EDU-DORA2 (Education thérapeutique et préventive face au Diabète et à l'Obésité à Risque chez l'Adulte et l'Adolescent) is being conducted in Belgium, Luxemburg and Lorraine to investigate potential working tracks for a multifactorial and multidisciplinary approach in the management of childhood obesity (Scheen *et al.* 2010).

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Drug therapy: actuality and perspectives

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The main role of regulators is to authorize the access to safe and efficacious medicinal products. The risk–benefit of a candidate drug should be positive for a specific disease and a target population. But is overweight or obesity as such a disease? Who should potentially be treated and be prescribed pharmacological agents? When so, what is considered to be a clinically relevant drug effect? Some answers are given for adults in 'Guideline on Clinical Evaluation of Medicinal Products used in Weight Control' by the Committee for Human Medicinal Products of the European Medicines Agency and for children in the 'Paediatric Addendum Guideline on Clinical Evaluation of Medicinal Products used in Weight Control'.

The simple conclusion of this guidance could well read: 'There is some room for drug therapy in childhood obesity, namely in severe cases and for limited duration, provided that the medicinal product is harmless and its effect sustained'. If indirect evidence demonstrates the risks linked to overweight, the impact of a drastic weight control on obesity-related complications needs to be prospectively demonstrated in clinical trial conditions to define who will really benefit from a pharmacological treatment. Ideally the clinical relevance of a treatment allowing to lose weight (or to maintain an 'ideal' weight) should translate in less complications later in life, an increased life expectancy and a better quality of life also based on improved self-esteem. In practice such a composite endpoint is not achievable in pharmaceutical trials in an acceptable time frame. More realistically, the surrogate marker is weight (loss) accepted as a primary endpoint in most clinical trials (CT). The way to conduct CT is currently driven by the experience gained from past investigations in the field. Weight losses are often transient since partial failure or full relapses are frequent. Patients should be obese as defined, and have a documented history of failing to lose weight by means of lifestyle modifications, before enrolment into the pharmacological phase of a study. Further confounding factors related or not to the drug studied may affect the outcome of trials. Therefore regulators are de facto suspicious and require a robust methodology to circumvent bias as much as possible. The lessons learnt from the past have also contributed to carefully monitor the safety of weight losing agents. The guidance recommends collecting information during the whole trial period. Particular attention should be given to adverse events signalled from adult CT. This data set should notably encompass the adverse events related to lipid profile, liver function, cardiovascular system function and rebound phenomenon.

For centrally acting anorectic agents it is recommended that special attention and monitoring is afforded to neuropsychiatric events such as depression, sleep pattern and nightmares, assessment of self-esteem, aggression or suicidality. In growing children height velocity should also be monitored and pubertal development assessed by determining Tanner stage at baseline and endpoint. Today the tools for a quicker development of pharmacological agents are available (EC Paediatric Regulation 1901/2006) and can be used for future candidate drugs.

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'Over' or 'bad'-nutrition?

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Food intake and behaviour are considered the most important etiological factor of obesity in childhood and adolescence. The efficacy of dietary treatment depends on the regard for different stages designed to help the child and his family to modify on the long term their dietary habits, behaviour and lifestyle.

The first stage in the dietary approach is to understand the child's way of life, physical activity level, the actual food habits and the level of food intakes as exactly as possible in terms of quality and quantity, meal by meal, snacks, candies, drank during day and night. The methodology of 24 h recall is applied during the consultation, completed by an FFQ, taking into account vitamins and minerals supplementations. This evaluation gives the opportunity to demonstrate possible 'over' consumptions as well as low intakes in some nutrients, inducing possibly specific nutritional deficiencies. The intakes are estimated as 'over' consumption or 'under' consumption by comparing with nutritional recommendations for the age, taking into account the physical activity level, and are not evaluated by comparing with dietary intakes of non-obese children of same age and sex.

As usually observed in the literature, energy intakes are frequently higher compared with recommended dietary allowances, taking into account a very low level of physical activity. Among our patients, we observed an over consumption of proteins, fat, saturated fatty acids, sucrose and sodium. We also frequently observed very low intakes in some nutrients in spite of hyper caloric diet. High consumption of fruit juice or sodas to the detriment of milk causes calcium deficiency. Avoiding vegetables, fruits, high fibre breads and cereals induce very low fibre consumption. The frequent high-fat diet is mostly characterized by an over consumption of saturated fatty acids while insufficient intakes of poly-unsaturated fatty acids, inducing a poor fat balance. It is also frequently observed that the parents avoid giving vitamin D supplementation, considering that vitamins in general increase obesity. The plasma 25-hydroxyvitamin D is below the normal range in about 35 % of our patients. Dietary habits and food intakes evaluation, including vitamins and minerals supplements, are necessary to elaborate feasible nutritional recommendations in order to correct over nutrition as well as nutrient deficiencies.

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Sleep loss and weight gain

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Epidemiology: Sleep disordered breathing (SDB) has a prevalence of 2 % in the general paediatric population and is mostly caused by adenotonsillar hypertrophy. In children with obesity SDB is diagnosed in 13–59 %.

Metabolic consequences: SDB in obese children is an independent risk factor for the metabolic syndrome. The severity of the sleep disorder is associated with the degree of metabolic deregulation. Possible links are systemic inflammation and oxidative stress. In SDB, increased concentrations of C-reactive protein and interleukin-6 and a decrease in interleukin-10 levels is observed. This inflammatory response is linked to the severity of SDB. Evidence for a role of oxidative stress is provided by an ongoing study of our group, showing higher uric acid concentrations, a parameter for oxidative stress, in obese children with SDB. Both the increased inflammatory response and the elevated uric acid levels disappear when SDB is treated with Aden tonsillectomy or weight loss.

Future research: First of all, the mechanisms by which these metabolic consequences develop are still unclear. I t is known that adipose tissue actively secretes adipokines. These molecules contribute to the pathogenesis of insulin resistance and other metabolic disorders. Therefore future studies focus on the effects of hypoxia on fat tissue and the excretion of such adipokines. Secondly, prospective studies are designed to evaluate the effects of the two therapeutic modalities for SDB in obese children: weight loss by diet plus physical activity and adenotonsillectomy.

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Psychological subtypes in obese children

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