Childhood obesity

Screening and prevention

Synthesis and recommendations

This report presents the synthesis and recommendations made by the group of experts brought together by the French institute of health and medical research (Inserm) within the framework of the procedure of Expertise collective (expert advisory opinions) to respond to questions raised by the French national health insurance fund for independant workers (CANAM) concerning screening for childhood obesity and its prevention.

The Centre for expertise collective of Inserm coordinated this work in cooperation with the Department for economic and social partnership for the preparation of the file and the documentation department for the literature search (Department of scientific information and communication).

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Foreword

The prevalence of childhood obesity is increasing steadily throughout the world. In France, it is estimated from regional studies that the prevalence of childhood obesity has more than doubled since the 1980s. The causes of this epidemic remain poorly understood despite the efforts of the scientific community working in the fields of epidemiology, pathophysiology, and genetics.

This rise in the prevalence of obesity might result from the increasingly sedentary lifestyle of western civilization associated with a reduction in daily physical activity and/or from changes in eating behavior, both quantitatively and qualitatively. These questions require responses in order to define effective prevention strategies.

The french national health insurance fund for independent workers (CANAM) requested an expert analysis from the Inserm on the potential ways of screening for and preventing childhood obesity based on the most recent scientific data.

In response to this request, the Inserm brought together a multidisciplinary group of experts with competence in the areas of epidemiology, sociology, anthropology, biology, neurobiology, physiology, and different clinical specialties including pediatrics, endocrinology, and nutrition.

The group of scientific experts structured their work around the following questions :

- What is the definition of childhood obesity? What prevalence data are available in France? What is the situation in France compared with other countries?
- What are the mid-term and long-term consequences of childhood obesity?
- What predictors of obesity are available? How useful are they as screening tools?
- What tools are available for diagnosis?
- What risk factors have been identified? What is the role of genetic factors and environmental factors related to nutrition and sedentary lifestyle?
- What advances have been made in genetics? Are they useful for screening high risk populations?
- What is the influence of early nutritional factors on the development of regulatory neuronal systems and on the constitution of the "obesity phenotype"? What is the role of prevention during the early phases of life?
- What cellular mechanisms are involved in the development of childhood obesity? What is the physiological role of white and brown adipose tissue?
- How can the role of physical activity in the prevention and treatment of obesity be studied?

Querying databases (Medline, Embase, Psychinfo, Pascal, and Sociological Abstracts) allowed us to select more than 1000 scientific articles.

During the seven working sessions organized between September 1999 and March 2000, the experts presented a critical analysis of the international literature and prepared a synthesis on the different aspects of childhood obesity. The final three sessions were devoted to the elaboration of the principal conclusions and recommendations.

At the end of this report, four communications provide further information on specific points concerning the different aspects of clinical management of overweight children and also on the impact of acquired knowledge on the evolution of products proposed by the food and agriculture industry.

Synthesis

The prevalence of obesity has risen steadily over the last few decades. This worldwide epidemic is largely related to changing lifestyle and has not spared the French population. Despite the difficulty in establishing a precise definition of childhood obesity, it was estimated in the 1980s that 6% of French children aged 5 to 12 years were obese. Fifteen years later the estimate rose to 10-12%. This rapid increase in the number of obese children raises important public health issues due to the potential long-term impact of obesity and its complications.

Several studies have been devoted to examining the respective roles of different risk factors of obesity, now recognized as a specific disease entity. Both genetic and environmental factors have been identified. In western countries, obesity and its complications - type 2 diabetes mellitus, high blood arterial pressure, cardiovascular diseases - occur more readily in adults living in relatively less favorable social situations. This correlation seems to be noted less among children.

Our understanding of obesity has been greatly improved by advances in genetics and a better knowledge of the molecular mechanisms regulating appetite and the development of fat mass. Whatever the complexity of these systems, excess body weight and obesity always result from an imbalance between energy intake and energy expenditure. Since there has been a steady decline in mean daily calorie intake in the general population for many years, the increasing prevalence of obesity is probably related to changes in energy expenditure induced by the trend towards a more sedentary lifestyle. Mean calorie intake in the general population is not however necessarily indicative of calorie intake in specific sub-populations. A few observational reports have shown an association between obesity and the number of hours children and adolescents spend watching television. Other factors, including nutritional factors, could also play a role in early childhood, while overweight may appear only many years later

Towards an international definition of childhood obesity

Obesity can be described as an excess of fat mass in the body, a condition associated with higher morbidity and mortality. The amount of body fat mass can be estimated with the body mass index (BMI), also called the Quetelet index. The BMI is defined as body weight (expressed in kg) divided by height (in meters) squared. In adults, obesity is defined as a BMI equal to or greater than 30 kg/m^2. For children, reference curves for BMI are needed because body composition is affected by age-dependent physiological variations.

