PEDIATRIC OBESITY
EDITORIAL
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How growing up sweet can turn sour

Today's infants and children are growing up in a much sweeter nutritional environment than previous generations. Negotiating added sweeteners, sugary beverages and sweet snack foods has become an important daily task in bringing up today's children. Even though sugary beverage consumption, which contributes the most to this phenomenon, is declining at least in the United States (1,2), there is no denying the generational shift in the nutritional landscape of children who are now growing up with much greater access and exposure to sweeter foods and beverages. As summarized in this issue (3), analysis of the food supply in the United States shows that >70% of foods contain sugar, and consumption of soft drinks, including juices, has increased fivefold since 1950 (4), and studies from across the globe not presented in this issue show sugary beverage consumption is rising very rapidly (5–8). This sweeter environment includes not just an increase in ordinary table sugar (sucrose), but a whole host of other alternative natural and artificial sweeteners that are appearing in the food supply, some of which are likely to have important consequences on growth and development relevant to obesity and associated disease risk that could be distinctly different from sucrose. While much research has been done to examine the 'sweeter' food environment and its effects on obesity and disease risk in general, much less research has considered how this phenomenon specifically affects growth and development of infants and children. In this special issue, we present a series of new work that focuses on this problem as it relates to paediatric populations.

The accompanying editorial by Bray and Popkin presents an update on an important hypothesis that these authors proposed 10 years ago (9). In their landmark paper, they discussed the impact of the appearance of high-fructose corn syrup (HFCS) in the food supply as a potential contributor to the obesity epidemic (10). Since this earlier publication, a new body of science has emerged and established the evidence for strong links between dietary sugars, especially fructose, and obesity and metabolic risk, including fatty liver disease, which notably has more than doubled in children in the last 10 years (11). Greater fructose consumption in adolescents has been shown to be associated with cardiometabolic risk and this is mediated through effects on increasing visceral adiposity (12). These findings suggest that greater exposure to fructose also probably contributes to the rise in paediatric fatty liver disease that is occurring (11), although specific data supporting this link have not yet been analysed. A new review by Stanhope *et al*. outlines how metabolism of the fructose moiety of sucrose explains many of these adverse metabolic effects (13). These effects are likely to be worse during growth and development because fructose promotes adipose tissue differentiation during growth (14). In support of this concept, the paper in this special issue by Disse *et al*. shows that children with fructose malabsorption have lower levels of obesity (15). Although not definitive, because this finding may also be explained by 'loss of calories' or effects of fructose in the gastrointestinal system promoting gut flora that would protect against obesity, this finding supports the concept of a more damaging effect of fructose on obesity during growth, and merits further investigation that should also include stronger measures of body composition/fat distribution and metabolic outcomes.

Also, in this issue, Morgan presents results of a systematic literature review on the links between HFCS and obesity in children (16). This analysis yielded mixed results with some studies showing an effect and others showing null effects. However, the number and quality of studies in this area are very limited and remain focused on body weight, rather than body fat distribution and metabolic risk as outcomes, and have not considered the increased fructose exposure that comes from fruit juices. For example, the impact of a shift towards use of HFCS and greater fruit juice consumption should be examined in the context of the estimated doubling of fatty liver disease among US children and adolescents that was recently reported (11).

Although some would argue that the overall consumption of sugar and fructose have declined in recent years (a trend found only at most in a few countries but not globally), it is important to point out that levels are still higher from a generational perspective, and that much of the world is experiencing major increases in sugar intake and hence fructose

consumption. This imbalance and shift towards more fructose in the food supply has important implications for the growing and developing infants and children (17). For example, the shift from drinking milk in infancy and childhood to sodas and juices has a major implication in fructose load because milk contains no fructose, whereas beverages and in particular fruit juices can be very high in fructose. In beverages made with HFCS, we recently showed higher than expected fructose content. This tips the balance from an equivalence of fructose and glucose that's found in sucrose, to ~50% more fructose than glucose in beverages made with HFCS (18). This would translate to a 12 fluid oz (350 mL) serving of soda made with HFCS having 23 g of free fructose with probably higher amounts in a similar serving size of fruit juice. Two such servings would be sufficient to almost reach the 90th percentile for population levels of fructose consumption for young children (19), without even taking into account the fructose that would be consumed from other natural sources (fruits) and contained in other foods and beverages made with either sucrose or HFCS. The impact of this imbalance towards greater amounts of fructose in the food supply on the obesity and metabolic risk during growth and development is an important area of future study, because the evidence suggests that fructose is obesogenic during these critical periods (17).

