiene products for children under the age of 6 years. 2005,sept 20.
  - › European Cosmetic Toiletry and Perfumery Association (COLIPA): The cosmetic directive of the European Union. In Dupuis J(ed),1995:Dir 76/768/EEC.
  - › Featherstone JDB: The science and practice of caries prevention. *J Am Dent Assoc*,2000;131:887-899.
  - › Fejerskov O, Thylstrup A, Larsen MJ: Rational use of fluorides in caries prevention: a concept based on possible cariostatic mechanisms. *Acta Odontol Scand*, 1981;39:241-249.
  - › Fejerskov O: Changing paradigms in concepts on dental caries: consequences for oral health care. *Caries Res* 2004; 38:182-191.
  - › Ferro R., Besostri A, Meneghetti B, Stellini E: Current severity of dental caries in 5- and 12year old children in the Veneto Region (Italy) . *Community Dent Health* 2007a; 24:88-92.
  - › Ferro R, Besostri A, Olivieri A, Stellini E, Mazzoleni S: Preschoolers' dental caries experience and its trend over 20 years in a North East Italian Health District. *Eur J Paediatr Dent* 2007b; 4:199-202.
  - › Formon SJ, Ekstrand J, Ziegler E: Fluoride intake and prevalence of dental fluorosis: trends in fluoride intake with special attention to infants. *J Publ Health Dent*,2000;60:131-139.
  - › Gillespie GM, Roviralta G (Eds): *Salt fluoridation*. Scientific Publication no.501 Pan American Health Organization (WHO-AMRO), Washington D.C.,1985.
  - › Health in Europe: Information and Data Interface (HEIDI): Dental caries in Europe. European Commission website last accessed 07.09.2013.
  - › Hellwig E, Lennon AM: Systemic versus topical fluoride. *Caries Res*,2004;38:258-262.
  - › Hong L, Levy SM, Broffitt B, Warren JJ, Kanellis MJ, Wefel JS, Dawson D: Timing of fluoride intake in relation to development of fluorosis on maxillary central incisors. *Community Dent Oral Epidemiol* 2006a;34:299-309.
  - › Hong L, Levy SM, Warren JJ, Broffitt B, Cavanaugh J: Fluoride intake levels in relation to fluorosis development in permanent maxillary central incisors and first molars. *Caries Res*, 2006b;40:494-500.
  - › Irish Oral Health Services Guideline Initiative. *Topical Fluorides: Evidence-based guidance on the use of topical fluorides for caries prevention in children and adolescents in Ireland*. 2008.
  - › \*Ismail AI, Hasson H: Fluoride supplements, dental caries and fluorosis: a systematic review. *J Am Dent Assoc* 2008;139(11):1457-1468.
  - › Kalsbeek H, Kwant GW, Groenoveld A: Caries experience of 15-year-old children in the Netherlands after discontinuation of water fluoridation. *Caries Res*, 1993;27:201-205.
  - › Leverett DH: Appropriate use of systemic fluoride: considerations for the 90's. *J Publ Health Dent*,1991;51:42-47.
  - › Leverett DH, Adair SM, Vaughan BW, Proskin HM, Moss ME: Randomised clinical trial of the effect of prenatal fluoride supplements in preventing dental caries. *Caries Res* 1997; 31:174-179.
  - › Locker D: benefits and risks of water fluoridation. An update of the 1996 Federal- Provincial Sub Committee Report,1999. Prepared for Ontario Ministry of Health and Long Term Care.
  - › \*Marinho VCC, Higgins JPT, Logan S, Sheiham A: Fluoride gels for preventing dental caries in children and adolescents (Review). *Cochrane Database of Systematic Reviews* 2002, Issue 1. Art.no. CD002280 republished online in 2009.
  - › \*Marinho VCC, Higgins JPT, Logan S, Sheiham A: Topical fluoride (toothpastes,mouthrinses,gels or varnishes) for preventing dental caries in children and adolescents. *Cochrane Database of Systematic Reviews*,2003b. issue 4 Art.no.: CD002782.
  - › \*Marinho VCC, Higgins JPT, Logan S, Sheiham A: Fluoride varnishes for preventing dental caries in children and adolescents (Review). *Cochrane Database of Systematic Reviews* 2002, Issue 1 Art.no.CD002279 republished online in 2009.
  - › Marinho VCC, Higgins JPT, Logan S, Sheiham A: Fluoride mouthrinses for preventing dental caries in children and adolescents (Review). *Cochrane Database of Systematic Reviews* 2003c, Issue 3. Art.no. CD002284 republished online in 2009.
  - › \*Marinho VCC, Higgins JPT, Logan S, Sheiham A: Fluoride toothpastes for preventing dental caries in children and adolescents (Review). *Cochrane Database of Systematic Reviews* 2003, Issue 1 Art. no. CD002278 republished online in 2009.