The World Health Organization (WHO) advocates the use of weight for height curves established by the National Center for Health Statistics (NCHS) to assess growth in children. Standard curves have been established for girls aged 0 to 10 years and for boys aged 0 to 11.5 years. For adolescents, the WHO recommends associating measurements of skin fold thickness with BMI. The standard BMI curves published by the WHO are based on American data. These WHO recommendations are not widely applied internationally making it difficult to compare the prevalence of obesity reported in studies conducted in different countries.

The International Obesity Task Force has examined the recommendations established by the European Childhood Obesity Group and has published a new definition of childhood obesity available on web site (http:/www.bmj.com/cgi/content/abridged/320/7244/1240 and http:/www.bmj.com/cgi/content/full/320/7244/1240). This new definition is based on BMI percentile curves established from data collected in different countries. Two threshold levels, defining degree 1 and degree 2 childhood obesity correspond to the percentile[1] curves of the standard BMI curve reaching 25 and 30 kg/m^2 respectively at 18 years. These levels correspond to the thresholds defining overweight and obesity in adults. A common international definition of childhood obesity would be useful to compare prevalences in different countries and to provide meaningful comparisons between studies investigating the factors associated with obesity.

Besides the importance of a uniform definition of obesity for epidemiological analysis, thresholds associated with increased long-term morbidity and mortality must be determined in older children and adolescents. Of course, these thresholds must be validated in different populations.

Weight and height curves : an easy-to-use screening tool for childhood obesity

In France, each child has a health booklet. Practitioners can use the standard growth curves (height and weight for age) printed in this booklet to record the child's growth and detect a trend towards obesity.

Since 1995, the health diaries also have standard BMI curves by age and gender. These curves take into account three variables - weight, height, and age - simultaneously. They provide a more precise assessment of body composition than the conventional curves expressed as weight for age and weight for height. With these BMI curves, it is easier to recognize changes in body composition during growth and thus to identify childhood obesity earlier.

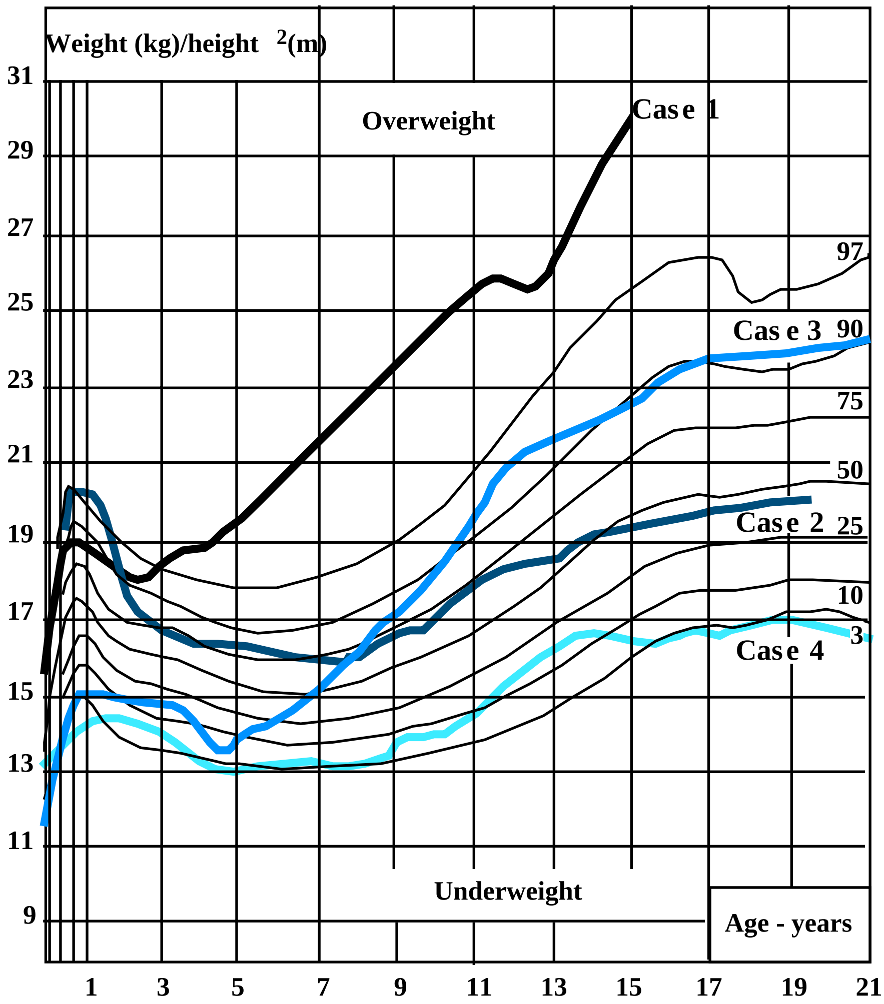
The standard BMI curves were established from reference data collected in the French population during an international longitudinal study on growth coordinated by the International Center for Childhood. These curves show that BMI, which reflects changes in body fat mass, increases during the first year of life then declines spontaneously up to the age of 6 years. The second rise in the BMI curve, starting by the age of 6 years is called the " adiposity rebound ". The risk of obesity in adulthood is higher when this rebound occurs earlier.