The paper in this issue by Piernas *et al*. presents a comprehensive analysis of purchase and intake patterns of foods and beverages containing caloric and low or non-caloric sweeteners in the United States as an example of dynamic shifts underway in one high-income country (20). This unique analysis identified a previously unexplored trend related to increasing purchase and consumption of products containing lower calorie sweeteners or a mixture of sweetener types in the same product including dual use of caloric and low-caloric sweeteners. This is an important issue for growing children because the impact of alternative sweeteners on obesity and associated disease risk is a virtually unstudied area. A recent study, for example, showed that sucralose in obese adults has subtle but important effects on glucose and insulin (21) that would increase the risk for type 2 diabetes. Thus, it is going to be critically important to get a better insight into how alternative sweeteners have particular effects on the regulation of energy balance and metabolic risk during growth and development. Piernas *et al*. also showed that over the last 10 years, the purchase and intake of foods and beverages made with caloric sweeteners has continued to decline in the United States (20). It is important to point out that despite this recent decline, levels of sugar consumption/purchase remain particularly high in vulnerable segments of the US population that are susceptible to obesity (e.g. Hispanic, African–American, low income) and are certainly higher from a generational perspective. This result is reflected by the findings of a similar paper in this issue by Slining and Popkin (3). This comprehensive analysis of the US food supply showed that trends in intakes of solid fats and sugars in the United States declined between 1994 and 2010 but still remain above recommended levels. Also, we must not ignore the rapid increase in marketing and consumption of these sugary beverages that is occurring globally (5–8,22,23).

Despite the growing evidence of the links between sugar consumption and obesity and metabolic risk in children, not all studies support this relationship, demonstrating heterogeneity in the population in these effects. For example, two papers by Jensen *et al*. in this issue examined the link between sugary beverage consumption and development of obesity in two non-US populations in Australia (24) and Denmark (25) but failed to demonstrate convincing evidence. Despite the lack of effects, these papers reveal important and relevant findings. In the first of these papers, longitudinal data between 2003 and 2008 from 1465 children and adolescents from Victoria, Australia, were analysed with a mean follow-up period of 2.2 years (24). This analysis showed 'limited evidence' of a link between sugary beverage consumption and change in obesity. However, the authors did find that higher consumption of fruit juices, and cordials was associated with higher obesity at follow-up. In the second paper, data from 359 6-year-old children in Denmark were analysed with follow-up data at ages 9 and 13 years, but failed to find convincing evidence of an effect of sugary beverage consumption on the development of obesity (25).

These findings are in contrast to several studies that demonstrate a link between sugary beverages and obesity in children as young as 2–4 years of age (26,27), as well as more rigorous intervention studies in older adolescents in the United States (28,29) and in the Netherlands (30). These mixed findings across the population point out a couple of important features that require further consideration (i) Assessment of accurate levels of beverage consumption is challenging in children and only accounts for partial contribution to patterns of total sugar and type of sugar consumption. (ii) The type of sugar used in the food supply varies globally. For example, neither Australia nor Denmark use HFCS in its food supply (31) so typical sodas in these countries are likely to be

predominantly sweetened with sucrose not HFCS, so overall fructose exposure may be lower in these countries. The findings in the study by Jensen *et al*. of a link between juices/cordials and obesity are interesting in this regard and might be explained by the higher fructose content in juices/cordials compared with other sweetened beverages being consumed in the absence of HFCS, and this study fits with an earlier Australian study on the effects of fruit juices on children (32). (iii) The effects of sugar on obesity has been shown to vary across different segments of the population. In the United States, for example, longitudinal and intervention studies have shown a stronger impact of dietary sugar on obesity in Hispanics compared with non-Hispanics (28,33). (iv) Outcome measures from the two studies by Jensen *et al*. were limited to body weight or skinfolds (24,25). Because studies have shown that higher levels of sugar/fructose have stronger effects on visceral and/or liver fat (34), future studies should focus on the impact of sugar/fructose on body fat pattern, especially visceral and/or liver fat as well as metabolic outcomes.

Although the links between increased sugar/fructose consumption and obesity and children remain mixed, one clear finding is that increasing sugar/fructose contributes to an altered body fat profile that would promote metabolic risk, as reviewed in the Bray and Popkin editorial (9). In addition, another clear finding is that higher levels of dietary sugar/fructose promote metabolic dys-regulation, especially in the obese state. This was clearly shown in a recent paper by Welsh *et al*. using National Health and Nutrition Examination Survey (NHANES) data in the United States to show that the impact of increasing levels of dietary sugar had little or no impact on insulin resistance and dyslipidemia in lean children and adolescents, but had adverse effects on these outcomes in obese children and adolescents (2). This concept is evidently demonstrated in this special issue in the paper by Wang *et al*. (35), using data from the QUébec Adiposity and Lifestyle InvesTigation in Youth study (2005–2008) that examined 632 Caucasian children aged 8–10 years from Québec, Canada. This analysis showed how greater consumption of sugar-sweetened beverages was associated with greater metabolic risk in overweight and obese children and children with impaired glucose tolerance, with no such relationships in normal weight children. Thus, being overweight or obese clearly exacerbates the adverse effects of increasing dietary sugar on metabolic risk during childhood.

