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PAPER

Clinical aspects of obesity in childhood and adolescence — diagnosis, treatment and prevention

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The level of fatness at which morbidity increases is determined on an acturial basis. Direct measurements of body fat content, eg hydrodensitometry, bioimpedance or DEXA, are useful tools in scientific studies. However, body mass index (BMI) is easy to calculate and is frequently used to define obesity clinically.

An increased risk of death from cardiovascular disease in adults has been found in subjects whose BMI had been greater than the 75th percentile as adolescents. Childhood obesity seems to increase the risk of subsequent morbidity whether or not obesity persists into adulthood.

The genetic basis of childhood obesity has been elucidated to some extent through the discovery of leptin, the *ob* gene product, and the increasing knowledge on the role of neuropeptides such as POMC, neuropeptide Y (NPY) and the melanocyte concentrating hormone receptors (MC4R). Environmental/exogenous factors contribute to the development of a high degree of body fatness early in life. Twin studies suggest that approximately 50% of the tendency toward obesity is inherited. There are numerous disorders including a number of endocrine disorders (Cushing's syndrome, hypothyroidism, etc) and genetic syndromes (Prader–Labhard–Willi syndrome, Bardet–Biedl syndrome etc) that can present with obesity.

A simple diagnostic algorithm allows for the differentiation between primary or secondary obesity. Among the most common sequelae of primary childhood obesity are hypertension, dyslipidemia and psychosocial problems.

Therapeutic strategies include psychological and family therapy, lifestyle/behavior modification and nutrition education. The role of regular exercise and exercise programs is emphasized. Surgical procedures and drugs used as treatments for adult obesity are still not recommended for children and adolscents with obesity. As obesity is the most common chronic disorder in the industrialized societies, its impact on individual lives as well as on health economics has to be recognized more widely.

This review is aimed towards defining the clinical problem of childhood obesity on the basis of current knowledge and towards outlining future research areas in the field of energy homoeostasis and food intake control.
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Definition of obesity in childhood and adolescence

The level of fatness at which morbidity increases is determined on an acturial basis. Direct measurements of body fat content, eg hydrodensitometry, bioimpedance or DEXA are useful tools in scientific studies; however, body-mass index (BMI; weight in kilograms divided by the square of the height in meters) is easy to calculate and is correlated sufficiently with direct measures of fatness. BMI is therefore frequently used to define obesity clinically. Accordingly, a child with a BMI above the 97th centile in regard to age and gender is considered to be obese.

In adults, a BMI greater than 28 kg/m^2 is associated with an increased risk of morbidity such as stroke, ischemic heart disease, sleep-apnea syndrome, orthopaedic diseases or type 2 diabetes mellitus. A central distribution of body fat is also associated with a higher risk of morbidity and mortality.[1–5] In addition and most importantly, an increased risk of death from cardiovascular disease in adults has been found in subjects whose BMI had been greater than the 75th percentile as adolescents.[3] Childhood obesity seems to increase the risk of subsequent morbidity whether or not obesity persists in adulthood.[2,6–8] A working definition of obesity in childhood has been a BMI greater than the 85th percentile. Morbid or severe obesity is defined as being characterized by a BMI above the 99th centile for age and gender.[5,9]

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Epidemiology of childhood obesity

The Bogalusa heart study found that 22% of the children surveyed in 1990 had a body mass index greater than the

85th percentile established in a similar survey conducted in 1980. There was little change in the cohorts of children with a BMI less than the 50th percentile. In contrast, there was a large increase in BMI in the cohorts with a BMI greater than the 50th percentile. In summary, over time, obese children have a tendency towards even more excessive weight.[4,8] It has become clear that childhood obesity has reached epidemic proportions in all industralized countries. The current age-adjusted prevalence may be as high as 20–30%. The prevalence of massive obesity as defined as a BMI > 25 kg/m^2 in French infants was found to be approximately 2% in 1996.[5] In the German state of Saxony approximately 8% of schoolchildren in third and fifth grade have been found to be obese (20% increased body weight in relation to height centile). In another survey of German public health authorities in Southern Germany 13% of the adolescents at the age of 13 y had been considered to be 'obese' as defined by their primary care physician (6th Kongreß für Jugendmedizin, Weimar, Germany, 11–13 March 2000, Büsching U, Kiess W, unpublished data).

