ABSTRACTS

ETHICS

WHAT DOES THE PRECAUTIONARY PRINCIPLE MEAN FOR EVIDENCE-BASED DENTISTRY?

Today there is increased recognition of the importance of the "precautionary principle" as applied to health care practices undertaken in the face of uncertain information about risks. Its purpose is to provide a compass for making better and more informed health care decisions. Its application requires broad thinking about potential adverse health effects, taking an interdisciplinary approach to science and science policy, and examining a wide range of alternatives to what might be potentially harmful procedures. Although often criticized as antiscientific, the precautionary principle challenges scientists and health-care professionals to be more explicit about overcoming uncertainties and to develop more effective tools for characterizing and preventing adverse health risks. How in various ways these challenges might be successfully met is a main focus of this article. In regard to dental practice, the role and application of the precautionary principle to water fluoridation and to amalgam fillings are considered in relation to their potential risk-benefit trade-offs.

Since its inception after World War II, water fluoridation has been promoted as a safe and effective way of preventing tooth decay. Nevertheless, over the years, various contradictory findings reported by reputable investigators have raised concerns about the safety and efficacy of the practice. A precautionary approach requires that these studies be carefully examined and weighed, not only for what they reveal about the limitations of fluoridation for reducing dental caries and creating adverse health effects, but also whether more effective reduction in cavities can be achieved through less potentially harmful means, such as better dental hygiene, strictly topical use of fluoride, and appropriate dietary interventions.

The second topic, the use of mercury amalgams for dental restorations, although long considered safe according to the American Dental Association, has come under increasing concern because of newer findings about the potential toxic hazards of mercury vapor released from amalgam fillings. The amount of mercury released is more than previously estimated and is in the range of known long-term toxicity. Here again, the precautionary principle urges that alternatives to amalgam fillings deserve more emphasis, as is now happening.

In conclusion, the precautionary principle is not at odds with but is entirely consistent with good public health policy. The justifiably laudable goal of having unequivocal evidence before taking action must be balanced by the importance of preventing illness and injury even in the face of ongoing uncertainties.

Authors: Tickner J, Coffin M.
Correspondence: Department of Community Health and Sustainability, University of Massachusetts at Lowell, Lowell, MA, USA. E-mail: Joel_Tickner@uml.edu
Keywords: Amalgam safety; Dental practice; Fluoride use and risks; Precautionary principle; Public health policy; Science-based decisions.
Source: J Evid Base Dent Pract 2006;6:6-15.

ENVIRONMENTAL ASSESSMENT

A HEALTH RISK ASSESSMENT FOR FLUORIDE IN CENTRAL EUROPE

In Central Europe, groundwater resources that exceed the World Health Organization guideline value of 1.5 mg F/L are widespread, and adverse effects of high-fluoride water on health have been reported. The aim of this project was to develop a geographic information system (GIS) to aid identification of areas where high-fluoride waters and fluorosis may be a problem; hence, where water treatment technologies should be targeted. The development of the GIS was based upon collation and digitization of existing information relevant to fluoride

risk in Ukraine, Moldova, Hungary, and Slovakia, assembled here for the first time in readily accessible form. In addition, geochemistry and health studies to examine relationships in more detail between high-fluoride drinking waters and health effects in the population were carried out in Moldova and Ukraine, where dental fluorosis prevalence rates of 60-90% in adolescents consuming water containing 2–7 mg F/L are found.

Authors: Fordyce FM, Vrana K, Zhovinsky E, Povoroznuk V, Toth G, Hope BC, Iljinsky U, Baker J.
Correspondence: FM Fordyce and BC Hope, British Geological Survey, West Mains Road, Edinburgh EH9 3LA, UK; E-mail: fmf@bgs.ac.uk
Keywords: Dental fluorosis; Fluoride risk assessment; Fluoride water; Geographic information system (GIS); Hungary; Moldova; Slovakia; Ukraine.
Source: Environ Geochem Health 2007;29(2):83-102.

Fluoride in the Environment

FLUORIDE OCCURRENCE IN PUBLICLY SUPPLIED DRINKING WATER IN ESTONIA

A total of 735 water samples from public water systems in Estonia serving 100 or more residents was analyzed for fluoride (F) using the SPADNS method. In order to specify the natural source of F, the chemical composition of the water of five aquifer systems utilized for water supply were included in the study. Tap water F concentrations ranged from 0.01 to 6.95 mg/L with F levels above 1.5 mg/L in nearly one-sixth of the samples and 41.6% below 0.5 mg/L. In southern Estonia, where a terrigenous Middle-Devonian aquifer system is exploited, the F concentration of most of the tap water is less than 0.5 mg/L, possibly promoting susceptibility to dental caries. In the western part of the country, groundwater used for drinking purposes originates from Ordovician and Silurian carbonate rocks. This water has a high F content of 1.5–6.95 mg/L associated with the abstraction depth, wherein the main controlling factors for dissolved F are the pH and the chemical composition of the of water.