Changes in a child's body composition can be followed with these curves. Different periods (when the child appears to become thinner or fatter) can be recognized : an overweight child who has not yet shown an adiposity rebound can still return to the mean (case n° 2); conversely, the risk of obesity is greater if the adiposity rebound occurs early (cases n° 1 and 3). The fact that the childhood curves of most adults with obesity exhibit an early rebound (before the age of 6 years) suggests that factors promoting the development of obesity could occur early in childhood.

The highest percentile curves delimit thresholds used to define excess weight in children. A BMI above the 97th percentile is generally considered to be a sign of obesity. However, weight status must be interpreted differently at the different ages. Before the age of 8 years

[1] A percentile is defined as the percentage of subjects with a BMI below the defined level. For example, 3% of the population has a BMI below the 3rd percentile.

most overweight children will not remain overweight. After this age, most children will remain in the same BMI chanel. The BMI curve is an objective tool for clinical assessment but, like conventional weight and height measurements, it cannot provide an indication of the real body composition or the risk of complications in adulthood. Further investigations using more sophisticated methods elaborated to measure body composition and biological criteria must be made when complementary information is needed.



Case 1 : fat at 1 year ; will stay fat after an early adiposity rebound (2 years)

Case 2 : fat at 1 year ; will return to the mean after a late adiposity rebound (8 years)

Case 3 : thin at 1 year ; will put on weight after an early adiposity rebound (4-5 years)

Case 4 : thin at 1 year ; will stay thin after a late adiposity rebound (8 years)

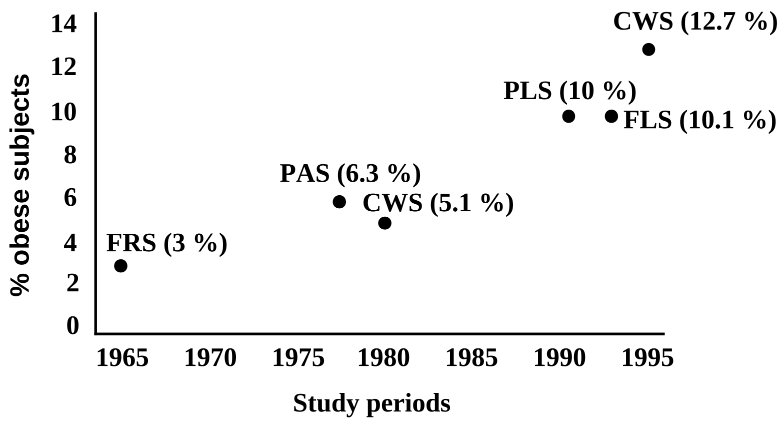
Time course of the BMI curve of four children

The prevalence of childhood obesity is above 10 % in France

Studies conducted both in industrialized and developing countries all point out a rapid rise in the number of overweight and obese children. The nutritional studies conducted in the United States (NHANES) during the 1970s revealed a steady rise in the number of overweight children.

When the BMI curves for French children born between 1955 and 1960 are compared with those for American children born during the same period, it can be seen that the 97th percentile for French children corresponds to the 85th percentile for American children. This means that 3 % of the French children were obese as compared to 15 % of the American children. By 1990-96, 10 to 14 % of 10 year old French children were obese as compared to 22 % in the US.

Three regional studies were conducted in 5 to 10 year old French children in the early 90s : . in the central and western parts of France by the Regional Health Institute (*IRSA*, *Institut Régional pour la SAnté*), in the Paris area by Inserm, and in the cities of Fleurbaix and Laventie (Fleurbaix-Laventie study). Using the 97th percentile to define obesity, these three regional studies showed that approximately 10 to 12 % of French children are obese. The prevalence of childhood obesity has thus shown a 3 to 4-fold increase over a 30-year period, rising from 3 % to 10-12 %. In the IRSA study, the prevalence of obesity among children aged 10 years rose from 5.1 % in 1980 to 12.7 % in 1996. Thus, although no comparable studies are available covering the entire French population, it can be estimated that the prevalence of obesity has more than doubled in France since the 1980s. In addition, several studies have demonstrated that the increase in the number of cases of severe obesity has risen more rapidly than the number of cases of moderate obesity.