Childhood obesity as a major burden for the economy

The financial burden of childhood obesity for industrialized societies can only be estimated. The annual economic costs due to medical expenses and lost income as a result of complications of adult obesity is approximately 70 billion dollars in the USA. At least another 30 billion dollars are thought to be spent on diet foods, products and programs to lose weight. If one is to calculate the prospective costs of obesity forms that have started at an early age, the prospective financial costs are even higher.[1,2,4,10] On the other hand, it is almost too ironic to state that sales and profits of the obesity treatment industry have already reached an enormous sum. Therefore, obesity in childhood and adolescence has already become a major factor in health care planning systems and within the health care industry as such.

Causes of and factors leading to childhood obesity

Multiple factors are related to the high incidence of childhood obesity. Both genetic/endogenous[11–17] and environmental/exogenous factors contribute to the development of a high degree of body fatness early in life (Table 1). In fact, twin studies suggest that at least 50% of the tendency toward obesity is inherited.[2,12] There is also increasing evidence that responsiveness to dietary intervention is genetically determined.[18–20]

The discovery of leptin and its receptors[11,13,14,16,17,21,22] has stimulated research on obesity in general to a great extent. It has become clear that the adipocyte product, leptin, feeds back body fatness to the hypothalamus and regulates food intake in rodents. The fact that in obese humans leptin serum levels are high has led to the hypothesis that leptin insensitivity contributes to the further progressive development of obesity in overweight humans. On the other hand, leptin administration to children with leptin deficiency leads to all of the following: (1) a striking decrease of food intake; (2) suppression of appetite; (3) continuous weight loss; and (4) restoration of endocrine disturbances.[14,23] Mutations and polymorphisms of the genes of other neuropeptides and hormonal regulators of appetite and weight control have been found in obese humans: mutations in the proopiomelanocorticotropin (POMC) gene and polymorphisms in the β-adrenergic receptor, and melanocorticotropin receptor, MC4R, have been shown to be associated with severe, morbid obesity.[15,24] These genetic defects are the first monogeneic disorders of weight control described. It is to be expected that other such monogenetic forms of obesity will be found. However, in general, a multifactorial aetiopathogenesis of obesity will prove to be present in most patients.

Exogenous factors such as overconsumption of fat-rich diets,[25] the excessive use of modern media (TV)[26] and lack of physical activity (sedentary life style) always contribute to the development of obesity in childhood and adolescence as well as in adults. Nutrition and diet early in infancy is thought to influence growth rate and body fatness beyond infancy. Some authors even strongly advocate that intrauterine growth retardation predisposes for the development of obesity and syndrome X later in life.[6,20] However, the evidence for fat patterning resulting from differences in fetal or early postnatal nutrition is still open to question.[18]

Table 1 Factors which contribute to the development of obesity

Genetic factors
Among others, polymorphisms and/or mutations in any of the following: β-adrenergic receptor, leptin, Ob-R, TNF, POMC, MC4R, NPY, NPY receptors
Environmental/exogenous factors
Increase of sedentary activities (ie TV viewing)
Decrease in physical activity
Shift in diet towards more fast/prepackaged foods with high fat/calorie content
Loneliness
Psychosocial/family problems

Differential diagnosis

'Exogenous obesity' which may also be referred to as 'simple' or 'primary' obesity is still by far the most common diagnosis in the obese child. However, apart from the above-mentioned monogenetic traits of morbid obesity there are numerous disorders that can also present with obesity early in life. Figure 1 shows a neonate with Prader–Willi syndrome, one of the syndromes associated with morbid obesity. These usually include genetic syndromes and also a variety of underlying disorders such as hypothalamic tumors, other brain lesions and endocrine disorders (Table 2). The diagnosis of primary or simple or 'exogenous' obesity

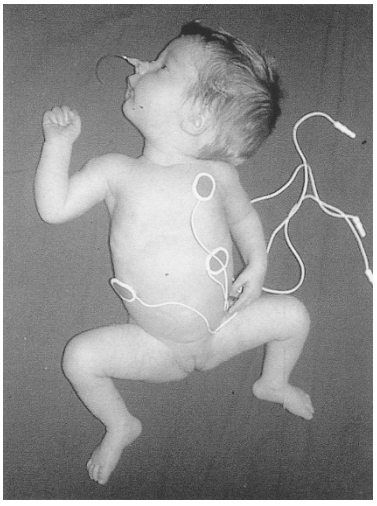

Figure 1 Neonate with Prader–Willi syndrome as proven by methylation test and molecular genetics. Note the fair hair colour and the presence of severe muscle hypotonia which required gastric feeding.

