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Review Article

Pediatric Oral Systemic Health: From Fetus to Adolescence

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Abstract

The oral systemic health link has now become well recognized and numerous publications have discussed the importance of the oral microbiome in the overall health of any individual. This is likely even more important in children and this influences their future health as they mature. What is particularly interesting is that the microbiome of a child is developed prior to birth and is related to the maternal oral microbiome. Early intervention to the mother prior to the child's birth, with proper sleep, exercise and dietary adjustments such as the limitation of added sugars and use of coconut oil, for example, will influence the developing child's microbiome. Direct influence with the polyols xylitol and erythritol to reduce pathogens, and probiotics to boost levels of commensals would also be required. Due to the extent of oral disease, and its tremendous associated costs, urgent action is required by all health professions.

Introduction

Every species depends on adaptation to survive. Humans have managed to survive and flourish while directly influencing the environment of the entire planet, encompassing all other forms of life. While there may be philosophical disagreements as to the inadvertent harm to our natural surroundings, the human species, homo sapiens, has been the only survivor of the hominins [1]. The biology of this success is intertwined in the coevolution of homo sapiens and the associated holobiome [2,3]. Chronic illnesses and debilitations appear to be increasing, requiring reflection into the evolutionary process, and the perturbations that have recently occurred creating this environment of now-declining health [4]. Current research would point to the "Hygiene hypothesis", overuse of anti-microbials, dietary shifts and the resultant decrease in human microbiome diversity [5,6]. The old model of looking for an increase in pathogens is flawed. Indeed, the fault lies with the decrease in commensals that not only compete directly with the pathogens, but also modulate the immune response of the host [7]. To improve the health of children, we must first improve the microbiome of the mother. The maternal microbiome sets the stage for the child's microbiome [8,9].

Pre-natal intervention has been studied with positive results reported by the supplementation of the mother with probiotics or polyols [10,11]. Published studies using xylitol that involve the nursing mother and child have demonstrated the decrease in the maternal transmission of mutans streptococci [12]. Certainly, intervention may be desired even earlier, preferably before pregnancy because it is also reported that antecedent use of antibiotics by the mother will influence the maternal microbiome [13]. The placental microbiome is most closely related to the maternal oral microbiome [14]. The presence of commensal bacteria in the placenta and developing fetus is essential to fetal immunological maturation [15]. The oral health of the expectant mother should then be considered primarily important to the oral systemic health of the fetus and later, the child. In addition, the placental microbiome appears to be developed quite early in the pregnancy, by maternal imprinting [14]. This maternal imprinting involves the transportation of viable commensals via circulating monocytes, properly creating a fetal microbiome to program the developing child [16]. Animal studies have demonstrated the transmission of maternal breast commensals into the amniotic fluid [17]. All this depends upon the mother actually having a healthy microbiome [18]. The maternal microbiome can be influenced in numerous ways including diet, exercise and probiotic supplementation [19-22]. Limiting added dietary sugar and the regular addition of polyols can help decrease the prevalence of pathogens before they are passed on to the child [12,23-25]. In the case of Early Childhood Caries, the reduction of maternal Candida albicans will reduce the biofilm formation by *Streptococcus mutans* potentially reducing the incidence of dental caries [26,27]. Some Lactobacilli, all probiotics such as *Lactobacilli rhamnosus*, have been demonstrated to inhibit *Candida albicans* [28-30]. Other supplements, such as N-acetyl cysteine, also have a reducing effect on Candida albicans levels [31-32]. Coconut oil in the form of Medium Chain Triglycerides (MCT) supplements has also been used to reduce levels of Candida albicans and is reportedly as effective as ketoconazole [33-35]. But it has also been reported that coconut oil has more beneficial components than just MCT, giving pause as to why whole coconut oil isn't utilized more [36]. Regardless, MCT may increase exercise endurance and encourage weight loss [37]. In addition, another natural product, propolis has also been demonstrated to inhibit *Candida albicans* and other oral pathogens [38-40]. If the expectant mother increases exposure to coconut oil or N-AC, the inhibitory effects may be beneficial in preventing the onset of ECC or, possibly *Candida albicans* systemic disease if prematurely born [41].

Vitamin K2 has also been reported as being very beneficial as an anti-caries agent and for activation of proper bone and dentin formation in concert with vitamins A and D [42]. This research isn't new, but recently furthered explored and reported [43]. Insufficient levels of Vitamin D have been linked to S-ECC in a number of studies [44-47]. With increased publications of the beneficial properties of these supplements, it is surprising that the dental profession has not enthusiastically adopted a more fully energetic policy on their role in preventing ECC, especially considering the lack of important micronutrients in the typical American fast food diet [48]. The method of birth has been greatly researched demonstrating that C-section results in an increase in childhood allergies and asthma [49]. The research implicates the lack of exposure to the bacteria of the birth canal and anus as being causative with the neonate's microbiome lacking maternal commensals [50]. After birth, either by vaginal delivery or C-section, breast feeding provides the infant with Human Milk Oligosaccharides which are much more than just food for bacteria as originally proposed for the child [51]. The HMOs also are antiadhesive antimicrobials that serve as soluble decoy receptors, preventing pathogens attachment to the infant's mucosal surfaces and thereby lowering the risk for viral, bacterial and protozoan parasite infections [52,53].