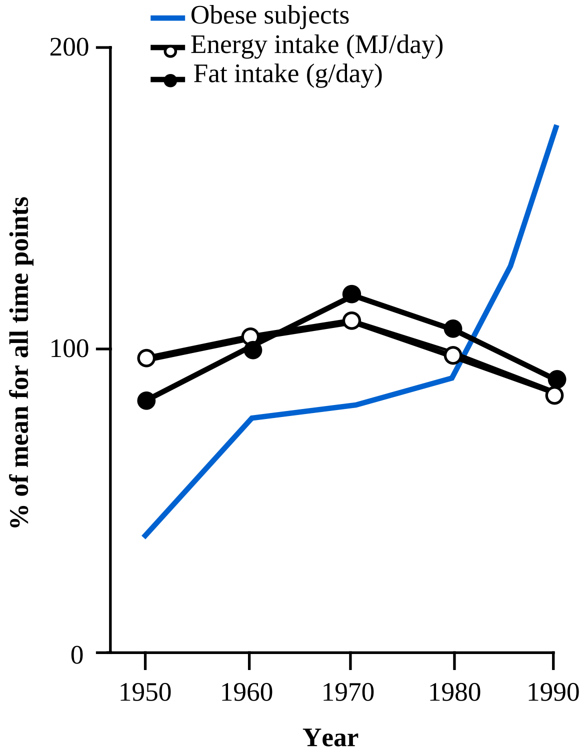


Prevalence of childhood obesity in France defined by BMI > 97th percentile using the reference French population. FRS : French reference study (at 10 years); PAS : Inserm study in the Paris area (7-12 years); CWS: IRSA study in central and western part of France (10 years); PLS: longitudinal study in the Paris area (8 years); FLS : Fleurbaix-Laventie study (5-12 years)

Generally, the rise in the prevalence of obesity occurs together with changes in the growth process of the general population : children are getting taller (longer leg length) and grow faster. The adiposity rebound and menarche occur earlier.

Changes in mean calorie intake cannot explain the increased prevalence of obesity in western populations

In most countries, studies of food intake have shown evidence of decreased calorie intake over the last few decades. But during this same period, there has also been an increase in the prevalence of obesity.



Secular trends in food intake in relation to obesity in Britain (from Prentice and Jebb, 1995)

These results would suggest that the increase in the prevalence of obesity is not related to increased daily calorie intake in these populations since there has been on the contrary a decrease of 200 to 300 kcal/d over the last few decades.

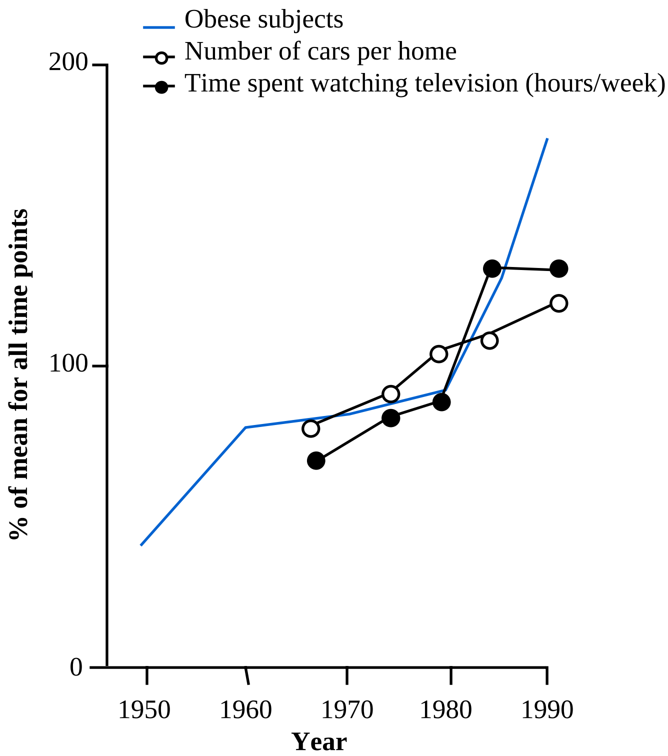
Studies conducted to demonstrate the relation between obesity and food intake have however provided contradictory data (food intake surveys are known for their lack of precision due to under-reporting of food intake or changes in eating behavior) and have been unable to establish a link between obesity and food intake. Recent studies have led to the hypothesis of a qualitative imbalance in nutrient intake early in life as a risk factor for the development of obesity.

Are modern eating habits involved ? Convincing research data are lacking to clearly demonstrate a link between obesity and specific eating habits. A better understanding of the cognition modes in obese subjects (eating habits, food representation) remains an important area of research.