Table 2 Disorders which can present with obesity in childhood—differential diagnosis of obesity disorders

Endocrine disorders
Cushing's syndrome
Hypothyroidism
Growth hormone deficiency
Hyperinsulinemia
(Pseudo)hypoparathyroidism (Albright's hereditary dystrophy)
Brain damage
Hypothalamic tumor/surgery/trauma
Genetic syndromes
Prader–Labhard–Willi syndrome
Alstrom
Bardet–Biedl
Carpenter
Cohen
Monogenetic disorders (for example, leptin deficiency, POMC mutation, leptin receptor mutation)
Primary (simple/'exogenous') obesity
(Multifactorial)

is usually easy to make and depends upon family and personal history and a careful physical exam (Figure 2).

Diagnostic algorithm

A simple diagnostic algorithm which aids in making a diagnosis in children and adolescents with obesity is shown in Figure 2. Usually, no laboratory investigations are recommended unless substantial co-morbidity such as hypercholesterolemia or liver disease must be suspected. However, a primary determination of serum concentrations of TSH, T3 and T4 is still carried out in most centers in Europe.[5]

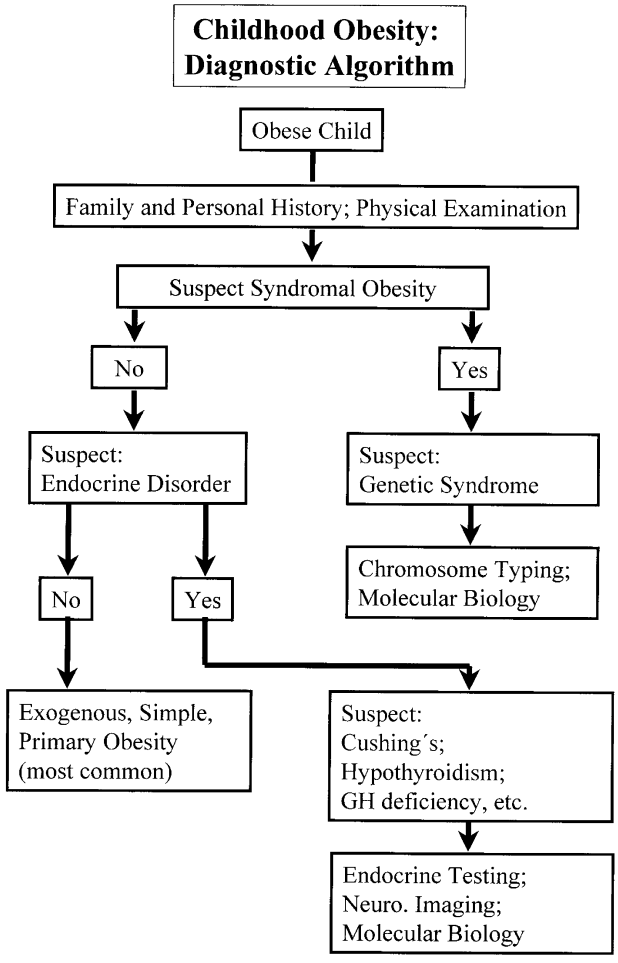

Figure 2 Diagnostic algorhythm for the diagnosis of obesity in childhood and adolescence. Note that 'simple/primary obesity' is by far the most common diagnosis in children and adolscents with obesity.

Co-morbidity in childhood obesity

Among the most common sequelae of primary childhood obesity are hypertension, dyslipidemia and psychosocial problems. A more complete list of co-morbidity disorders is shown in Table 3. These disorders which arise from overweight and subsequent biochemical changes actually predispose for yet again additional co-morbidity such as cardiovascular disease in early adulthood. Since approximately 85% of obese children of school age will stay obese in adulthood, the co-morbidity represents a major health burden in industrialized societies.[1,2,4] In addition, childhood obesity seems to increase the risk of subsequent morbidity whether or not obesity persists in adulthood. It is therefore essential to carefully examine all obese children with respect to the presence of co-morbidity. Such examinations should include blood pressure monitoring and check of lipid status. The opinion of orthopedic surgeons and child psychiatrists

Table 3 Co-morbidity of childhood obesity

Psychosocial — psychiatric
Poor self image, social isolation, autoaggression, suicide, promiscuity, drug and alcohol addiction, bulimia, binge eating, smoking, (enuresis)
Cardiovascular
Accelerated atherosclerosis, hypertension
Endocrine and gynecological
Hyperinsulinemia, insulin resistance, early puberty, polycystic ovaries, dysmenorrhea
Metabolic
Dyslipidemia
Respiratory
Hypoventilation, sleep apnea, snoring
Orthopedic
Slipped capital femoral epiphyses, coxa vara, Blount's disease, Legg-Calve–Perthes disease
Others
Paronychia, akanthosis nigricans, striae rubrae

should be sought much more frequently than is being done so currently.