Authors: Karro E, Indermitte E, Saava A, Haemer K, Marandi A.
Correspondence: Enn Karro, Institute of Geology, University of Tartu, Vanemuise 46, 51014 Tartu, Estonia; E-mail: enn.karro@ut.ee
Keywords: Estonia; Fluoride water; Groundwater; Public water supply.
Source: Environ Geol 2006;50(3):389-96.

Dental Effects

RELATIONSHIP BETWEEN DENTAL CARIES EXPERIENCE (DMFS) AND DENTAL FLUOROSIS IN 12-YEAR-OLD PUERTO RICANS

Objectives: To examine the relationship between DMFS (decayed, missing, and filled surfaces of permanent teeth) and the community fluorosis index (CFI) scores and between individual DMFS and NIDR (National Institute of Dental Research)/Dean Index fluorosis scores. *Design:* A population-based, cross-sectional study. *Setting:* Public and private schools of Puerto Rico. *Subjects:* 1,435 students age 12. *Method:* A probabilistic stratified sample was selected from 11 regions of Puerto Rico according to the type of school (public and private) and setting (urban and rural). Children were examined using NIDR criteria for DMFS and dental fluorosis. Regression analysis was used to determine the relationship between DMFS means and CFI scores. Individual level DMFS was regressed on NIDR/Dean Index scores to test for linear and deviation from linear relationships. *Results:* There was no statistically significant relationship between regional DMFS and CFI scores and between individual level fluorosis scores when dichotomized as 0–2 as the referent level. However, the referent level of 3–4 showed a statistically significant higher DMFS with increasing levels of fluorosis. Gender and school setting were statistically significant in all models: females and public school attendance were associated with increased DMFS. *Conclusion:* No ecological relationship between CFI and DMFS scores was found in 12-year-old children in Puerto Rico. Moderate and severe fluorosis was, however, associated with higher DMFS levels relative to lower

fluorosis scores, though this finding may be associated with restorations placed for cosmetic reasons. While controlling severe fluorosis is desirable, this will have little impact on overall high caries in Puerto Rican children. These findings suggest caution when interpreting caries experience using the DMFS index in populations with differing fluorosis levels.

Authors: Elías-Bonita AR, Psoter W, Elías-Viera AE, Jiménez P, Toro C.
Correspondence: Prof Augusto R. Elías-Bonita, DMD, MSD, University of Puerto Rico Medical Sciences Campus, School of Dentistry Research Center, PO Box 365067, San Juan, Puerto Rico 00936-5067; E-mail: aelias@rcm.upr.edu
Keywords: Community fluorosis index (CFI); Dean index of fluorosis; Dental caries; DMFS; Puerto Rican children.
Source: Community Dent Health 2006;23:244-50.

CARIES AND FLUOROSIS IN 6- AND 9-YEAR-OLD CHILDREN RESIDING IN THREE COMMUNITIES IN IRAN

OBJECTIVES: The aim of this study was to investigate the caries and fluorosis prevalence among 6- and 9-year-old students in three communities in Iran with varying urbanization and fluoride in piped water. METHODS: Data were obtained from 523 dental examinations of 6- and 9-year olds in an upper middle class district in Teheran (T) (0.3 mg F/l), the city of Semnan (S) (1.3 mg F/l), and the village of Dibaj (D) (0.2 mg F/l). RESULTS: Children in the naturally fluoridated city of Semnan showed slightly higher dmfs/dfs (SD) scores for both 6-year olds [S: 9.1 (9.2), T: 7.2 (7.4), D: 7.1 (6.1)] and 9-year olds [S: 6.0 (6.2), T: 4.4 (4.2), D: 5.0 (4.7)], whereas the mean dmft/dft scores as well as the numbers of caries-free children were comparable. A lower prevalence of dental restorations was reported for both Semnan and Dibaj compared with Teheran. A higher prevalence of fluorosis [Tooth Surface Index of Dental Fluorosis (TSIF) 3-7] was observed in the naturally fluoridated city of Semnan compared with the low-fluoridated communities. CONCLUSIONS: The ingestion of naturally fluoridated water (1.3 mg F/l) seemed to have a negligible effect on caries prevalence, but resulted in higher prevalence of dental fluorosis. It is emphasized that the study population was not adjusted for socioeconomic status, availability of dental care nor for exposures to other sources of fluoride. Nevertheless, it can be concluded that caries prevalence in Iran is quite low compared with that in other countries in the Middle East and that the elevated fluoride levels in the drinking water in Semnan may contribute to the development of mild to severe fluorosis.

