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Childhood obesity and Craniofacial growth: recapitulating orthodontic implications

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ABSTRACT

Childhood obesity is a significant concern in many countries and is a condition of systemic inflammation to an impaired immunity. It is usually characterized by a low-grade inflammation depending mostly on the release of cytokines, adipokines and reactive oxygen. There is a vast difference of craniofacial morphology in obese and normal adolescents. The visceral adipose tissue (VAT) is the primary source of pro-inflammatory cytokines in obese individuals. This narrative review article focuses on the profile of immune response and illustrates the craniofacial morphological changes in obese adolescents. Furthermore, interventional studies which were aimed at preventing early occurrence of malocclusion in obese adolescents is elaborated.

Key words : **Adolescents, childhood obesity, craniofacial morphology, immunity, malocclusion, visceral adipose tissue**

INTRUDUCTION

Childhood obesity, defined as excess of body fats which impairs the quality of life in an individual[1,2,3] is a significant factor all over the world and most common in affluent countries. There has been dramatic increase in number of overweight (BMI >25 kg/m2) and obese (BMI >30 kg/m2) adults in recent years.[4,5,6] There appears significant shift in the prevalence of childhood obesity which occurred between 1980 and 2004, doubling in just 25 years (from 15.0% in 1980 to 32.9% in 2004) globally.[7,8,9] The number of children who were classified as extremely obese (BMI>40kg/m2 increased from 0.9% in 1960 to 5.1% in 2004 globally.10 Lot of current studies recently mention about the risks of type-2 diabetes mellitus, hypertension, hypercholesterolemia, dyslipidemia, hyperinsulinemia, respiratory disorders and increased risk of cancers in obese individuals.[10,11,12] Genetic, epigenetic, environmental factors, health status, basal metabolism, physical exercise, race, hormonal balance, imbalanced diets and sedentary lifestyle contribute to obesity and overweight, irrespective of socio-economic status.[13-17]

PREVALENCE

Overweight is defined as a BMI of 25-29 and obesity is BMI of 30 or greater.[18,19,20] Recent surveys found that there is gradual upward trend in body weight which is equivalent to a 0.2kg rise in body weight/year at any age.[17] Investigators have used Body Mass Index (BMI) to measure the overweight of an individual.[18]

Race and ethnicity: The prevalence of obesity shows striking and significant disparities with regards to race and ethnicity in children.[21,22] While childhood obesity is clearly a major public health issue in United States, the increased prevalence of obesity is not only limited to this country; indeed, obesity is now a global epidemic. The distribution of childhood obesity in 2–19 years old children with regards to race showed similar trends as seen in adults. The prevalence of obesity was lower among non-Hispanic white children compared to non-Hispanic African American children and Mexican American children.[22] When gender and race were considered, higher rates of obesity were seen in Mexican American boys than in non-Hispanic white boys. Non-Hispanic African American girls had higher rates of

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obesity than non-Hispanic white girls.[23] Various countries across the globe —North America, Central America, South America, Western Europe, the Middle East, Eastern Europe—report that minimum 40% of their population are overweight or obese.[24,25] while east Asian countries such as China, Japan, Vietnam, and India report decreased rates of obesity.[25] Over the past 10 years, the World Health Organization (WHO) has recognized the increasing trend in overweight or obese children,] and meticulous attention is now being given to the global implications associated with this increase.[23] In various analysis of the leading causes of global mortality, childhood obesity and being overweight were among the top 10 etiologies for each.[26-30]

HORMONAL VARIATIONS AND OBESITY

The mechanisms which control and regulate craniofacial growth and development are very complex and interactions between hormones, genes, nutrients and epigenetic factors will determine the final morphology of craniofacial bones.[31-35] Usually GH deficiency exhibits decreased anterior and posterior facial heights and small sized cranial bases bones.[36-40] Obese adolescents exhibit higher levels leptin, a hormone which secretes white adipose tissue for controlling appetite, rapids the process of skeletal growth by accelerating the production of gonadotrophin releasing hormone hence influencing the onset of malocclusions.[41,42] So, some authors say that there is increased maxillary and mandibular sizes , prognathic jaws and smaller mandibular plane angles in obese children.[42,43]

Human beings have the unique ability to deposit fats and then utilize during starvation. But, consumption of food in large quantities leads to increase of fat deposits. Obese adolescents consume more fats and have more irregularity of eating pattern than non-obese adolescents.[44] Sleep pattern and duration also contributes inversely to BMI and the circumference of waist.[44] Puberty is a critical period in females since there is a risk of obesity due to early menarche (<11years).[45] Evidence indicates that childhood obesity is associated with cardiovascular events in adult life and even increased levels of cholesterol.[44] The major complications of childhood obesity include high levels of triacyl glycerides, low levels of lipoprotein cholesterol and defective glucose metabolism.[44]