Therapeutic approach

Because obesity is a risk factor for numerous medical disorders, psychosocial problems and excess mortality, it is indeed imperative that effective treatment be developed and be widely available and instigated. Therapeutic strategies include psychological and family therapy interventions, lifestyle/behavior modification and nutrition education. The role of regular exercise and exercise programs is emphasized.[2,5,10,27] Intermittent exercise (high intensity followed by low intensity sports) results in greater reduction in weight and fat. Such approaches also increase compliance/adherence rates of the youths. Multidisciplinary outpatient treatments are considered to be the most effective.[10,27] In most countries, networking of primary care physicians, public health/school medicine institutions, specialists of pediatric and adolescent medicine, social workers, child psychologists and dietitions as well as sport educators could be achieved. Health insurance providers and policy makers should strongly support such networking concepts. Using such approaches, some workers have reported high success rates and sufficient long-term weight reduction in small groups of children studied.[27] However, longterm treatment probably also including extended pharmacotherapy may be neccesary for the majority of very obese adolescents.[28] Table 4 lists some drugs used in obesity management in adults.

However, great care should be exerted when antiobesity medication is to be prescribed to children. Several previously widely used medications have recently been withdrawn from the market because of concerns about side effects in adults. Most if not all of these drugs have not yet been studied in respect to efficacy, safety and long-term effects in children and adolescents.[10] It is therefore of great concern that some of these drugs are being prescribed to youngsters by primary care physicians upon parental request (own observations) outside any scientific follow-up studies and without careful and systematic long-term follow-up.

Table 4 Drugs used in obesity management (*note*: not recommended for use in children)

Approved for the use in adult obesity in some countries
Sibutramine
Phentermine
Mazindol
Diethylpropion
Orlistat
Drugs under development
Leptin and leptin agonists
Brain and gut peptide agonists or antagonists
β_3-agonists
MC4R agonists

Laparoscopic adjustable gastric banding is being increasingly considered to be the treatment of choice in very obese adults.[29,30] Early complications of such interventions and significant late complications such as pouch dilatation and stomach slippage have been rare.[29] However, in one series, in 7.5% of 146 cases operated on, reoperations were necessary.[31] Recommendations of an international workshop on gastric banding for adult obesity are summarized in the following: (1) good patient selection has to be made; (2) standard surgical practice has to be adhered to; and last but not least, (3) no surgery must be performed without the support of an interdisciplinary team which has to include internists, psychologists and dietitians.[29] Whether or not such invasive treatment options will ultimately be considered in children is still subject to debate. There is literally no experience with the procedure in children.

Prevention

As prevention has to start very early in life and perhaps even before extrauterine life,[6] a population and community approach for prevention seems to be reasonable. However, primary prevention has been proven difficult or impossible in most societies at this point of time. Again a multidisciplinary team approach is needed to develop and secure preventive strategies. Good nutrition and modest exercise for pregnant women as well as monitoring of intrauterine growth of the child are mandatory. After birth, rapid weight gain should be avoided and principles of good nutrition and physical activities should be taught at all ages. A recent study by von Kries *et al* found that the prevalence of obesity in children who had never been breast-fed was 4.5% as compared to 2.8% in breast-fed children. It was concluded by these authors that in industrialized countries promoting prolonged breast-feeding may help decrease the prevalence of obesity in childhood.[20] Children's food choice can be

influenced by early intervention and guidance.[25] Parents should be encouraged to make healthy foods easily available to the child and serve these foods in positive mealtime situations in order to help their child to develop healthy food habits. As for treatment startegies, multidisciplinary teams should be formed. Such teams should always include a physician, a nutrition specialist and a psychologist but mainly consist of school nurses, teachers and kindergarden teachers.

Perspectives

Obesity is the most common chronic disorder in children and adolscents in the industrialized societies. In some countries, the prevalence of obesity in childhood and adolscence has become much higher than that of the allergic disorders including both asthma and eczema. Childhood obesity is associated with substantial co-morbidity and late sequelae. While diagnostic strategies are clear and straightforward, treatment remains difficult and frustrating both for the patient, family and the multidisciplinary team caring for children and adolescents with obesity. In our opinion, much more attention should be given to prevention and the development of preventive strategies at all ages. Prevention should in any case start very early in life. New drugs are being developed that promise to be useful for treatment and secondary prevention. However, no data are available for the use of such agents in childhood and adolescence.

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