COMMENTARY

How sugar-containing drinks might increase adiposity in children

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Many epidemiological studies have concluded that intake of carbohydrate (CHO) or even sucrose bears no relation with body adiposity, or the relation may be a negative one.[1] Children and adults who ingest large amounts of CHO, sucrose, or both are leaner than their peers. The high intake of CHO in some respondents might reflect high levels of physical activity. Another reason for the lack of relation between CHO intake and adiposity may be inaccuracy in assessing intake—the "doubly-labelled water method" used for measuring energy expenditure in free-living individuals has recently cast doubt on the validity of self-reported food intake for adults, although such data are more valid for children.[2] Yet another reason could be that very active children need and ingest much sugar.

In today's *Lancet* David Ludwig and colleagues provide convincing new evidence about the relation between sugar intake and development of adiposity in children. They show that consumption of sugar-sweetened beverages is an independent risk factor for obesity in children aged 11–12 years. What could account for such an association? Perhaps it is, as suggested by Ludwig and colleagues, the well-demonstrated fact that compensation at subsequent meals for energy consumed in the form of a liquid is less complete than for energy consumed in solid form.[3]

There have been many studies showing that energy compensation in adults is, at best, approximate, even with solid foods. In free-living human beings, weekly food diaries reveal no adjustment of intake over 1 or a few days.[4] Under experimental conditions, a pre-load is commonly given to find out whether human beings adjust later intake according to the energy or nutrient content of the pre-load. In adults, all possible responses have been found, from no compensation to rather accurate compensation.[5] Compensation seems to be especially poor if the pre-load is a liquid product.[6] In addition, adults compensate better for a dilute pre-load (by eating more at the next occasion) than for a dense pre-load (by eating less at the next occasion). Imperfect compensation could easily lead to occasional or chronic excess of intake over expenditure, resulting in progressive accumulation of body fat over a lifetime.

Children do better than adults in pre-load experiments. Pre-school children showed both unconditioned and conditioned adjustment of intake at their next meal as a function of the energy contained in a liquid or semisolid pre-load.[7,8] They were more accurate in their energy compensation than were young adults.[9] Slightly older children (9–10 years), however, ate the same amount at lunch whatever the energy content of liquid pre-loads.[10] In adolescents, some compensation occurred at dinner after semisolid snacks the energy content of which had covertly been varied.[11] Compensation improved with repeated exposure to the snacks, thereby demonstrating a learning effect. Compensation for energy consumed in liquid form, which can be observed in very young children (4–5 years), is lost rapidly in the following years, for as yet unknown reasons. Perhaps learning to eat in response to social signals rather than to physiological ones contributes to the decrease in ability to compensate adequately.

The notion of energy density has cast light on the compensation issue. The very high energy density of the diet in developed countries makes compensation for energy excess very difficult, even though it would facilitate compensation for energy deficits.[12] The foods available to children certainly make it difficult for them to compensate for excess energy intake, either ingested in liquid or solid form, whatever their ability to do so under well-controlled laboratory conditions.

In Ludwig and colleagues' study the average body-mass index (BMI) was high (corresponding to the 85th centile of the most recent reference values[13]) and a large proportion of the children were obese. It would be interesting to study the relation between intake of sugar-sweetened beverages and body adiposity over a broader range of BMI values. Overweight or obese children are less accurate than their lean peers in compensating for previous energy intakes.[14] Perhaps many children in Ludwig and colleagues' study had pre-existing difficulties with energy regulation that explained why they were fat at the start of the experiment, and why they did not compensate well for sugar-sweetened drinks over the 21 months of the study. Although the physiological rise in BMI values occurs at all BMI levels between these ages,[13] the high level of adiposity in this sample is indicative of an overweight or obesity-prone population whose ability to regulate energy is not ideal.

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Molecular cytogenetics in cancer

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Since identification of the Philadelphia-chromosome in patients with chronic myeloid leukaemia,[1,2] more than 25 000 cases of haematological cancers and 11 000 cases of solid tumours have been karyotyped and reported by July, 2000.[3] Recurrent and characteristic chromosome abnormalities, commonly of major diagnostic and prognostic importance, have been observed in many malignant tumours.

Generally, chromosome aberrations are either balanced, with relocation but without visible gain or loss of material, or unbalanced, with gain or loss of chromosome material. From both a biological (panel) and a diagnostic point of view, the two types of aberration differ greatly. Reciprocal balanced translocations with mutual exchange of material between two chromosomes and inversions with relocation of material within the same chromosome both originate from two double-strand breaks of DNA followed by their illegitimate recombinations. Topoisomerase II[4] and V(D)J-recombinase[5] have been involved in these events.

Biological differences between general types of chromosome aberration

	Recurrent balanced	Recurrent unbalanced
Origin	Double-strand breaks of DNA followed by illegitimate recombinations, mediated by topoisomerase II, or VDJ-recombinase	Diffuse damage of DNA with gain or loss of chromosome material
Genetic effect	Chimeric fusion genes with a dominant effect or gene activation	Chromosomal gain or loss or activating the effects of mutations of putative recessive genes

Chimeric gene fusions in AML and related diseases with recurrent balanced chromosome aberrations