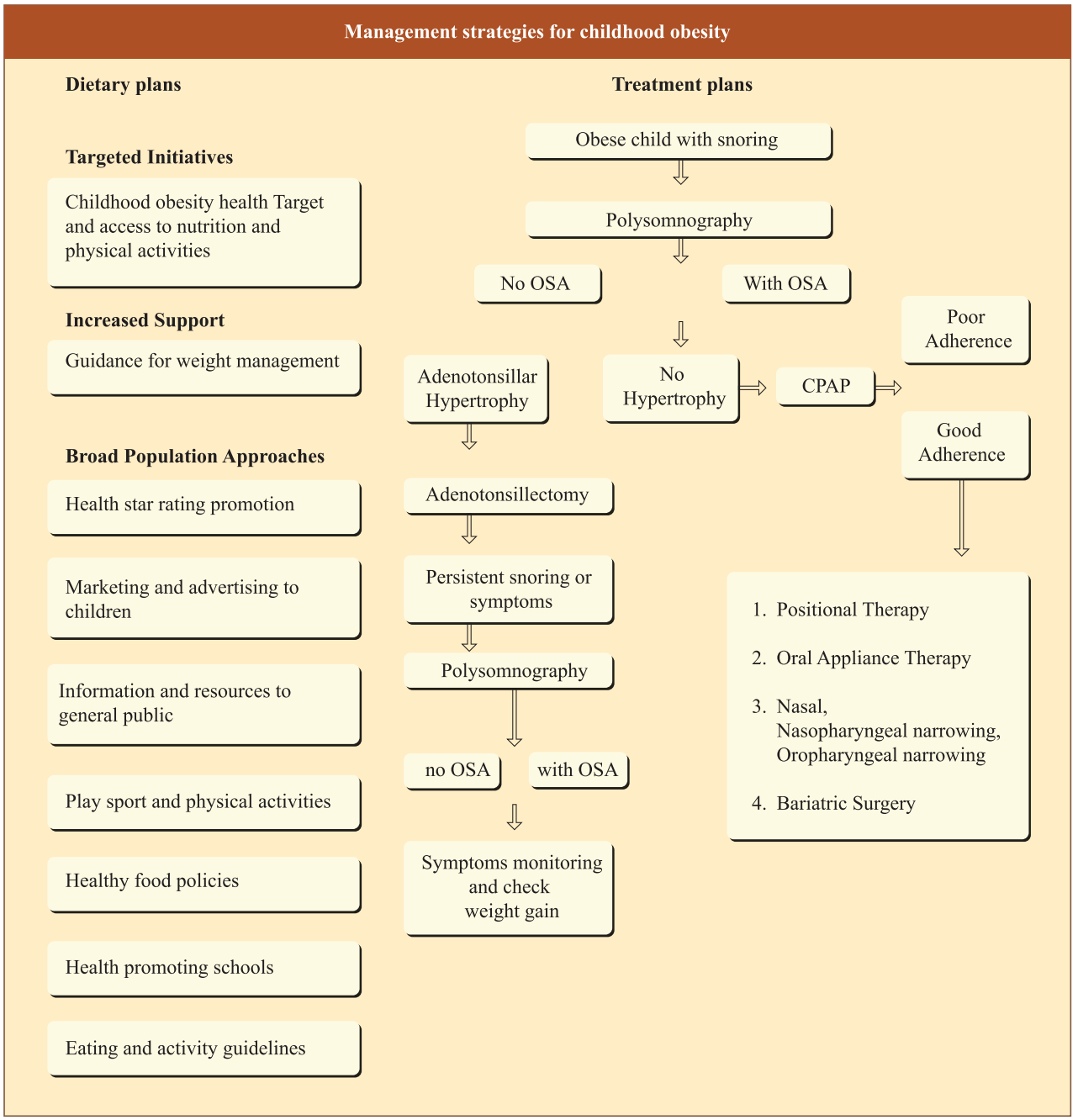
ALTERATIONS OF INNATE AND ADAPTIVE IMMUNITY IN OBESITY

Obesity is often associated with systemic inflammation and impaired immunity.[44,45] It is reported that the visceral adipose tissue(VAT) is the most common source of pro-inflammatory cytokines through experimental as well as animal studies.[45-52] Macrophages with an inflammatory phenotype account for 40-60% of VAT immune cells in obesity and are called as 'classically activated macrophages' (M1).[53-56] Large amounts of TNF-alpha, IL-6, IL-12 ,IL-1beta and MCP-1 (monocyte chemotactic protein-1) are secreted by M1.[57] In non-obese groups , macrophages are termed as 'alternatively activated macrophages (M2)' and they secrete IL-10 and IL-1 receptor antagonist which exert anti-inflammatory activities.[58] M1 macrophages seem to favor insulin resistance and their deactivation process helps against insulin resistance.[59-61] Obese animals expressed increased amounts of adipose tissue-derived necrosis factor (TNF)-alpha.51 and proved association between C-reactive protein, interleukin(IL)-6 and developing risk of type-2 diabetes.[52]

VAT contains increased numbers of T helper (Th) CD4+, T cytotoxic CD8+ and B cells. Th1 cells produce interferon (IFN)- gamma which in turn polarizes M1 macrophages and increase release of TNF-alpha.62-69 Increase in Th17 cells in obese humans, lead to great expression and release of IL-17 and Th17 dependent mechanism is considered as.70-72 important etiology associated to autoimmune disorders in obese individuals.[73] T-regulatory (Treg) cells are reduced in obese mice and humans.[66-67] Depletion of Treg cells lead to high insulin levels and decreased insulin receptor signaling.[68] This particular data suggests that anti-inflammatory role exerted by Treg cells with the release of IL-10 suppress obesity induced inflammation.[69]

OBESITY INFLUENCING SKELETAL MATURATION

Knowledge of skeletal development is important because early orthodontic treatment directed towards improving skeletal discrepancies completely depends on the nature and period of skeletal development. The most evaluated skeletal maturity indicators depend on either stage of bone development in hand-wrist radiographs or shape and size of cervical vertebrae as observed in lateral cephalogram.[74-78] Literature suggest that leptin plays an important role in skeletal growth through the activation of various mediators like insulin-like growth factor 1 and sex hormones.[79] Leptin might act directly on the skeletal growth centers and its receptors have been found in the cartilaginous growth centers that are significantly involved in skeletal maturation.[79] Hence, an obese child would have a mechanism of central resistance to leptin and an increased leptin sensitivity at a peripheral level causing increased differentiation and proliferation of chondrocytes, which can lead to precocious skeletal maturation.[79] Increasing the level of controversy, some authors mentioned that increased body weight could be a result of puberty, rather than a determining factor.[80] Comparing skeletal maturity evaluated from hand-wrist and lateral cephalograms between the obese and normal-weight



subjects yielded different results.[80] Obese children had a higher mean cervical vertebral maturation score compared with the controls which is related to earlier skeletal maturation.[81] It is a fact that discrepancy between the skeletal and chronologic ages because of systemic conditions or medications might jeopardize treatment results. It is time for orthodontic clinicians to consider body mass index standard deviations as part of their patient evaluation while considering growth modification with either orthopedic or functional appliance treatment plans.[83]

OBESITY AND DENTAL DEVELOPMENT

Costacurta et al carried out a study using the method codified by Demerjian and reported that obese girls had more advanced dental age when compared to non-obese girls.84 These results were in concordance with that of Hilgers et al. who showed that dental development acceleration was

significantly higher for obese girls than boys.[85] Briefly, the results highlighted out of these studies emphasized a correlation between accelerated dental maturity and increasing BMI percentile.[86] In contrast, Eid et al. did not find a correlation between dental maturity and body mass index in Brazilian children.[87] which could be attributed to genetic and/or dietary factors. Additionally, based on the results of a study increasing BMI percentile accelerates dental age and affects treatment duration such as in serial extraction or space maintenance.[88] When permanent teeth erupt at an early stage in obese children, they may not have good oral hygiene habits leading to increased incidence of caries lesions.[88]

FACIAL SOFT TISSUE MORPHOLOGY IN OBESE PATIENTS

Obese individuals have reported to show increased growth activity at dentofacial complex, but without any pronounce deviations in facial components and proportions when compared to the control group pertaining to a specific age.[89] Even though obese children have a decreased level of GH, controversial literature exists saying increase as well decrease in craniofacial diameter. Specifically, facial prognathism is a characteristic feature of male and female obese individuals and is considered the effect of increased maxillary and mandibular lengths. Some reports found a combination of facial prognathism with smaller than average cranial base angle.[90,91] It is also reported that obese females exhibited lesser inclination of maxilla, increased incisor inclination and larger alveolar prognathism than control group.