The prevalence of obesity increases with sedentary lifestyle

Energy expenditure due to physical activity has decreased in industrialized countries due to more comfortable living conditions (motorized transportation, elevators, central heating, air-conditioning) and sedentary leisure activities (television, video games). Certain studies have demonstrated that the time spent watching television during childhood is predictive of obesity during adolescence.

In children, energy expenditure resulting from physical activity can be estimated with different tools or markers : estimation of the relation between total energy expenditure and basal metabolism (measurements based on double-labeled water and oxygen consumption); questionnaires on different physical activities and periods of inactivity (time spent watching television or playing video games, motorized transportation….); accelerometric analysis of movement. Each of these techniques has its drawbacks. Nevertheless, all of the methods used to estimate the level of physical activity appear to show an association between increased prevalence of childhood obesity and the trend towards a more sedentary lifestyle. However, the cause and effect relation remains to be demonstrated.



Secular trends in time spent on sedentary activities in relation to obesity in Britain (from Prentice and Jebb, 1995)

Genetic predisposition in common obesity is established but the genes implicated remain to be identified

The influence of genetic factors in predisposition to obesity is a well-established fact. Epidemiology studies on genetics have identified the role of heredity in determining the level and the evolution of body mass. These studies have examined obesity-linked phenotypic segregation in families followed for several generations or followed cohorts of monozygous twins separated early in life. Depending on the type of study, the heredity factor in obesity is estimated to vary from 10% to 80%, further illustrating the methodological imprecision.

Inheritance of obesity by type of study

Type of study	Inheritance (%)
Family studies	25 – 55
Twin studies	50 – 80
Adoption studies	10 – 30

Studies manipulating food intake in pairs of monozygous twins over several weeks have demonstrated that differences in responses between pairs of twins are greater than within a pair of twins, showing that, under defined environmental conditions, heredity intervenes in the predisposition to weight gain.

Once the genetic predisposition to obesity has been established, two important questions arise when one considers the potential impact, in terms of public health, of the search for genes implicated in obesity.

- Does genetic predisposition to obesity depend on a small number of frequent variants with an additive effect or is it related to rare variants among a large number of different genes?
- Can genetic predisposition to common obesity be identified easily and, if identified, can it be used to establish targeted preventive measures for patients "at risk"?

Certain family studies on obesity-related phenotype segregation would suggest that up to three major genetic determinants could be transmitted via mendelian or non-mendelian inheritance. A few of these studies suggest that body fat mass and body mass index (BMI) could be influenced by the presence of a single gene. No data has emerged to confirm these hypotheses and different types of genetic studies searching for genes predisposing to obesity have not provided convincing evidence to date.

There are three categories of studies designed to demonstrate genetic variations predisposing to obesity : studies searching for mutations among groups of candidate genes; studies on associations; and studies screening the entire genome.

Genes implicated in single-gene forms of obesity

Gene	Role of gene product	Symptoms associated with obesity	Number of cases (Number of families)
LEP *(leptin)*	Defect in signal from adipose tissue to brain	Hypogonadotrophic hypogonadism	5 (2)
LEPR *(leptin receptor)*	Defect in signal from adipose tissue to brain	Hypogonadotrophic hypogonadism	3 (1)
PCSK1 *(Protein convertase subtilisin/kexin type 1)*	Defective maturation of POMC	Hyperproinsulinemia Hypocortisolism Hypogonadotrophic hypogonadism	1 (1)
POMC *(pro-opiomelanocortin)*	Absence of ACTH, αMSH and ßendorphin precursors	Corticotropic insufficiency	2 (2)
MC4R *(melanocortin 4 receptor)*	Defective binding of MC4R ligands (αMSH)	None	> 14 (>10)

Studies on candidate genes have basically led to the description of mutations causing rare syndromes of morbid obesity. In these studies, individual genes are chosen for study because they are associated with clinical symptoms also associated with obesity. Families expressing the first identified forms an obesity syndrome linked to a single gene were described in 1996. These families had mutations of genes coding for leptin and prohormone convertase 1. Subsequently, mutations of the leptin receptor gene and the pro-melanocortin gene were also discovered. These mutations produce rare forms of obesity associated with other endocrine disorders distinguishing them from common obesity.

Technological progress has allowed the extension of such studies of evaluation of mutations of genes responsible for a small but significant proportion of the cases of common obesity. Recently, the mutations of type 4 melanocortin receptor (MC4R) have been identified. It would appear that MC4R mutations occur in 1 to 3% of all obese children. These mutations are currently the most frequent cause of single-gene obesity in humans. In addition, and unlike the preceding genes, they cause obesity without associated symptoms.