Authors: Meyer-Lueckel H; Paris S; Shirkhani B; Hopfenmuller W; Kielbassa A M
Correspondence: Hendrik Meyer-Lueckel, Department of Operative Dentistry and Periodontology, School of Dental Medicine, Charite - Universitatsmedizin Berlin, Germany; Email: hendrik.meyer-lueckel@charite.de
Source: Community Dent Oral Epidemiol 2006;34(1):63-70.

FLUORIDE INTAKE FROM FOOD AND LIQUID IN JAPANESE CHILDREN LIVING IN TWO AREAS WITH DIFFERENT FLUORIDECONCENTRATIONS IN THE WATER SUPPLY

The purpose of this study was to estimate the average daily amount of fluoride from the diet ingested by Japanese children of ages susceptible to dental fluorosis in two areas with different fluoride concentrations in the water supply. Thirty-eight children aged 2–8 years participated in a survey of fluoride intake. Twenty-one out of 38 children lived in an area in which the community water fluoride concentration averaged 0.555 ppm (moderate fluoride area: MFA), and 17 lived in a low fluoride area (LFA), with F ranging between 0.040 and 0.131 ppm. To measure the fluoride intake, diets were collected with a duplicate-diet technique. The fluoride concentrations in each sample were measured using the diffusion technique of Taves and the F ion selective electrode. Meanwhile, after clinical examinations for dental caries and fluorosis, 228 subjects aged 13-15 years were selected for analysis from the same communities. The mean DMFT in the MFA was significantly lower than that in the LFA. The severest grade of dental fluorosis observed was “very mild” according to Dean's fluorosis index in both areas. The total daily fluoride intakes were 0.0252-0.0254 mg F/kg/day in the MFA and 0.0126-0.0144 mg F/kg/day in the LFA. Differences in the fluoride concentration of drinking water in this study were reflected in the fluoride intake from the diet in a typical Japanese diet.

Fluoride 40(1)69–74
January-March 2007

Authors: Nohno K, Sakuma S, Koga H; Nishimuta M, Yagi M, Miyazaki H.
Correspondence: K Nohno, Department of Oral Health Science, Graduate School of Medical and Dental Sciences, Niigata University, Gakkocho-Dori, Niigata, Japan. Email: no2@dent.niigata-u.ac.jp
Keywords: Dental fluorosis; Dental caries; Dietary fluoride; Fluoride intake; Japanese children; Japanese diet.
Source: Caries Res 2006;40(6):487-93.

Editor's Note: In view of the well-known slower eruption rates of permanent teeth in young children exposed to higher levels of fluoride intake, this report of a significantly lower mean DMFT (decayed, missing, filled permanent teeth) in the moderate fluoride area than in the low fluoride area may also reflect the presence of fewer erupted permanent teeth at a given child's age for DMFT comparison.

HEALTH/TOXIC EFFECTS IN ANIMALS

EFFECT OF FLUORIDE INTOXICATION ON ENDOMETRIAL APOPTOSIS AND LIPID PEROXIDATION IN RATS: ROLE OF VITAMINS E AND C

A study was made of the effect of fluoride (F) intoxication on lipid peroxidation in endometrial tissue and the protective effects of combinations of vitamins E and C in rats. In addition, apoptotic changes in endometrial tissue were also examined. The experimental groups were: a control group; a group treated with 100 mg F/L (F group); and a group treated with 100 mg F/L (F plus vitamins E and C (F + Vit group). The F and F + Vit groups were treated orally with fluoride for 30 days. Vitamins E and C were injected simultaneously at doses of 50 mg/kg day by mouth and 20 mg/kg day body wt intraperitoneally, respectively. Extensive DNA strand breaks, the typical biochemical feature of apoptosis, were detected with the use of the terminal deoxynucleotidyl transferase (TdT)-mediated dUTP-biotin nick and labeling (TUNEL) method. Elevated malondialdehyde (MDA) levels in the uterine tissue revealed a significant increase in lipid peroxidation in the F group compared with the controls ($p<0.05$). Vitamins E and C significantly reduced the F-induced lipid peroxidation in the F + Vit group compared with the F group ($p<0.05$). Diffuse apoptosis in glandular epithelium and stromal cells was found in endometrial tissues of F treated rats by the TUNEL method. The severity of these lesions was reduced by administration of vitamins E and C. These results indicate that subchronic administration of F causes endometrial apoptosis and that lipid peroxidation may be a molecular mechanism involved in F-induced toxicity. Furthermore, treatment with a combination of vitamins E and C reduced endometrial apoptosis caused by F.