Considering the vertical plane relationships, there exists reports mentioning a greater posterior facial height with no alteration in anterior facial height in obese individuals creating a more upward and forward rotation pattern. It is reported that the growth changes in lower posterior face are responsible for increased posterior dimension in obese children and vital areas of growth are mainly the mandibular condyles and alveolar processes.[89] The soft tissue profile of obese individuals appear to be straight and is attributed to large mandibular length and anterior position of pogonion. In contrast, cephalometric studies conducted on patients with GH deficiency, reported small anterior and posterior cranial base, decreased posterior facial height, and small posterior mandibular height.[90] One study, which looked into the relationship between low BMI (less than 30) and craniofacial features in obstructive sleep apnoea patients reported short anterior cranial base, small and retrognathic mandible.[89]

OBESITY AND ITS RELATION TO RESPIRATION AND SLEEP

Obesity is considered an important risk factor for the development and progression of obstructive sleep apnoea (OSA).[91-93] Recent data showed that obese children have a 46% prevalence of OSA in comparison to normal weight children (33%).[94] Furthermore, patients with mild OSA who increase 10% of their baseline weight are at a six-fold risk of OSA progression, and an equivalent weight loss can result in 20% improvement in severity of OSA. Obesity may worsen OSA because of fat deposition at certain sites surrounding the upper airway. This results in a decreased lumen and increased collapsibility of the upper airway and is considered a predisposing factor to apnea.[92] However, the relationship between OSA and obesity is very complex. Factors such as decreased physical activity levels and increased appetite, particularly for refined carbohydrates contributes to weight gain in OSA patients.[95] There exists genetic polymorphisms which might influence both sleep apnea and obesity. Patel et al96 reported a correlation between AHI and anthropomorphic adiposity measures mentioning that obesity could explain 50% of the genetic variance in obstructive sleep apnea.

Hormones related to obesity, weight control, satiety, and energy expenditure may be altered in OSA. Leptin is a hormone secreted by adipose tissue and binds to the ventral medial nucleus of hypothalamus, called as the satiety center leading to signal the brain that the body has had enough to eat.[97-99] Popko et al mentioned that polymorphisms of the leptin receptor[97] is involved in energy homeostasis and body weight regulation which are significantly correlated with OSA and obesity when compared with healthy controls. Hyperleptinemia is believed to be accompanied by desensitized cellular responses to leptin, therefore the effect of leptin is not achieved.[100] Ghrelin, a hormone produced by cells lining the stomach, stimulates appetite and thus is considered a counter-regulator to leptin. Ghrelin is increased during reduced sleep and has been shown to stimulate appetite, and might lead to obesity and worsening of OSA.[101] Thus, there exists a close correlation between obesity, sleep deprivation and OSA and share common pathophysiologic features of metabolic dysregulation.98 Weight loss may improve these conditions and hence might constitute a potential intervention for these patients Type of Diet and molecular changes especially related to inflammation Obesity is often related to large amounts of production of reactive oxygen species (ROS) from sources like mitochondria and nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, which can increase the amount of body fat. Oxidative stress reduces the release of adiponectin with an increase in TNF-alpha and PAI-1 (plasminogen activator inhibitor) leading to a prothrombogenic status and insulin resistance.[102,103] The overexpression of NOX-2 (the catalytic core of NADPH oxidase) and dependent oxidative stress suggests a condition

of endothelial dysfunction.[104] Recent data reported that dietary anti-oxidants influence metabolic as well as inflammatory markers associated with low grade systemic inflammation.[102] Low grade inflammation is determined by the ratio of IL-17 and IL-10. Normal weight children who followed dietary recommendations and emphasized practiced physical activity (PA) had a reduction of BMI and increase in IL-10 salivary levels.[103] while those who were unable to attend dietary recommendations and did not practice PA had increase in BMI and IL-7 salivary levels while IL-10 salivary levels were even low.[104,105] Increased levels of IL-17 in these children with higher BMI are due to intake of junk food (hypercaloric food) and decreased PA and can be responsible for presence of low grade inflammation.[103]

The Expert Committee of American Medical Association recently concluded that there is a vital evidence that eating away from home, specifically fast food, is a risk factor for childhood obesity.[105,106] Some evidence suggests that a disproportionate number of fast food restaurants are situated near schools.[107,108] Students with fast food restaurants within 0.5 miles of their home were more prone to be overweight or obese. Fast food meals for children were introduced in the late 1970s and have been very popular with adolescents.[107] In terms of composition, fast food is high in total fat and TFAs, have high caloric density and offer less nutritional value and lead to obesity epidemic.[107,108] National School Lunch Program (NSLP) evaluation revealed that only 3% of the fast food meals met the NSLP criteria in terms of their percentage of energy from fat and carbohydrates. Children's meals are often offered with toys, which promotes brand recognition and frequent visits to the restaurant. Studies have found that children aged 3–6 years view, understand, and memorize advertising when cartoon characters are used.[108] The fast food advertisements seemed to focus on building brand recognition and associations using logos and cartoon characters.

Increased consumption of soft drinks has been associated with metabolic syndrome and cardiovascular risk as the number of calories consumed in sodas and fruit juices has increased significantly over years.[109] Along with this, the consumption of milk has been decreased by almost 38% contributing to the expansion of the obesity epidemic. Prospective studies have linked increased intake of sweetened beverages directly proportional with increased weight gain.110 Fructose typically comes from 3 sources: sucrose, high fructose corn syrup (HFCS), and fruits. The amount of fructose in fruits, which is relatively less compared to that in soft drinks, seems to entice individuals to consume other nutrients. In contrast, the HFCS added to soft drinks contains high concentrations of fructose and has no nutritional benefits.[110] and is identified as a possible independent risk factor for the development of obesity.[110]

MEASURING PARAMETERS FOR CHILDHOOD OBESITY AND A CRITICAL COMPARATIVE EVALUATION.

Obesity is the next important epidemiologic battle for physicians, public health experts, government officials and the public. Obesity has already surpassed smoking as the most pressing public health threat. Health initiatives should now be developed to effectively prevent obesity and diseases associated with it. Obesity is potentially more problematic since adequate nutrition is essential to survival; hence, abstinence from food is never an option. As changes to the healthcare systems in United States are discussed, plans should be offered that directly and aggressively target childhood obesity through health initiatives and prevention programs

- Food Labeling: Labeling the nutritional content of food products has been proposed as a method to allow consumers to make informed choices about the types of foods they consume. The only problem with these labels is that they appear in small print and people do not read them. Again, the information provided as part of this is always difficult for consumers to comprehend. Little data exist to show that labeling food products has improved the habits of eating.[111] Further, majority of consumers are unaware of the dietary content of restaurant foods. The Nutrition and Education Labeling Act of 1994 exempted restaurants from providing nutritional labeling of their products.[112] Recently, New York City mandated that fast food companies provide nutritional labeling for their products.[112] Overall, there may be a small role for nutritional labeling, but use of this technique along with other strategies or regulation of nutritional content can be expected to alter eating habits or prevent childhood obesity-related consequences.

