Alarming Trends in Childhood and Adolescent Obesity in Israel

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Childhood obesity is a chronic and serious public health problem associated with a large variety of related co-morbidity [1-3]. Greater degrees of obesity throughout childhood are associated with clustering of cardiovascular risk factors, mostly driven by obesity related insulin resistance [4]. Importantly, childhood obesity tends to track into adulthood in a significant proportion of those presenting with it. Specifically, while 25– 50% of obese toddlers and pre-school children, respectively, will be obese in young adulthood, more than 70% of obese children and adolescents aged 6–18 years will remain obese in young adulthood [5].

Beyond the early appearance of obesity driven morbidity in early childhood, longer exposure to obesity status during childhood is associated with a worse metabolic phenotype compared to adolescents who developed obesity later [6]. Notably, increased childhood body mass index (BMI), even within the normal range, confers increased risk for all-cause mortality and specifically mortality related to cardiovascular disease [7]. Thus, early appearance of obesity in younger children poses a triple jeopardy of immediate development of morbidity, increased risk of morbidity in later childhood, and risks of obesity in adulthood. The prevalence of childhood obesity is on the rise in some parts of the world and seems to have plateaued in others [8]. Yet, the situation in Israel, a Middle Eastern country with an ethnically diverse population, is not clear.

The evaluation of obesity involves comparing anthropometric measures to population-derived reference values. The distribution of these measures is defined using standard statistical tools. The upper/lower 5% is usually considered a threshold for defining a deviation from the norm. To have clinical relevance, this threshold is used to evaluate whether it confers increased risk for a pathological outcome. It is critical to use a reference population that is as representative as possible to the patient population to reach valid clinical conclusions.

There are two commonly used pediatric growth tables: the U.S. Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO). Israel is a Western country with regard to living conditions and nutrition patterns, yet it has a very ethnically diverse population. Therefore, it is not trivial to choose the most representative population to be used as a growth chart reference.

In this issue of Israel Medical Association Journal (IMAJ), Gabbay and colleagues [9] provided a large-scale analysis of anthropometric measurements of Israeli children and adolescents and compared their distribution with both CDC and WHO growth tables. The findings are important and alarming: boys and girls demonstrate a BMI that is significantly higher compared to the CDC and WHO benchmarks consistently along the entire age range of 4 to 18 years. The finding that Israeli children have a slightly shorter final height compared to both reference charts does not explain the findings regarding BMI, specifically in the younger children. The most significant finding is that the deviation toward a greater BMI already appears by the age of 4 years and may be evident even earlier. Importantly, this alarming finding is not explained by choosing the wrong reference for comparison.

Management of obesity at any age is challenging. While obese adults have a standard lifestyle modification approach and a modest selection of pharmacological options for obesity management [10], the possibilities for treatment of children, specifically younger than 12 years of age, are limited. Popular bariatric surgical options are reserved for morbidly obese adolescents and are less relevant for younger children with lower degrees of obesity with or without related comorbidity. Importantly, the success rate of lifestyle and behavioral modification programs for obese children are modest and largely non-sustainable [11]. This situation leaves us with only one potentially effective strategy to address the alarming findings described by Gabbay et al. [9]: primary prevention programs against obesity.

As Gabbay et al. [9] showed, Israeli children deviate upward in the BMI charts already by 4 years of age. This means that the window of opportunity for obesity prevention is during pregnancy and in the infant and toddler years. The wealth of data in the literature indicates that a combination of dietary measures and in-
increased physical activity can reduce the risk of obesity (standardized BMI and BMI) in young children aged 0 to 5 years [12]. There is some evidence that isolated dietary interventions may be beneficial, while focusing solely on increased physical activity does not appear to be effective in children of this age group.

A critical window of opportunity for childhood obesity prevention is during pregnancy and the perinatal period. Increasing evidence indicates that intrauterine exposure to maternal obesity significantly increases the risk of early obesity development in the offspring [13]. Moreover, increased gestational weight gain, independent of degree of obesity, is also associated with early development of obesity in the offspring [14]. Thus, it is crucial to encourage and promote prevention programs before and throughout pregnancy aiming at breaking the inter-generational cycle of obesity [15].