Studies on the segregation of identified gene variants and on the phenotypic expression related to energy metabolism in carriers of these mutations should allow a more precise description of the respective role of the environment in the development of obesity in genetically predisposed subjects.

Associations studies examine frequent genetic variants observed within a given gene (exons, introns) or in regions regulating gene expression. These studies compare the frequency of these variants in different groups of subjects (case-control studies) or compare a quantitatively measurable phenotype between subjects with and without the variant (cohort studies). Theoretically, such studies can detect a weak effect of a variant on a phenotype in a small population. These studies are technically simple and inexpensive and many have been conducted, but methodological and publication bias (studies demonstrating a positive association are more readily published) remain a constant problem. In the near future, one can expect to see many more of these studies describing a positive association, but no genetic variant described to date demonstrates a significant effect on the development of common obesity.

Genome screening studies in obese families

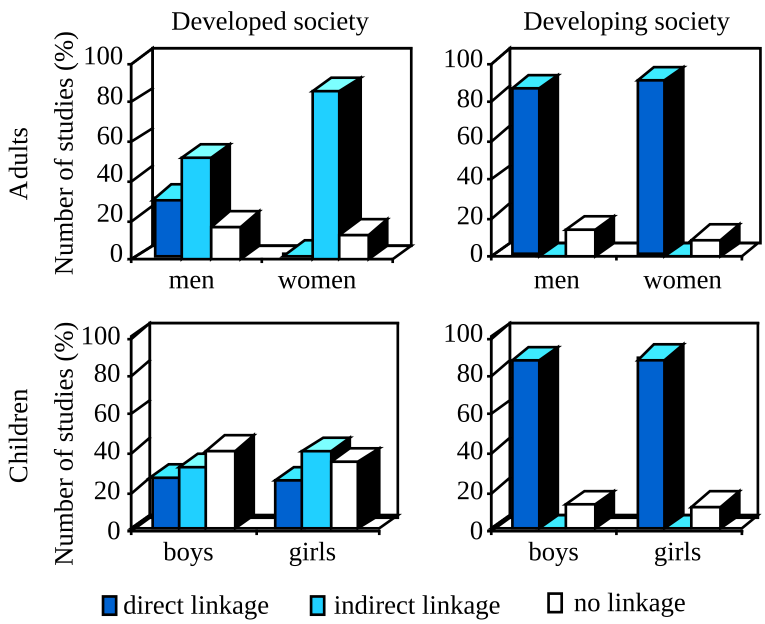
Population	Number of individuals	Chromosome linkage	Phenotype
Pima indians	874	11q21-22	% fat mass
		3p24.2-p22	
		11q23-24	Energy expenditure
Mexican Americans	>5000	2p21	Leptinemia
French	514	10p	Obesity
		2p	Leptinemia
		5cen-q	Leptinemia
Americans	513	20q13	Obesity

To identify the genetic basis of the predisposition to obesity, one can also screen the entire genome. Here, the aim is to demonstrate a genetic link between markers chosen at regular intervals on the genome and a qualitative characteristic (obesity) or a quantitative variable (BMI). These are family studies that involve several hundred people. Theoretically, these studies can localize recognized or unrecognized genes associated with several rare mutations or frequent variants predisposing to obesity. Unfortunately, because of their design, these studies can only demonstrate genes with a sufficiently significant effect (i.e. those accounting for a significant percentage of the phenotypic variation or observed in a significant subgroup of the families). Screening studies have provided a considerable amount of data on genes responsible for several single-gene diseases, but, despite the description of several gene linkages, have not yet led to the discovery of genes whose alterations would be responsible for multiple-gene diseases. For obesity, the gene linkages identified by different research teams are not in general agreement. A large number of genes probably contribute to the predisposition to obesity observed in different populations.

Even though genetic predisposition to obesity appears to be a well-established fact, we still have no reliable evidence suggesting how many genes are involved. We do not know which variants are active nor how they interact. Consequently, it is too early to propose genome screening as a useful public health tool.

Obesity and socio-economic status : an uncertain relation in childhood

There is an undeniable relation between the distribution of obesity in a given adult population and social and economic status. In developed societies, obesity is more frequent in women on the lower end of the social ladder; for men, the trend is less marked. In developing societies, the frequency of obesity increases with rising social position, irrespective of gender.



Link between obesity and social and economic status (from Sobal and Stunkard, 1989)

In France, a Sofres poll taken in 1997 confirmed that obesity is more frequent in low income families. The rate of obesity was 4.3% among people in the higher income bracket and 12.1% among those in the lower income brackets (less than 1000 euros/month). The poll also demonstrated significant regional differences, the phenomenon being more marked in specific regions (Nord, Auvergne, Lorraine, Languedoc).