- Eliminating Trans Fat in New York City, Denmark, and Beyond: The average daily per capita intake of TFAs in the United States has been shown to increase heart diseases risk and the most leading health organizations have introduced the complete removal of TFAs from foods.[113] Because of the great efforts in New York City and Denmark, legislation to ban artificial TFAs from restaurants has been passed by 1 state legislature, 10 local city governments, and the country of Puerto Rico are considering almost similar legislation.[113] To achieve this objective, consumers would need to read labels and become educated about the TFA content, and healthcare providers would need to provide counsel on TFA-free alternatives. The best option is to decrease the use of industrially produced TFAs and shift towards the use of

safer fats in both packaged goods and restaurant food.[113]

- Taxation of High Calorie Beverages: The current debate is how to decrease the consumption of high-calorie beverages in school systems of United States. Two ideas which have been proposed are to increase taxation on high calorie beverages and to restrict their availability in schools.[114] The current level of taxation on high calorie beverages is insufficient to decrease consumption. Newly proposed legislative strategies have suggested increasing the tax on non-diet soda, fruit drinks and flavored milk.[114]

MANAGEMENT STRATEGIES

- Diet plan for obese individuals: Prevention seems to be one of the accurate strategy to fight childhood obesity. Lots of reports mention that there are several factors which are to be given importance in the prevention of obesity.[115] Breast feeding is very useful in decreasing the risk of childhood obesity. Dietary regulations like limited intake of sugar, sweetened beverages and meals with vegetables and fruits, avoiding junk foods and encouraging limited amounts of food is considered useful steps in reducing the incidence of obesity.

- Increasing activity and reducing sedentary plans: Increase in physical activities reducing sedentary life should be promoted to prevent childhood obesity. Walking, cycling, swimming and other play activities should be encouraged to prevent obesity in the initial phase itself. Home environment should be improved to encourage more physical activities for children.[115]

- Pharmacological methods - Prebiotics and Probiotics: Prebiotics are non-digestible dietary fibers which stimulate the growth and activity of gut bacteria. There are many experimental studies which demonstrated the anti-obesogenic effects of prebiotics.[115] In infants receiving formula rich in prebiotics (galacto-oligosaccharides, fructo-oligosaccharides), there was increase in bifido bacteria thus reporting the possibility of adipocyte growth influences through modulation of microbiota composition.[116] With reference to childhood obesity, maternal supplementation in the first and third trimester with probiotics did not change prenatal and postnatal growth rates. But, breastmilk of these mothers was rich in Staphylococcus and Lactobacillus which led to development of neonatal microbiota and decreased incidence of obesity in children.[116] Synbiotics, which is a combination of pre-and probiotics modulate the microbiota and intestinal immunity.[116] Studies even reveal that children treated with synbiotic (Protexin), exhibited a decrease in weight as well as TNF-alpha and IL-6 with an increase in adiponectin.[116]

Management strategies in childhood OSA with special emphasis on craniofacial morphology associated with obesity:

Sleep fragmentation is a vital consequence of OSA. Experimental sleep deprivation, as well as self-reported short sleep have been associated to metabolic dysregulation independent of childhood obesity and OSA, elaborating important interactions between these conditions and increasing the complexity of treatment.[95] Currently, continuous positive airway pressure (CPAP) is the mainstay of treatment of OSA. Weight loss may be an effective therapy in overweight and obese patients, who may comprise 70% of subjects with OSA.[97] Weight loss through bariatric surgery, has been shown to decrease the severity and symptoms of OSA.[98] Weight loss may elicit important and significant changes in cholesterol, insulin resistance, leptin, inflammatory markers, and endothelial function.

Oral appliances are important management options for obese children with OSA.[117] Oral devices can be broadly broken in to mandibular repositioning appliances (devices that direct the movement of the lower jaw forward) and tongue retaining appliances (prevents the tongue from falling backward in sleep). The devices significantly increase the pharyngeal airway mechanically and have been proved to be efficacious in the treatment of mild to moderate OSA in obese individuals.[118] A review of OSA treatments showed that the trial suffered significant methodological shortcomings like inappropriate randomisation and lack of an intention-to treat analysis.[119] Other studies have concluded that in a subset of patients the use of an oral appliance would allow patients better to tolerate their CPAP therapy.[120]

The presence of a maxillary transverse deficiency where the upper teeth are too narrow to occlude with the mandibular teeth is often found in children with OSA.[121] This may be treated with rapid maxillary expansion (RME). The studies have all been small and randomized double blind trials may be needed for RME to gain wider acceptance but the treatment may be a reasonable approach for obese children with this specific orthodontic abnormality.[125] It has been reported in a study that an anteriorly titrated mandibular position reduced Obstructive Sleep Apnea severity, enlarged the velopharynx, and decreased the curvature of the anterior velopharyngeal wall.[123] Hence it was proposed that this change in the upper airway curvature associated with mandibular advancement may affect the severity of Obstructive Sleep Apnea through its effect on airflow dynamics.[123] Maxillomandibular advancement through funactional appliances is prescribed as a functional and curative treatment for OSA in obese children.124 It can

result in improvement in the quality of life and reduction in OSA health-related risks.[124] Mandibular advancement appliances have been evaluated to be effective in the treatment of mild to moderate OSA.[124] Treatment with removable functional appliances, like Twin Block appliance, has also been used to help growing pediatric OSA patients with a stimulation of mandibular growth.[124]

CONCLUSIONS

Childhood obesity is so common in western countries and garners special attention currently due to increased orthodontic malocclusions and food related diseases in these subjects. A regular intake of junk foods can result in systemic inflammation in obese children. Interventional studies show the identification of gut microbiota associated in the development of obesity. Diets containing synbiotics are recommended to prevent noxious effects of obesity. Literature is replete which depicts marked differences in the craniofacial morphology between obese and normal children. Obese children have typical features of bimaxillary prognathism and larger facial dimensions.

