

# Gene-environment relationships in dento-alveolar complex: The tooth as an early marker of exposure to environmental pollutants

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#### Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010

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Mild Fluorosis





Undefined hypomineralization

Caries on MIH

MIH, fluorosis, caries are the most common environmental enamel defects

	Prevalence (	both sexes)	Male prevale	ence	Female prev	alence
	Total (thousands)	Proportion of population (%)	Total (thousands)	Proportion of population (%)	Total (thousands)	Proportion of population (%
Dental caries of permanent teeth	2 431 636	35-29%	1194051	34.37%	1237585	36-23%
Tension-type headache	1431067	20.77%	655 937	18.88%	775131	22-69%
Migraine	1012944	14.70%	371072	10.68%	641873	18.79%
Fungal skin diseases	985 457	14-30%	516167	14.86%	469291	13.74%
Other skin and subcutaneous diseases	803 597	11.66%	417129	12.01%	386 468	11-32%
Chronic periodontitis	743187	10-79%	378 407	10.89%	364780	10.68%
Mild hearing loss with perinatal onset due to other hearing loss	724689	10.52%	386147	11.11%	338 543	9.91%
Acne vulgaris	646488	9-38%	311349	8.96%	335140	9.81%
Low back pain	632 045	9-17%	334793	9.64%	297 252	8.70%
Dental caries of baby teeth	621507	9-02%	352 0 85	10.13%	269 421	7-89%
Moderate iron-deficiency anaemia	608 915	8-84%	269596	7.76%	339 319	9-93%
Other musculoskeletal disorders	560 978	8.14%	262779	7.56%	298199	8.73%
Near sighted due to other vision loss	459 646	6-67%	235 052	6.77%	224 593	6.58%
Mild iron-deficiency anaemia	375 438	5-45%	152 523	4.39%	222 915	6-53%
Asthma	334 247	4-85%	160346	4.61%	173 901	5.09%
Neck pain	332 049	4.82%	135134	3.89%	196 915	5.77%
Chronic obstructive pulmonary disease	328 615	4-77%	168 445	4.85%	160 170	4-69%
Genital prolapse	316 897	4-55%		200	316 897	9.28%
Major depressive disorder	298 441	4.33%	111441	3.21%	187000	5-48%
Pruritus	280 229	4-07%	117758	3.39%	162 471	4-76%
Anxiety disorders	272 777	3-96%	95731	2.76%	177 046	5-18%
Nild anaemia due to hookworm disease	260 254	3.78%	149572	4.30%	110681	3-24%
Osteoarthritis of the knee	250785	3.64%	88885	2.56%	161900	4-74%
Schistosomiasis	238366	3.46%	124289	3.58%	114 077	3-34%
Eczema	229761	3.33%	104259	3.00%	125 502	3-67%
Jncomplicated diabetes mellitus	227 588	3-30%	114 817	3.30%	112 771	3-30%
Jterine fibroids	225 259	3.23%	-		225 259	6.60%
Sexually transmitted chlamydial diseases	215 621	3.13%	85675	2.47%	129 946	3.80%

Dental decay has been listed at the most frequent inflammatory pathology

#### **Global Burden Chronic Disease 2010 WHO**

## **MIH definition and prevalence**

MIH « Molar Incisor Hypomineralization » HSPM «hypomineralized second primary molar »



### Diagnosis

- -Well demarcated creamy white to brown lesions on one to four permanent first molars
- -Associated with affected incisors
- -Hypoplasia / Substance loss / enamel breakdown
- -Atypical caries and restoration
- -Sensitive teeth

(Weerheijm 2001, 2003)



#### Prevalence

-MIH prevalence varies between 2 and > 40% depending on studies

-Mean prevalence turns around 15-18% children 6 to 9 years old worldwide according to the most recent published data

## MIH etiology - association with environmental conditions





AN EMERGING PATHOLOGY





SELECTIVE DENTAL DEFECTS Specific window of time

with a similar prevalence than other pathologies associated to exposure to EDCs

	Mineraliz	ation of p	ermanent fi	irst molars	and incisors	s į	
Ł	birth	1	2	3	4	5	years

A link with exposure to endocrine disruptoring chemicals?

## Classification

✤ 1428 substances → EDC (May 2018) (endocrinedisruption.com)

<u>Xeno-estrogens</u>: PCBs (polychlorinated biphenyl), PBDE (polybromated biphenyls ether), phthalates, alkylphenols, bisphenol A, genistein, UV filters, pesticides, conservatives, cadmium nanoparticles, diesel nanoparticles

Xeno-androgens: PCBs, UV filters (benzophenone-4)

<u>Anti-estrogens</u>: PBDE, flavones and isoflavones (phytoestrogens), UV filters (benzophenone-4), insecticides, phthalates

Anti-androgens: PCB#138, organochlorinated pesticides, UV filters (benzophenone-4), bisphenol

A, vinclozolin, diesel nanoparticles

Disruption of thyroid axis: PCBs, dibutylphtalate, bisphenol A, pesticides, triclosan, perfluorated

compounds, UV filters, PBDEs, DEHP

Disruption of corticoid axis: hexachlorobenzene

Aryl carbon receptor (AhR) activation : dioxins (TCDD)

### Comparison between human MIH affected teeth and BPA treated rat incisors



Control - Score: 0 BPA - Score: 1S BPA - Score: 2S BPA - Score: 3 AS BPA - Score: 3b AS



D100



MIH

Jedeon et al., Am J Pathol, 2013

#### The time-window of sensitivity to low-dose BPA



#### Enamel microscopic structure (SEM)



### **Quantification of Enamel Matrix proteins**



BPA increased the level of enamelin adsorbed to crystal

Jedeon et al., Am J Pathol, 2013



Jedeon et al., Am J Pathol, 2013

#### **ENAMEL DEFECTS, EARLY MARKER OF EXPOSURE TO EDCs**



#### **BPA disrupts amelogenesis preferentially in male rats**





Jedeon et al., Endocrinology, 2014

### Expression of sex steroid receptors in rat dental epithelium



Jedeon, et al., Endocrinology, 2016



## **Uncharacterized enamel hypomineralizations**



Control



Mild Fluorosis









Increasing fluorosis prevalence

#### Interference between various environmental pollutants including endocrine disruptors?

### **Complementary hypomineralyzing effects of NaF and BPA**



Hierarchical Clustering

### BPA and fluoride have complementary hypomineralyzing effects on enamel



 Exposure to BPA weakens enamel making it more susceptible to frequent mineralization defects, Molar Incisor Hypomineralization and Dental Fluorosis
INCREASED PREVALENCE OF DF and INCREASED SUSCEPTIBILITY TO fluoride

 Our study identifies a small group of genes involved in systemic enamel hypomineralization, some of them also reported in genetic enamel pathologies ENAMELOME

#### Jedeon, et al., JBMR, 2016

#### Environmental pollutants

Metabolism-cancer .... MIH, fluorosis, caries

BPA, anti-androgenic EDCs, Phthalates, Fluoride ...

Ethics EDC-free Reconstruction

Dental prevention products, medical devices, resins, materials



**Indirect exposure** 

Leaching of monomers (Bis-GMA, Bis-EMA, Bis-DMA), Mercury, Triclosan, Fluoride ...