For children, available data do not demonstrate any significant link between obesity and economic or social status in developed countries. A few recent studies have demonstrated an inverse relationship in adolescent girls after puberty. In developing countries, the frequency of obesity is clearly greater in groups with a higher social status.

Considering these observations, social science studies have examined the social mechanisms that might explain how the distribution of obesity moves from a random distribution in the child population to one favoring a particular social category in the adult population, particularly women. Most of these studies have demonstrated that obese subjects are victims of discrimination in developed countries.

Several reports have shown how negative attitudes towards obese subjects can lead to discrimination involving a wide range of human relationships : access to higher education, employment, income, career advancement, family life.

Obesity plays an important role in changing social status, which is affected by educational level, occupational activity, and marriage. The impact of these three factors is different for men and women. For men, education and occupation have a predominant effect, while for women, marriage is more important, although the trend is on the decline. A thin woman is more likely to marry a man with a higher social status while a heavier women is more likely to marry a man with a lower social status.

Obesity also has a negative effect on educational level and career advancement. People exercising an influential role in the community (assessment, direction) evaluate obese individuals more negatively than thin individuals. Such negative attitudes are observed not only in the community in general but also within medical institutions.

After identifying the discrimination against obese subjects, social science studies have examined ways of helping obese individuals cope with this discrimination. Four steps are described : recognition, awareness of the discrimination phenomenon; anticipation of the discriminatory effect depending on the context or the people involved; development and promotion of immediate and long-term reaction mechanisms enabling the subject to cope with discrimination and community policies aimed at changing negative social attitudes against obesity.

The prevailing attitude towards thin and fat individuals is a highly variable and highly culture-dependent, social phenomenon. The Human Relation Area Files contain data concerning body fatness for 58 non-western traditional cultures and in 81% of them, the social image of ideal female beauty is one of a plump “full-flesh” body. The capacity to store fat is seen as a sign of good health and vitality and persons with an abundant supply of adipose tissue reach high social positions with power and prestige.

Obesity in childhood and adolescence is associated with increased cardiovascular morbidity in adulthood

Severe childhood obesity is associated with a variety of disorders including orthopedic (early development of genu valgum or even genu varum and tibia vara), respiratory (sleep apnea), metabolic (glucose intolerance) and endocrine (ovarian dysfunction) conditions requiring medical care.

Children with moderate obesity present few or no clinical signs. Nevertheless, mean blood pressure, total cholesterol, triglycerides, and the LDL/HDL cholesterol ratio are higher in moderately obese children than in thinner children. In addition, obese children have hyperinsulinemia, sometimes associated with glucose intolerance. Hepatic steatosis is also more frequent.

Long-term epidemiology studies have examined the relation between the degree of obesity during childhood and disease development or death. These studies are our only source of information on risks associated with childhood obesity. It must be recalled however that these studies included individuals who were obese children during the first half of the 20^{th} century when living conditions were much different than they are today.

Epidemiology studies are in general agreement that childhood obesity is associated with a 50 to 80% higher mortality during adulthood. The imprecision of the available data is due to differences in methodology. Factors involved include :

- the type of study : some studies have compared mortality in a group of obese adolescents (18-20 years) with national health statistics, while others have followed individual subjects over periods running up to 55 years;
- the age at which the children were first examined : age has ranged from 2 months to 20 years;
- the definition of childhood obesity used (from BMI ≥ 75^{th} percentile to BMI ≥ 31 kg/m^2 at 18 years, clinical criteria, hospitalization for childhood obesity).

Most of the studies comparing boys and girls have found a higher mortality risk in boys. The observed over-mortality is basically related to cardiovascular disorders. The only study with BMI data at adulthood suggests that the increased risk associated with childhood obesity cannot be explained entirely by the persistence of obesity into adulthood.

The probability that childhood obesity will persist into adulthood increases with the age of the child, with the severity of the obesity, and with family history of obesity. The risk associated with a family history of obesity is greater if the child is young. It must be recalled however that most adults who are obese today were not obese before puberty.

Obesity during childhood and adolescence persisting into adulthood

Obesity	Risk of persistent obesity in adulthood (%)
Before puberty	20 – 50
After puberty	50 - 70

Until now preventive measures were not successful

There have been few public health measures specifically designed to prevent obesity. Several projects implemented in different countries have focused on a community approach aimed at modifying the risk of cardiovascular disease in the general population. These projects are designed to limit fat intake through nutrition education and promotion of physical activity. For some of these preventive measures the impact on obesity was estimated. An example of an intervention program is the Finnish project conducted in North Carelia. This project was designed to reduce markers of cardiovascular risk (serum cholesterol, blood pressure, smoking) over a twenty year period. The goal was to reduce mortality in the middle age population. During this period, mean BMI decreased in women but increased in men.