REFERENCES:

1. Stevens GA, Singh GM, Lu Y, Danaei G, Lin JK, Finucane MM, et al. National, regional, and global trends in adult overweight and obesity prevalences. Popul Health Metr. 2012;10(1):22.
2. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of Childhood and Adult Obesity in the United States, 2011-2012. JAMA. 2014 Feb 26;311(8):806.
3. Von Ruesten A, Steffen A, Floegel A, van der ADL, Masala G, Tjønneland A, et al. Trend in obesity prevalence in European adult cohort populations during follow-up since 1996 and their predictions to 2015. PloS One. 2011;6(11):e27455.
4. Barquera S, Campos-Nonato I, Hernández-Barrera L, Pedroza A, Rivera-Dommarco JA. [Prevalence of obesity in Mexican adults 2000-2012] Salud Pública México. 2013;55(Suppl 2):S151–60.
5. Malik VS, Pan A, Willett WC, Hu FB. Sugar-sweetened beverages and weight gain in children and adults: a systematic review and meta-analysis. Am J Clin Nutr. 2013 Oct 1;98(4):1084–102.
6. Devaux M, Sassi F. Social inequalities in obesity and overweight in 11 OECD countries. Eur J Public Health. 2013 Jun 1;23(3):464–9.
7. Aitsi-Selmi A, Bell R, Shipley MJ, Marmot MG. Education modifies the association of wealth with obesity in women in middle-income but not low-income countries: an interaction study using seven national datasets, 2005-2010. PloS One. 2014;9(3):e90403.
8. Malik VS, Willett WC, Hu FB. Global obesity: trends, risk factors and policy implications. Nat Rev Endocrinol. 2013 Jan;9(1):13–27.
9. Tran KT, Eriksson B, Nguyen TC, Horby P, Bondjers G, Petzold M. DodaLab - an urban health and demographic surveillance site, the first three years in Hanoi, Vietnam. Scand J Public Health. 2012;40(8):765–72.
10. Chuc TN, Diwan VK. FilaBavi, a demographic surveillance site, an epidemiological field laboratory in Vietnam. Scand J Public Health. 2003;31(62):3–7.
11. Fernandes MM. A national evaluation of the impact of state policies on competitive foods in schools. J Sch Health. 2013;83(4):249–55.
12. Iannotti RJ, Wang J. Trends in physical activity, sedentary behavior, diet, and BMI among US adolescents, 2001-2009. Pediatics. 2013;132(4):606–14.
13. Goran MI, Ulijaszek SJ, Ventura EE. High fructose corn syrup and diabetes prevalence: a global perspective. Glob Public Health. 2013;8:55–64.
14. Malik VS, Pan A, Willett WC, Hu FB. Sugar-sweetened beverages and weight gain in children and adults: a systematic review and meta-analysis. Am J Clin Nutr. 2013;98:1084–1102.
15. Mozaffarian D, Benjamin EJ, Go AS, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics–2015 update: a report from the American Heart Association. Circulation. 2015;131:e29–322.
16. American Diabetes Association. Economic costs of diabetes in the U.S. In 2012. Diabetes Care. 2013;36:1033–1046.
17. Lloyd-Jones DM, Hong Y, Labarthe D, et al; American Heart Association Strategic Planning Task Force and Statistics Committee. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. Circulation. 2010;121:586–613.
18. Li C, Ford ES, Zhao G, Balluz LS, Giles WH. Estimates of body composition with dual-energy X-ray absorptiometry in adults. Am J Clin Nutr. 2009;90:1457–1465.
19. Lee SY, Chang HJ, Sung J, Kim KJ, Shin S, Cho IJ, Shim CY, Hong GR, Chung N. The impact of obesity on subclinical coronary atherosclerosis according to the risk of cardiovascular disease. Obesity (Silver Spring). 2014;22:1762–1768.
20. Freedman DS, Ford ES. Are the recent secular increases in the waist circumference of adults independent of changes in BMI? Am J Clin Nutr. 2015;101:425–431.
21. Xi B, Mi J, Zhao M, Zhang T, Jia C, Li J, Zeng T, Steffen LM; Public Health Youth Collaborative and Innovative Study Group of Shandong University. Trends in abdominal obesity among U.S. children and adolescents. Pediatrics. 2014;134:e334–e339.
22. Wang DD, Leung CW, Li Y, Ding EL, Chiuve SE, Hu FB, Willett WC. Trends in dietary quality among adults in the United States, 1999 through 2010. JAMA Intern Med. 2014;174:1587–1595.
23. Schwingshackl L, Hoffmann G, Kalle-Uhlmann T, Arregui M, Buijsse B, Boeing H. Fruit and vegetable consumption and changes in anthropometric variables in adult populations: a systematic review and metaanalysis of prospective cohort studies. PLoS One. 2015;10:e0140846.
24. Boggs DA, Palmer JR, Spiegelman D, Stampfer MJ, Adams-Campbell LL, Rosenberg L. Dietary patterns and 14-y weight gain in African American women. Am J Clin Nutr. 2011;94:86–94.