Despite the mixed findings and gaps in our understanding related to the impact of dietary sugars on obesity and metabolic risk in paediatric populations, most would support that a major focus of current public health efforts should be to reduce overall consumption of sugars, especially fructose. For reasons described previously, this is a critically important issue in infants and children because of the underlying effects of excess sugars, particularly fructose, on growth and development of adipose tissue, brain and other organ systems during these critical periods. Children are also particularly vulnerable to this issue because food companies target marketing efforts of sugary foods and beverages heavily towards children, because these are the very foods that children crave and therefore drive higher sales and profits. Consequently, targeting food and beverage marketing practices is an important public health strategy to curtail this problem. In the current issue, Brinsden and Lobstein performed a detailed comparison of recent voluntary pledges by the food and beverage industry to reduce children's marketing exposure to energy-dense foods and beverages (36). They compared the recently developed and about to be launched schemes that were proposed by the industry in the United States and by European Union as well as three government-led schemes. This interesting analysis examined 178 different products and evaluated which ones would be approved for marketing under the different schemes. They showed that the industry-led voluntary pledges would allow 40–50% of products to be advertised, whereas the government-led schemes would be more restrictive, with a proposal from Denmark being the most restrictive allowing only 7% of products to be advertised to children (36). Interestingly, the government-led schemes appear to have more stringent criteria relating to sugar content of foods and beverages. This analysis confirms that we should not rely on industry-led initiatives in these public health efforts.

To summarize, the following issues arise from the shift towards a sweeter nutritional environment and are specific to infants and children during growth and development. These issues merit further consideration and future research relative to the potential adverse effects of increasing sugar and particularly fructose exposure during these critical periods that can turn a period of ‘sweet growth’, fuelled by sweet foods and beverages, into a ‘sour outcome’ of lifelong risk for obesity and related metabolic complications:

1. The effects of increased dietary sugar on obesity and metabolic risk are variable across studies and across populations. This merits further investigation to understand why some segments of the population such as Hispanics, for example (28), appear to be

more vulnerable to the negative effects of increasing sugar during growth and development. This could potentially be explained by metabolic, behavioural and/or genotypic differences between individuals and subgroups, and/or exposure differences explained by use of different/varied sweeteners in the food supply in different countries.

2. Obesity exacerbates the effects of sugar on metabolic outcomes during growth and development. Thus, efforts to reduce sugar should focus on the overweight and obese, and would benefit from focus not just on obesity as an outcome but also on reducing metabolic risk.

3. Increased exposure to sugar/fructose can be a 'double-edged sword' because of the dual effects of links to obesity as well as links to metabolic risk, either through direct effects of increased sugar/fructose or additional effects mediated through obesity.

4. A generational shift in the food supply towards greater fructose exposure, from either sucrose or alternative sweeteners that are higher in fructose content, affects the development of obesity and adverse metabolic outcomes during critical periods when adipose tissue is being laid down and during periods of brain and cognitive development related to appetite regulation. This is important because fructose has very different effects on the brain (37) and appetite regulation (38) that favour the development of obesity.

5. There is a need for a better evaluation of how much fructose we are really consuming due to the high likelihood of 'hidden fructose' in the food supply. Actual fructose consumption levels are difficult to estimate because of unclear regulations governing the fructose content of HFCS, the increasing use of fruit sugar and the increasing shift towards juice consumption in children that may have higher and unknown amounts of fructose, even if present in natural levels. For example, fructose content in popular beverages sweetened by HFCS can account for up to 65% of the sugar content (18,39).

6. Fructose is likely to have a complicated 'dose effect' on adverse metabolic outcomes that is driven not only just by consumption but, as suggested by Ludwig (40), also by the rate and dose at which the liver is exposed to fructose. This is an important issue because fructose is metabolized almost exclusively in the liver from where the adverse effects arise (41). Thus, free fructose (from HFCS, fruit juices, fruit sugar, free fructose added to foods as a sweetener) will likely have greater potential impact on adverse metabolic outcomes as compared with fructose liberated from sucrose, and the slower release and lower amounts of fructose liberated from fruit consumption.

7. There is a major gap in our understanding of how exposure to alternative non-caloric sweeteners affects obesity and metabolic risk over the long term during growth and development. This is an important area because of widespread and increasing use of a wide variety of different sweeteners in the food supply.

8. Broad public health efforts are needed using various approaches to change our cultural norms and 'wean' our children and ourselves as a society to lower levels of dietary sugar/fructose consumption, and should focus on marketing strategies that specifically target babies, infants and children.

9. Type of sugar matters, because it is the metabolism of the fructose moiety that has such adverse effects. This issue is likely even more problematic in growing infants and children because fructose appears to have obesogenic effects during growth and development of adipose tissue and multiple organ systems involved with obesity and associated chronic disease risk (17).

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