Authors: Güney M, Oral B, Take G, Giray SG, Mungan, T.
Correspondence: Mehmet Güney, Department of Obstetrics and Gynecology, Faculty of Medicine, Suleyman Demirel University, Isparta, Turkey. E-mail: mguney@med.sdu.edu.tr
Keywords: Endometrial apoptosis; Fluoride intoxication; Lipid peroxidation; Rat endometrial tissue; Vitamins E and C.
Source: Toxicology 2007;231(2-3):215-23.

HEALTH/BIOLOGICAL EFFECTS IN ANIMALS

SODIUM FLUOROACETATE POISONING (REVIEW)

Sodium fluoroacetate was introduced as a rodenticide in the US in 1946. However, its considerable efficacy against target species is offset by comparable toxicity to other mammals and, to a lesser extent, to birds; and its use as a general rodenticide was therefore severely curtailed by 1990. Currently, sodium fluoroacetate is licensed in the US for use against coyotes, which prey on sheep and goats, and in Australia and New Zealand for eliminating unwanted introduced species. The extreme toxicity of fluoroacetate to mammals and insects stems from its similarity to acetate, which has a pivotal role in cellular metabolism. Fluoroacetate combines with coenzyme A (CoA-SH) to form fluoroacetyl CoA, which can

substitute for acetyl CoA in the tricarboxylic acid cycle and reacts with citrate synthase to produce fluorocitrate, a metabolite of which then binds very tightly to aconitase, thereby halting the cycle. Many of the features of fluoroacetate poisoning are, therefore, largely direct and indirect consequences of impaired oxidative metabolism. Energy production is reduced and intermediates of the tricarboxylic acid cycle subsequent to citrate are depleted. Among these is oxoglutarate, a precursor of glutamate, which is not only an excitatory neurotransmitter in the CNS but is also required for efficient removal of ammonia via the urea cycle. Increased ammonia concentrations may contribute to the incidence of seizures. Glutamate is also required for glutamine synthesis and glutamine depletion has been observed in the brain of fluoroacetate-poisoned rodents. Reduced cellular oxidative metabolism contributes to a lactic acidosis. Inability to oxidise fatty acids via the tricarboxylic acid cycle leads to ketone body accumulation and worsening acidosis. Adenosine triphosphate (ATP) depletion results in inhibition of high energy-consuming reactions such as gluconeogenesis. Fluoroacetate poisoning is associated with citrate accumulation in several tissues, including the brain.

Fluoride liberated from fluoroacetate, citrate, and fluorocitrate is a calcium chelator, and there are both animal and clinical data to support hypocalcaemia as a mechanism of fluoroacetate toxicity. However, the available evidence suggests the fluoride component does not contribute. Acute poisoning with sodium fluoroacetate is uncommon. Ingestion is the major route by which poisoning occurs. Nausea, vomiting and abdominal pain are common within 1 hr of ingestion. Sweating, apprehension, confusion, and agitation follow. Both supraventricular and ventricular arrhythmias have been reported, and nonspecific ST- and T-wave changes are common, the QTc may be prolonged and hypotension may develop. Seizures are the main neurological feature. Coma may persist for several days. Although several possible antidotes have been investigated, they are of unproven value in humans. The immediate, and probably only, management of fluoroacetate poisoning is therefore supportive, including the correction of hypocalcaemia.

Authors: Proudfoot AT, Bradberry SM, Vale JA.
Correspondence: Alex T Proudfoot, National Poisons Information Service (Birmingham Centre), City Hospital, Birmingham, UK.
Keywords: Citric acid cycle; Fluoroacetate poisoning; Rodenticide; Sodium fluoroacetate.
Source: Toxicol Reviews 2006;25(4):213-9.