25. Hu FB. Resolved: there is sufficient scientific evidence that decreasing sugar-sweetened beverage consumption will reduce the prevalence of obesity and obesity-related diseases. Obes Rev. 2013;14:606–619.
26. Agladıoglu SY, Cetınkaya S, Savas Erdeve S, Onder A, Kendırcı HNP, Bas VN, Aycan Z. Diabetes mellitus with Laron syndrome: case report. J Pediatr Endocrinol Metab. 2013;26:955–8.
27. Huffman DM, Farias Quipildor G, Mao K, Zhang X, Wan J, Apontes P, Cohen P, Barzilai N. Central insulin-like growth factor-1 (IGF-1) restores whole-body insulin action in a model of age-related insulin resistance and IGF-1 decline. Aging Cell. 2015.
28. Hepler C, Gupta RK. The expanding problem of adipose depot remodeling and postnatal adipocyte progenitor recruitment. Mol Cell Endocrinol. 2017;445:95–108.
29. Scheja L, Heeren J. Metabolic interplay between white, beige, brown adipocytes and the liver. J Hepatol. 2016;64:1176–1186.
30. Harwood HJ., Jr The adipocyte as an endocrine organ in the regulation of metabolic homeostasis. Neuropharmacology. 2012;63:57–75.
31. Viana-Huete V, Guillen C, Garcia-Aguilar A, et al. Essential role of IGFIR in the onset of male brown fat thermogenic function: regulation of glucose homeostasis by differential organ-specific insulin sensitivity. Endocrinology. 2016;157:1495–1511.
32. Tchernof A, Despres JP. Pathophysiology of human visceral obesity: an update. Physiol Rev. 2013;93:359–404.
33. Amato MC, Pizzolanti G, Torregrossa V, Misiano G, Milano S, Giordano C. Visceral adiposity index (VAI) is predictive of an altered adipokine profile in patients with type 2 diabetes. PLoS ONE. 2014;1969;9:e9.
34. Verheggen RJ, Maessen MF, Green DJ, Hermus AR, Hopman MT, Thijssen DH. A systematic review and meta-analysis on the effects of exercise training versus hypocaloric diet: distinct effects on body weight and visceral adipose tissue. Obes Rev. 2016;17:664–690.
35. Berry DC, Jiang Y, Graff JM. Emerging roles of adipose progenitor cells in tissue development, homeostasis, expansion and thermogenesis. Trends Endocrin Met. 2016;27:574–585.
36. Tchoukalova YD, Votruba SB, Tchkonia T, Giorgadze N, Kirkland JL, Jensen MD. Regional differences in cellular mechanisms of adipose tissue gain with overfeeding. Proc Natl Acad Sci U S A. 2010;107:18226–18231.
37. Jankovic A, Korac A, Buzadzic B, et al. Redox implications in adipose tissue (dys)function – A new look at old acquaintances. Redox Biol. 2015;6:19–32.
38. Bays H. Central obesity as a clinical marker of adiposopathy; increased visceral adiposity as a surrogate marker for global fat dysfunction. Curr Opin Endocrinol. 2014;21:345–351.
39. Hardy OT, Czech MP, Corvera S. What causes the insulin resistance underlying obesity? Curr Opin Endocrinol. 2012;19:81–87.
40. Pellegrinelli V, Rouault C, Rodriguez-Cuenca S, et al. Human adipocytes induce inflammation and atrophy in muscle cells during obesity. Diabetes. 2015;64:3121–3134.
41. Sun K, Kusminski CM, Scherer PE. Adipose tissue remodeling and obesity. J Clin Invest. 2011;121:2094–2101.
42. Gurzov EN, Tran M, Fernandez-Rojo MA, et al. Hepatic oxidative stress promotes insulin-STAT-5 signaling and obesity by inactivating protein tyrosine phosphatase N2. Cell Metab. 2014;20:85–102.
43. Junnila RK, List EO, Berryman DE, Murrey JW, Kopchick JJ. The GH/IGF-1 axis in ageing and longevity. Nat Rev Endocrinol. 2013;9:366–376.
44. Hill CM, Fang Y, Miquet JG, Sun LY, Masternak MM, Bartke A. Long-lived hypo-pituitary Ames dwarf mice are resistant to the detrimental effects of high-fat diet on metabolic function and energy expenditure. Aging Cell. 2016;15:509–521.
45. Romero CJ, Wolfe A, Law YY, et al. Altered somatotroph feedback regulation improves metabolic efficiency and limits adipose deposition in male mice. Metabolism. 2016;65:557–568.
46. Baquedano E, Ruiz-Lopez AM, Sustarsic EG, et al. The absence of GH signaling affects the susceptibility to high-fat diet-induced hypothalamic inflammation in male mice. Endocrinology. 2014;155:4856–4867.
47. Berryman DE, Lubbers ER, Magon V, List EO, Kopchick JJ. A dwarf mouse model with decreased GH/IGF-1 activity that does not experience life-span extension: potential impact of increased adiposity, leptin, and insulin with advancing age. J Gerontol A Biol Sci Med Sci. 2014;69:131–141.
48. List EO, Berryman DE, Funk K, et al. The role of GH in adipose tissue: lessons from adipose-specific GH receptor gene-disrupted mice. Mol Endocrinol. 2013;27:524–535.
49. List EO, Berryman DE, Funk K, et al. Liver-specific GH receptor gene-disrupted mice have decreased endocrine IGF-I, increased local IGF-I, and altered body size, body composition, and adipokine profiles. Endocrinology. 2014;155:1793–1805.
50. Russo VC, Azar WJ, Yau SW, Sabin MA, Werther GA. IGFBP-2: the dark horse in metabolism and cancer. Cytokine Growth Factor Rev. 2015;26:329–346.
51. DeMambro VE, Le PT, Guntur AR, et al. Igfbp2 deletion in ovariectomized mice enhances energy expenditure but accelerates bone loss. Endocrinology. 2015;156:4129–4140.
52. Yau SW, Russo VC, Clarke IJ, Dunshea FR, Werther GA, Sabin MA. IGFBP-2 inhibits adipogenesis and lipogenesis in human visceral, but not subcutaneous, adipocytes. Int J Obesity (Lond) 2015;39:770–781
53. Nguyen KH, Yao XH, Erickson AG, Mishra S, Nyomba BL. Glucose intolerance in aging male IGFBP-3 transgenic mice: differential effects of human IGFBP-3 and its mutant IGFBP-3 devoid of IGF binding ability. Endocrinology. 2015;156:462–474.
54. Christians JK, Bath AK, Amiri N. Pappa2 deletion alters IGFBPs but has little effect on glucose disposal or adiposity. Growth Horm IGF Res. 2015;25:232–239.
55. Kusminski CM, Bickel PE, Scherer PE. Targeting adipose tissue in the treatment of obesity-associated diabetes. Nat Rev Drug Discov. 2016;15:639–660.
56. Lanes R. Cardiovascular risk in growth hormone deficiency: beneficial effects of growth hormone replacement therapy. Endocrinol Metab Clin. 2016;45:405–418.
57. Ciresi A, Amato MC, Pizzolanti G, Giordano C. Serum visfatin levels in ac-romegaly: correlation with disease activity and metabolic alterations. Growth Horm IGF Res.