HMO's also reportedly modulate epithelial and immune cell responses, reducing excessive mucosal leukocyte infiltration and activation, lowering the risk for necrotizing enterocolitis and providing the infant with sialic acid, a potentially essential nutrient for brain development and cognition [54,55]. Formula does not have the same protective properties that breastmilk does and sadly, many pediatric dentists criticize breast feeding as being cariogenic, even though published research links the associated dental caries to additional carbohydrate intake and night feeding [56,57]. The benefits of breast feeding have been well documented, and the need to adjust the preventive dentistry protocol to accommodate breast feeding should be evident [58]. Although the World Health Organization recommends two years, mothers probably should breast feed their infants for a least a year, the time interval reported to be the found in early hominins, Australopithecus africanus [59]. Another benefit from breast feeding, besides developing the microbiome and immune modulation, could be regulation of metals, especially zinc and copper, protecting the neurological development of the infant [60-62].

Streptococcus mutans has long been considered the key pathogen for the development of dental caries, the most prevalent chronic disease of humans [63-65]. Efforts to reduce the levels of *Streptococcus mutans* in infants and children with xylitol and preventing dental caries have been successful, raising the question as to why this is not standard dental practice. 66-67 However, other bacterial and fungal organisms have now been closely identified with the development of dental caries [68]. *Scardovia wiggsiae* is a Bacillus bacterium found extensively associated with Severe-Early Childhood Caries [69]. *Scardovia wiggsiae* and *Slackia exigua* have been reported to be involved in the early caries development [70]. *Candida albicans*, a fungal organism, helps with the biofilm production by increasing the extracellular polysaccharide matrix which protects *Streptococcus mutans* from anti-microbials and commensals such as *Streptococcus oralis* [71]. Lactobacilli inhibit the colonization of *Candida albicans*, hence decreasing the polysaccharide matrix, exposing the *Streptococcus mutans* to the bactericins or hydrogen peroxide of its natural competitors, other Streptococcus species [72]. Streptococcus oralis produces hydrogen peroxide that inhibits the anaerobic *Streptococcus mutans* growth [73,74]. Indeed, Probiora probiotic, a commercially available probiotic product, contains *Streptococcus oralis*, *uberis* and *rattus*, and claims to inhibit several key dental pathogens [75-77]. Probiotics have been reported to be an important adjunct in preventive dental care [78-80].

Erythritol and xylitol are polyols that have been extensively researched and demonstrated to have notable anti-cariogenic and anti-periodontal disease properties [81,82]. Polyols (particularly the non-hexitol alditols or sugar alcohols erythritol and xylitol) have been found effective in inhibiting the transition to and maturation of biofilms from planktonic cells [83]. Xylitol clearly inhibited the formation of mixed species biofilms, which included *Porphyromonas gingivalis* in vitro [84]. Erythritol suppressed the maturation of gingivitis biofilms and contributed to a healthier oral ecosystem [85]. *Porphyromonas gingivalis* takes advantage of early colonizers (Streptococci and Candida) to provide attachment and protection within the biofilm matrix. Polyols can reduce extracellular polysaccharide production and interfere with biofilm matrix elaboration, thereby reducing adherence and biofilm development [86-88]. Streptococci and Candida utilize common dietary sugars sucrose and D-glucose for preferred energy sources, as well as for polysaccharide production. Higher glucose concentrations stimulate Candida growth. Compared with common D-sugars, xylitol induced the lowest adhesion and biofilm formation on either Streptococcus mutans or Candida albicans [89]. In addition, xylitol has been demonstrated to decrease the levels of cariogenic bacteria while having little effect on beneficial bacteria [90]. The discovery of bacteriophages specific for certain strains of *Streptococcus mutans* also show great promise in the management of pediatric oral health [91]. With the costs of dental disease rapidly escalating, now (2010) estimated at 442 billion US dollars, all effective measures to prevent oral disease should be urgently started in the pediatric population [92].

The Airway evaluation of the infant/toddler is of paramount importance during the first Age One examination [31]. Airway issues in children have been linked to future obesity, diabetes and behavioral issues [94,95]. Mouth breathing increases the oral microbiome pathogenic potential, as the incoming air will reduce the protective nature of the saliva [96]. Studies have demonstrated the correlation between oral disease and airway pathology [97,98]. Sleep Disturbed Breathing in children has been extensively reviewed in the literature, describing an ever-increasing pathologic chain of events [99,100]. Amongst the deleterious effects of mouth breathing are lower and mid-facial adaptations, orthodontic malocclusions, potential speech issues, esthetic concerns, sleep disturbed bruxism, and future temporomandibular joint dysfunctions [101-104]. The key to the future health of children is effective preventive care. What becomes a serious morbidity in adulthood started in childhood. Now more than ever, pediatric health care providers need to emphasize the connection between the oral health of children and their systemic health, with all the future ramifications now clearly reported in the scientific literature. The importance of the oral microbiome, its role as a "gateway" microbiome, and the systemic connection need to be more fully explained to patients, parents and all health care professionals.

Interestingly, the oral health care of the child starts before birth, requiring the participation of all involved in pre-natal care. It is now obvious that what is most important may be the microbiome, and how it is affected by the environment, diet, sleep, exercise, antibiotics, polyols and probiotics. The microbiome then modulates the immune system, allergies, resistance to pathogens, auto-immune responses, and ultimately patient health and longevity. At last, there seems to be great interest in the importance of pediatric and general oral health due to the crisis that poor oral health is bringing upon us [105]. We should be concerned that research studies from several countries have all reported neurotoxicity effects from relatively low levels of fluoride in children [106-111]. Our over reliance on fluoride to create fluorapatite to inhibit decay seems inadequate at best. Perhaps this means that the time has come to treat a bacterial disease, as a bacterial disease. After all, dental caries and periodontal disease, and to a great extent downstream comorbidity including atherosclerosis, diabetes, strokes, inflammatory Alzheimer's, diabetes, and many systemic illnesses, can be traced back to a "dysbiosis" started in infancy.

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