SODIUM FLUORIDE INGESTION INDUCED OXIDATIVE STRESS IN BUCCAL MUCOSA OF RATS

Effects of NaF on buccal mucosa from female and male rats were examined. The animals were divided by gender into three groups (15 rats/group): a) control group, b) group that received 1 ppm of NaF added to drinking water, and c) group that received 50 ppm of NaF added to drinking water. After one week five rats from each group were sacrificed weekly, and buccal mucosa was isolated. Malondialdehyde (MDA) and the activity of the antioxidant enzymes superoxide dismutase (SOD) and catalase were determined. Although none of the animals presented signs of fluoride intoxication, buccal mucosa from both the female and male rats showed a significant increase in MDA concentration after four weeks of treatment with 50 ppm of NaF. This latter dose of NaF significantly increased the activity of catalase and SOD after two weeks of treatment in both genders of the rats. The treatment with NaF produces changes in the buccal mucosa indicatives of an oxidative stress.

Authors: Gutierrez-Salinas J, Morales-Gonzalez JA.
Correspondence: Jose Gutierrez-Salinas, Laboratorio de Bioquimica y Medicina Experimental, Division de Investigacion Biomedica, ISSSTE Centro Medico Nacional, Mexico City, Mexico.
Keywords: Anti-oxidant enzymes; Buccal mucosa; Oxidative stress; Rat buccal mucosa.
Source: Revista Mexicana de Ciencias Farmaceuticas 2006;37(3):11-22. [in Spanish].

HEALTH /BIOLOGICAL EFFECTS IN HUMANS

STRUCTURAL FORMS OF FLUORIDES IN BONE TISSUE OF ANIMALS UNDER CHRONIC FLUORIDE INTOXICATION

High-resolution solid-state ^{19}F NMR was used to examine the chemical structural forms of fluorine introduced into the bone tissue of Wistar rats exposed for 30 days to fluoride inhalation. Three structural forms of F were found to be deposited in the bone tissue: a solid phase of F-apatite and mobile nanoparticles of CaF_2 and MgF_2 (or $KMgF_3$) with a concentration ratio of approximately 2:2:1. Afterward, during 30 days of rehabilitation, this ratio remained constant, but the total F content in the bone tissue decreased approximately by one-third, and the F-apatite phase was transformed into disordered fluoro- and hydroxyapatite. A protective effect of the zeolitic enterosorbent (clinoptilolite) on F binding in the intoxication process apparently occurred, as well as a promotional effect of this enterosorbent on F excretion during the post-fluoride rehabilitation.

Authors: Gabuda SP, Gaidash AA, Kozlova SG, Allan NL.
Correspondence: SP Gabuda, A V Nikolaev Institute of Inorganic Chemistry, Siberian Division, Russian Academy of Sciences, Novosibirsk, Russia.
Keywords: Bone fluoride; ^{19}F NMR; Fluoride intoxication; Fluoride structures in bone; Rat bone.
Source: J Structural Chem 2006;47(2):258-66.

EXPERIMENTAL STUDIES OF THE PATHOGENESIS OF CHRONIC FLUORIDE INTOXICATION

Studies are presented of the pathogenesis of occupational fluorosis based on an experimental model of chronic fluoride intoxication (CFI). In early stages of CFI, fluoride and calcium in the body are in a compensatory relationship. Later, they are disturbed. The high ionic reactivity of fluoride in CFI is associated with hypocalcemia that triggers parathyroid hyperactivity. This results in hyperproduction of PTH, which is unrelated to the development of secondary hyperparathyrosis. CFI is also accompanied by elevated calcitonin having a hypocalcemic and hypophosphatemic action. The experiments revealed doubling of the content of collagen fragments of bone tissue in urine of animals with CFI thereby reflecting resorption of bone tissue. Serum osteocalcin increased three-fold as it was unable to be included in the bone tissue. There was also activation of lipid peroxidation in subnormal activity of respiratory enzymes.

Authors: Mikhailova NN, Anokhina AS, Ulanova EV, Fomenko DV, Kizichenko NV.
Correspondence: NN Mikhailova, Lab. Eksp. Gig. Issled. GU NII Kompleksnykh Problem Gig. Profzabol., SO RAMN, Novokuznetsk, Russia.
Keywords: Chronic fluoride intoxication; Hyperparathyrosis; Hypocalcemia; Lipid peroxidation; Osteocalcin.
Source: Patol Fiziol Eksp Ter 2006;(3):19-21. [in Russian].

CORRECTION

Effect of fluoride on growth and feed intake of juvenile giant freshwater prawn *Machrobrachium rosenbergii (De-man)* by S Adhikari, Ajaz Ahmad Naqvi, and N Sarangi in Fluoride 2006;39(4):313-7.

The formula for calculating weight gain percentages, p. 315, should have had D as the denominator rather than C. The correct formula was $(C - D) \times 100/D$, where C was the final weight (g), and D was the initial weight (g).