2015;25:240–246.
58. Stanley TL, Grinspoon SK. Effects of growth hormone-releasing hormone on visceral fat, metabolic, and cardiovascular indices in human studies. Growth Horm IGF Res. 2015;25:59–65.
59. Bredella MA, Gerweck AV, Lin E, et al. Effects of GH on body composition and cardiovascular risk markers in young men with abdominal obesity. J Clin Endocrinol Metab. 2013;98:3864–3872.
60. Oto Y, Tanaka Y, Abe Y, et al. Exacerbation of BMI after cessation of growth hormone therapy in patients with Prader-Willi syndrome. Am J Med Genet A. 2014;164:671–675.
61. Ruby MA, Massart J, Hunerdosse DM, et al. Human carboxylesterase 2 reverses obesity-induced diacylglycerol accumulation and glucose intolerance. Cell Reports. 2017;18:636–646.
62. Ferrante E, Malavazos AE, Giavoli C, et al. Epicardial fat thickness signifi-cantly decreases after short-term growth hormone (GH) replacement therapy in adults with GH deficiency. Nutr Metab Cardiovas. 2013;23:459–465.
63. Cortez M, Carmo LS, Rogero MM, Borelli P, Fock RA. A high-fat diet increases IL-1, IL-6, and TNF-alpha production by increasing NF-kappaB and attenuating PPAR-gamma expression in bone marrow mesenchymal stem cells. Inflammation 2013;36:379–86.
64. Kumar NP, Sridhar R, Banurekha VV, Jawahar MS, Nutman TB, Babu S. Expansion of pathogen-specific T-helper 1 and T-helper 17 cells in pulmonary tuberculosis with coincident type 2 diabetes mellitus. J Infect Dis 2013;208:739–48.
65. Lecube A, Pachon G, Petriz J, Hernandez C, Simo R. Phagocytic activity is impaired in type 2 diabetes mellitus and increases after metabolic improvement. PLoS One 2011;6:e23366.
66. Allard R, Leclerc P, Tremblay C, Tannenbaum TN. Diabetes and the severity of pandemic influenza A (H1N1) infection. Diabetes Care 2010;33:1491–3.
67. Deng J, Liu S, Zou L, Xu C, Geng B, Xu G. Lipolysis response to endoplasmic reticulum stress in adipose cells. J Biol Chem 2012;287: 6240–9.
68. Charland KM, Buckeridge DL, Hoen AG, Berry JG, Elixhauser A, Melton F, Brownstein JS. Relationship between community prevalence of obesity and associated behavioral factors and community rates of influenzarelated hospitalizations in the United States. Influenza Other Respir Viruses 2013;7:718–28.
69. Ferrante AW, Jr. The immune cells in adipose tissue. Diabetes Obes Metab 2013;15(Suppl 3):34–8.
70. Norseen J, Hosooka T, Hammarstedt A, Yore MM, Kant S, Aryal P, Kiernan UA, Phillips DA, Maruyama H, Kraus BJ, et al. Retinol-binding protein 4 inhibits insulin signaling in adipocytes by inducing proinflammatory cytokines in macrophages through a c-Jun N-terminal kinaseand toll-like receptor 4-dependent and retinol-independent mechanism. Mol Cell Biol 2012;32:2010–9.
71. Uysal T, Ramoglu SI, Basciftci FA, Sari Z. Chronologic age and skeletal maturation of the cervical vertebrae and hand-wrist: is there a relationship? Am J Orthod Dentofacial Orthop 2006; 130:622-8.
72. Mahajan S. Evaluation of skeletal maturation by comparing the hand wrist radiograph and cervical vertebrae as seen in lateral cephalogram. Indian J Dent Res 2011;22:309-16.
73. Flores-Mir C, Mauricio FR, Orellana MF, Major PW. Association between growth stunting and dental development and skeletal maturation stage. Angle Orthod 2005;75:935-40.
74. Sadeghianrizi A, Forsberg CM, Marcus C, Dahll€of G. Craniofacial development in obese adolescents. Eur J Orthod 2005;27: 550-5.
75. Baccetti T, Franchi L, McNamara JA Jr. The cervical vertebral maturation (CVM) method for the assessment of optimal treatment timing in dentofacial orthopaedics. Semin Orthod 2005;11:119-29.
76. Ochoa BK, Nanda RS. Comparison of maxillary and mandibular growth. Am J Orthod Dentofacial Orthop 2004;125:148-59.
77. Akridge M, Hilgers KK, Silveira AM, Scarfe W, Scheetz J, Kinane DF. Childhood obesity and skeletal maturation assessed with Fishman's hand-wrist analysis. Am J Orthod Dentofacial Orthop 2007;132:185-90
78. Baccetti T. Improving the effectiveness of functional jaw orthopedics in Class II malocclusion by appropriate treatment timing. Orthod Fr 2010;81:279-86.
79. Caprioglio A, Levrini L, Nosetti L, Berini J, Macchi A, Tagliabue A, et al. Prevalence of malocclusion in preschool and primary school children with habitual snoring and sleep-disordered breathing. Eur J Paediatr Dent 2011;12:267-71.
80. Wardie J, Carnell S, Haworth CM, Plomin R. Evidence for a strong genetic influence in childhood adiposity despite the force of the obesogenic environment. Am J Clin Nutr 2008; 87:398-404.
81. Costacurta M, Di Renzo L, Bianchi A, Fabiocchi F, De Lorenzo A, Docimo R. Obesity and dental caries in paediatric patients. A cross-sectional study. Eur J Paediatr Dent 2011;12:112-6.
82. Goulding A, Taylor RW, Jones IE, Manning PJ, Williams SM. Spinal overload: a concern for obese children and adolescents? Osteoporos Int 2002;13:835–40.
83. Pinero J, Rabinovich RR, Alaia MJ, Feldman DS, Otsuka NY. Does body mass influence skeletal age: An analysis using the Tanner-Whitehouse 3 method. J Orthopaedics 2012; 9: e2.
84. Costacurta M, Sicuro L, Di Renzo L, Condò R, De Lorenzo A, Docimo R. Childhood obesity and skeletaldental maturity. Eur J Paediatr Dent 2012; 13: 128- 132.
85. Flores-Mir C, Mauricio FR, Orellana MF, Major PW. Association between growth stunting with dental development and skeletal maturation stage. Angle Orthod 2005; 75: 935-940.
86. Zangouei-Booshehri M, Ezoddini-Ardakani F, Agha Aghili H, Sharifi A. Assessment of the relationship between body mass index (BMI) and dental age. Health 2011; 3: 253-257
87. Chaumoitre K, Lamtali S, Baali A, Saliba-Serre B, Lahmam A, Aboussad A, et al. Influence of socioeconomic status and body mass index on bone age. Horm Res Paediatr 2010; 74: 129-35.
88. Javadinejad S, Karami M, Hashemnia N. Association between body mass index and dental development in 7-15 year old children in the city of Isfahan-Iran in the year 2008. J Mashhad Dent Sch 2010; 34: 109-116.
89. Mack KB, Phillips C, Jain N, Koroluk LD. Relationship