Data from 22 European countries clearly indicates that breastfeeding is associated with lower risk of childhood obesity. Specifically, compared to children who are breastfed for at least 6 months, the odds of being obese are significantly higher among children never breastfed or breastfed for a shorter period [16]. Moreover, breastfeeding may attenuate BMI increase in children with a genetic susceptibility to obesity, defined using an obesity-specific genetic risk score constructed from genome-wide significant genetic variants [17]. Specifically, it was shown that exclusive breastfeeding in infancy delays the age of adiposity rebound. Thus, exclusive breastfeeding may present a major factor in preventing obesity among children at high risk due to genetic factors.

The increase in childhood obesity prevalence across the world has been associated with a rise in the consumption of highly processed fast foods and sugar sweetened beverages, starting at a very early age. These changes in dietary habits and the nature of food intake among children may partly explain the rise in childhood obesity observed in recent years [18]. It is reasonable to assume that the greater energy intake in young children who consume large amounts of soft drinks and calorie dense highly processed foods are not compensated for by increased physical activity or a decrease in other dietary elements resulting in a chronic calorie surplus. Specifically, with regard to young children, consumption of sugar sweetened beverages often reduces the consumption of healthier beverage options such as water or nutrient-dense beverages such as milk. Moreover, a higher added sugar intake in childhood is associated with an adverse metabolic phenotype of cardiovascular risk factor clustering, independent of total energy intake, physical activity, or degree of obesity [19]. Thus, simple interventions aimed at minimizing exposure to sugar sweetened beverages and highly processed food before the age of 3 years may have a tremendous impact on obesity occurrence [3].

The main message of the WHO European Childhood Obesity Surveillance Initiative [20] is that primary prevention is critical to reduce childhood obesity prevalence. It is simpler and more effective to act on the adoption of healthy eating habits in pregnant women, infants, and toddlers than to intervene with diets in children who already have developed overweight or obesity status. Such prevention should focus on critical periods of opportunity, including pre-conception, pregnancy, infancy, and early childhood. Israel has the ideal infrastructure (Tipat Halav), which is used for pregnancy counseling care as well as infant well care visits and vaccination administration, to implement such interventions. This infrastructure can be used for nutritional education during and after pregnancy and for the identification of infants and toddlers who are gaining weight inappropriately. Such intervention can address abnormal weight gain, which will be much more difficult to manage later. Therefore, primary prevention programs focusing in very early childhood should be prioritized at a national level.

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References


Capsule

Targeting the SARS-CoV-2 main protease

Vaccines are an important tool in the fight against COVID-19, but developing antiviral drugs is also a high priority, especially with the rise of variants that may partially evade vaccines. The viral protein main protease is required for cleaving precursor polyproteins into functional viral proteins. This essential function makes it a key drug target. Qiao et al. designed 32 inhibitors based on either boceprevir or telaprevir, both of which are protease inhibitors approved to treat hepatitis C virus. Six compounds protected cells from viral infection with high potency, and two of these were selected for in vivo studies based on pharmokinetic experiments. Both showed strong antiviral activity in a mouse model.

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Eitan Israeli

Capsule

The STAR-T cells to treat cancer

Chimeric antigen receptor T (CAR-T) cells have revolutionized treatment for hematological cancers, but this success has not translated to solid tumors. To address this challenge, Liu et al. engineered a synthetic T cell receptor and antigen receptor (STAR) that combines the specificity of a CAR and the internal signaling machinery of an endogenous T cell receptor. STAR-T cells outperformed their CAR-T cell counterparts in controlling multiple murine tumors and did not display evidence of the exhaustion frequently observed in CAR-T cells. These results suggest that STAR-T cells may be an attractive option for treating patients with solid tumors.

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Capsule

Keeping cGAS silent

Cells detect microbial and self-DNA in the cytosol as a danger signal that triggers immune and inflammatory responses. Paradoxically, a large fraction of a DNA-sensing enzyme called cGAS is tightly associated with the chromatin, especially during mitosis. Li et al. uncovered two mechanisms that prevent cGAS from being activated by the chromatin DNA. First, cGAS is hyperphosphorylated as cells enter mitosis, thereby inhibiting its DNA-binding and liquid-liquid phase separation, which promotes cGAS activation. Second, chromatin-bound cGAS is unable to oligomerize, a process required for its activation. Together, these mechanisms ensure cGAS inactivation during cell division to prevent autoimmune reactions.

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A word is not a crystal, transparent and unchanging; it is the skin of living thought and changes from day to day as does the air around us.

Oliver Wendell Holmes, Jr. (1841–1935), American jurist who served as an Associate Justice of the Supreme Court of the United States from 1902 to 1922.