  - › Marinho VCC, Higgins JPT, Sheiham A, Logan S: Combination of topical fluoride (toothpastes, mouthrinses, gels, varnishes) versus single topical fluoride for preventing dental caries in children and adolescents. *Cochrane Database of Systematic Reviews* 2004, Issue 1 Art.no. CD002781. republished online in 2009.
  - › Marinho VCC, Higgins JPT, Sheiham A, Logan S: One topical fluoride (toothpastes or mouthrinses or gels or varnishes) versus another for preventing dental caries in children and adolescents (Review). *Cochrane Database of Systematic Reviews* 2004, Issue 1. Art.no. CD2780. republished online in 2009.
  - › Marthaler TM: Changes in dental caries 1953-2003. *Caries Res*,2004;38:173-181.
  - › Nacacche H, Simard PL, Trahan L: Factors affecting the ingestion of fluoride dentifrice by children. *J Publ Health Dent*,1992;52:222-226.
  - › New Zealand Guidelines Group. *Guidelines for the use of fluorides*. Wellington: New Zealand Ministry of Health; 2009.
  - › Pizzo G, Piscopo MR, Pizzo I, Giuliana G: Community water fluoridation and caries prevention: a critical review. *Clin Oral Invest*,2007;11(3):189-193.
  - › Poulsen S: Fluoride-containing gels, mouth rinses and varnishes: an update of evidence of efficacy. *Eur Arch Paediatr Dent*,2009;10(3):157-161.
  - › Rozier RG, Adair S, Graham F, Iafolla T, Kingman A, Kohn W, Krol J, Levy S, Pollick H, Whitford G, Strock S, Frantsve-Hawley J, Aravamudhan K, Meyer D M: Evidence based clinical recommendations on the Prescription of Dietary Fluoride Supplements for Caries Prevention: A Report of the American Dental Association Council on Scientific Affairs *JADA* 2010; 141(12):1480-1489.
  - › Sà Roriz Fonteles C, Zero DT, Moss ME, Fu J: Fluoride concentration in enamel and dentin of primary teeth after pre- and postnatal fluoride exposure. *Caries Res* 2005;39:505-508.
  - › Scottish Intercollegiate Guidelines Network. *Prevention and management of dental decay in the preschool child*. November 2005. [www.sign.ac.uk](http://www.sign.ac.uk) last accessed 05/21/2012.
  - › Scottish Dental Clinical Effectiveness Programme: *Prevention and management of dental caries in children*. Dental Clinical Guidance. (april 2010) [www.scottishdental.org/cep](http://www.scottishdental.org/cep)
  - › Simard PL, Nacacche H, Lachapelle D, Brodeur JM: Ingestion of fluoride from dentifrices by children aged 12 to 24 months. *Clin Pediatr*, 1991;30:614-617.
  - › \*Tubert-Jeannin S, Auclair C, Amsallem E, Tramin P, Gerbaud L, Ruffieux C, Schulte AG, Koch MJ, Rège-Walther M, Ismail A: Fluoride supplements (tablets, drops, lozenges or chewing-gums) for preventing dental caries in children (Review). *Cochrane Database of Systematic Reviews* 2011, Issue 12. Art. No. CD 0075992.
  - › \*van Rijkorn HM, Truin GJ, van't Hof MA: A meta-analysis of clinical studies on the caries-inhibiting effect of fluoride gel treatment. *Caries Res*,1998; 32(2):83-92.
  - › Vilhena FV, Olympio KPK, Lauris JRP, Delbem ACB, Buzalaf MAR: Low fluoride acidic dentifrice: a randomized clinical trial in a fluoridated area. *Caries Res*, 2010;44(5):478-484.
  - › \*Walsh T, Worthington HV, Glenny AM, Appelbe P, Marinho VCC, Shi X: Fluoride toothpastes of different concentrations for preventing dental caries in children and adolescents. *Cochrane Database of Systematic Reviews* 2010, Issue 1 . Art. no.CD007868.
  - › Warren JJ, Levy SM: Current and future role of fluoride in nutrition. *Dent Clin of North America*,2003;35:390-391.
  - › Wefel JS: Effects of fluoride on caries development and progression using intra-oral models. *J Dent Res*,1990;69(Spec No):626-633.
  - › Zero DT: Fluoride concentrations in plaque, whole saliva and ductal saliva after application of home-use topical fluoride. *J Dent Res*,1992;71:1768-1775.
  - › Zimmer S, Jahn KR, Berthel CR: Recommendations for the use of fluoride in caries prevention. *Oral Health and Preventive Dent*,2003;1:45-51.
  - › \*Systematic reviews assessed in the database "Health Evidence" – Canadian Institutes of Health Research - web site last accessed 23.09.2013.