between body mass index percentile and skeletal maturation and dental development in orthodontic patients. Am J Orthod Dentofacial Orthop 2013; 143: 228-234.
90. Chaudhry K, Agarwal A, Rehani U. Interrelationship among dental, skeletal and chronological ages in urban and rural female children. Inter J Clin Pediatr Dent 2010; 3: 79-86.
91. Fatima SS, Rehman R, Chaudhry B. Body mass index or body fat! Which is a better obesity scale for Pakistani population? JPMA. 2014;64(11):1225–8.
92. Baccetti T, Franchi L, McNamara JA Jr. The Cervical Vertebral Maturation (CVM) method for the assessment of optimal treatment timing in dentofacial orthopedics. Semin Orthod 2005; 11: 119-129.
93. Ayatollahi SM, Ghoreshizadeh Z. Prevalence of obesity and overweight among adults in Iran. Obes Rev 2010; 11: 335-337.
94. Mirzazadeh A, Sadeghirad B, Haghdoost AA, Bahrein F, Rezazadeh Kermani M. The Prevalence of Obesity in Iran in Recent Decade; a Systematic Review and MetaAnalysis Study. Iranian J Publ Health 2009; 38: 1-11.
95. Ziaoddini H, Kelishadi R, Kamsari F, Mirmoghtadaee P, Poursafa P. First nationwide survey of prevalence of weight disorders in Iranian children at school entry. World J Pediatr 2010; 6: 223-227.
96. NCD Risk Factor Collaboration (NCD-RisC). Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19.2 million participants. Lancet. 2016;387:1377–96.
97. Flegal KM, Kit BK, Orpana H, Graubard BI. Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis. JAMA. 2013;309:71–82.
98. Innes KE, Selfe TK, Agarwal P. Prevalence of restless legs syndrome in North American and Western European populations: a systematic review. Sleep Med. 2011;12:623–634.
99. Brand S, Gerber M, Beck J, Hatzinger M, Puhse U, Holsboer-Trachsler E. High exercise levels are related to favorable sleep patterns and psychological functioning in adolescents: a comparison of athletes and controls. J Adolesc Health. 2010;46:133–141.
100. Kline CE, Sui X, Hall MH, et al. Dose-response effects of exercise training on the subjective sleep quality of postmenopausal women: exploratory analyses of a randomised controlled trial. BMJ Open. 2012;2:e001044.
101. Trenkwalder C, Paulus W. Restless legs syndrome: pathophysiology, clinical presentation and management. Nat Rev Neurol. 2010;6: 337–346
102. Daniele TM, de Bruin VM, AC EF, de Oliveira DS, Pompeu CM, de Bruin PF. The relationship between physical activity, restless legs syndrome, and health-related quality of life in type 2 diabetes. Endocrine. Epub December 1, 2012.
103. Esteves AM, Mello MT, Benedito-Silva AA, Tufik S. Impact of aerobic physical exerise on Restless Legs Syndrome. Sleep Sci. 2011;4: 45–48.
104. S. Virtue and A. Vidal-Puig, "Adipose tissue expandability, lipotoxicity and the Metabolic Syndrome—an allostatic perspective," Biochimica et Biophysica Acta, vol. 1801, no. 3, pp. 338–349, 2010.
105. P. A. Permana, C. Menge, and P. D. Reaven, "Macrophagesecreted factors induce adipocyte inflammation and insulin resistance," Biochemical and Biophysical Research Communications, vol. 341, no. 2, pp. 507–514, 2006.
106. J. A. Chavez and S. A. Summers, "Lipid oversupply, selective insulin resistance, and lipotoxicity: molecular mechanisms," Biochimica et Biophysica Acta, vol. 1801, no. 3, pp. 252–265, 2010.
107. P. Perez-Martinez, F. Perez-Jimenez, and J. Lopez-Miranda, "n-3 PUFA and lipotoxicity," Biochimica et Biophysica Acta, vol. 1801, no. 3, pp. 362–366, 2010.
108. C. T. Chen, Z. Liu, M. Ouellet, F. Calon, and R. P. Bazinet, "Rapid β-oxidation of eicosapentaenoic acid in mouse brain: an in situ study," Prostaglandins Leukotrienes and Essential Fatty Acids, vol. 80, no. 2-3, pp. 157–163, 2009.
109. L. M. Beckman, T. R. Beckman, and C. P. Earthman, "Changes in gastrointestinal hormones and leptin after Roux-en-Y gastric bypass procedure: a review," Journal of the American Dietetic Association, vol. 110, no. 4, pp. 571–584, 2010.
110. M. Takikawa, S. Inoue, F. Horio, and T. Tsuda, "Dietary anthocyanin-rich bilberry extract ameliorates hyperglycemia and insulin sensitivity via activation of amp-activated protein kinase in diabetic mice," Journal of Nutrition, vol. 140, no. 3, pp. 527–533, 2010.
111. O. Hamdy and C. Carver, "The why WAIT program: improving clinical outcomes through weight management in type 2 diabetes," Current Diabetes Reports, vol. 8, no. 5, pp. 413–420, 2008.
112. Pil, L.; Putman, K.; Cardon, G.; De Bourdeaudhuij, I.; Manios, Y.; Androutsos, O.; Lateva, M.; Lotova, V.; Zych, K.; Gó ´zd ´z, M.; et al. Establishing a method to estimate the cost-effectiveness of a kindergarten-based, family-involved intervention to prevent obesity in early childhood. Obes. Rev. 2014, 15, 81–89.
113. Moodie, M.L.; Herbert, J.K.; de Silva-Sanigorski, A.M.; Mavoa, H.M.; Keating, C.L.; Carter, R.C.; Waters, E.; Gibbs, L.; Swinburn, B.A. The cost-effectiveness of a successful community-based obesity prevention program: The be active eat well program. Obesity 2013, 21, 2072–2080.
114. Hayes, A.; Lung, T.; Wen, L.M.; Baur, L.; Rissel, C.; Howard, K. Economic evaluation of "healthy beginnings" an early childhood intervention to prevent obesity. Obesity 2014, 22, 1709–1715.
115. Seburg, E.M.; Olson-Bullis, B.A.; Bredeson, D.M.; Hayes, M.G.; Sherwood, N.E. A review of primary care-based childhood obesity prevention and treatment interventions. Curr. Obes. Rep. 2015, 4, 157–173.
116. Dietz, W.H.; Gortmaker, S.L. New strategies to prioritize nutrition, physical activity, and obesity interventions. Am. J. Prev. Med. 2016.
117. Villa MP, Rizzoli A, Rabasco J, Vitelli O, Pietropaoli N, Cecili M, et al. Rapid maxillary expansion outcomes in treatment of obstructive sleep apnea in children. Sleep Med. 2015;16(6):709-16.
118. Tapia IE, Marcus CL. Newer treatment modalities for pediatric obstructive sleep apnea. Paediatr Respir Rev. 2013;14(3):199-203.
119. Tarasiuk A., Greenberg-Dotan S., Simon-Tuval T., et al.

Elevated morbidity and health care use in children with obstructive sleep apnea syndrome. Am J Respir Critical Care Med. 2007;175(1):55–61.

120. Reuveni H., Simon T., Tal A., Elhayany A., Tarasiuk A. Health care services utilization in children with obstructive sleep apnea syndrome. Pediatrics. 2002;110(1 I):68–72.
121. Conley R. S., Legan H. L. Correction of severe obstructive sleep apnea with bimaxillary transverse distraction osteogenesis and maxillomandibular advancement. Am J Orthod Dent Orthop 2006;129(2):283–292.
122. Jacobson R. L., Schendel S. A. Treating obstructive sleep apnea: the case for surgery. Am J Orthod Dent Orthop 2012;142(4):435–442.
123. Oliveira De Felippe N. L., Da Silveira A. C., Viana G., Kusnoto B., Smith B., Evans C. A. Relationship between rapid maxillary expansion and nasal cavity size and airway resistance: short- and long-term effects. Am J Orthod Dent Orthop. 2008;134(3):370–382.
124. Timms D. J. The effect of rapid maxillary expansion on nasal airway resistance. Brit J of Orthod. 1986;13(4):221–228.

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