For children, school cardiovascular prevention programs have produced disappointing results in terms of reduced BMI and skin fold thickness. Among the nine studies conducted in the United States, Norway, Crete, Israel, and Russia and published between 1966 and 1992, three showed a significant reduction in BMI and two out of five a significant decrease in skin fold thickness. The intervention consisted of education focusing on the impact of physical activity and eating habits on health.

More recently, the Child and Adolescent Trial for Cardiovascular Health (CATCH) enrolled 4000 third grade children in the United States. This 2.5-year trial associated an education program and actions aimed at changing eating habits and physical activity. Early in the study the investigators observed a reduction in body mass index and in tricipital skin fold thickness, but the trend disappeared as the study continued. Nevertheless, changes in food intake and physical activity levels were documented. Other studies, including the Cardiovascular Health in Children (CHIC) study in North Carolina, the Fitness and Nutrition Intervention on Cardiovascular Health Study in Australia, and the Dietary Intervention Study in Children (DISC) in the United States employed different intervention methods, but all showed a very modest effect on adiposity.

There could be several explanations for the disappointing results of these intervention programs :

- these studies were not specifically designed to prevent obesity;
- the chosen interventions had little or no long-term efficacy;
- the tools used to assess the actions were inappropriate : an intervention designed to reduce body fat mass and increase lean mass does not affect BMI; skin fold thickness varies greatly between observers;
- changes in adiposity induced by puberty make it difficult to identify changes induced by the intervention.

The few studies specifically designed to prevent obesity in school children have involved much smaller samples, usually children in one school. A recent project conducted in the United States was basically aimed at reducing the number of hours third grade children spend watching television or playing video games. The project, which was managed by teachers for seven months, intended to teach how to become a discriminating television consumer. The parents participated in the study and were given an information letter. The observed increase in BMI, skin fold thickness and waist measurements was significantly greater in the control group than in children participating in the intervention study. A reduction of the time spent in sedentary activities could be a major objective for programs designed to prevent obesity. The short-term efficacy of such interventions appears to be demonstrated, but the long-term effect remains to be proven. One interventional study, the Pathways study, has been initiated in the United States : 2000 American Indian school children and a control group are participating. The efficacy of the intervention, an education program on good eating habits and increased energy expenditure through physical activity but with no specific indications concerning reducing calorie intake, will be assessed on precise estimates of body fat mass.

In France, the Fleubaix-Laventie Health Study I (Fleubaix and Laventie are two cities in northern France) began in 1992. This study tested the effect of nutritional education as an integral part of the school curriculum taught by teachers for five years from kindergarten through junior high-school. This study demonstrated the feasibility of programs aimed at reducing food-related risks in school children through increased awareness, both by children and their families.

In a prospective epidemiology study, the Fleurbaix-Laventie Health Study II, which began in 1999, 1000 to 1200 school children will be followed for four years. The aim is to analyze factors leading to weight gain (genetic factors, hormonal factors, physical activity, food intake, lifestyle) in a normal population living in an ordinary environment. The results will be analyzed with the aim of elaborating an adapted preventive policy.

Diagnosis of obesity is based on auxology and gets more accurate by measuring fat mass distribution

One might question the usefulness of a discussion concerning such an obvious diagnosis as childhood obesity. But in real clinical situations, the diagnosis is not always easy to establish.

Obesity is defined as an excess of fat mass, an entity that cannot be measured directly. Body composition, and in particular the fat mass, evolves with growth, differently in boys and girls. Ethnic origin affects the distribution of body fat and perturbed growth during childhood influences body proportions. In addition to these elements, the subcutaneous or intra-abdominal localization of abdominal adipose tissue is associated from childhood with different levels of cardiovascular risk. The risk is higher when fat is deposited in an intra-abdominal localization, probably in relation with biological mechanisms or different genotypes.

In infants born at term, fat mass constitutes 13 to 15% of total body weight. This proportion then varies with age. After the pre-puberty rebound, there is an increase in body fat in girls and a decrease in boys. Early in adulthood, 20 to 25% of the female body is composed of fat while in males, the percentage is 15 to 20%.

Evolution of fat mass by age

Period	Fat mass / body mass (%)
Birth	13 – 15
5 – 6 months	25 – 26
18 months	21 – 22
5 – 6 years	12 – 16
Adult	20 – 25 (women)
	15 – 20 (men)

In children, most of the fat mass is subcutaneous. North American studies have however shown that starting at the age of 7 years, Caucasian children have a greater intra-abdominal fat mass than Afro-American children.

Anthropometric measurements - body weight, height, circumferences (waist, hip, upper arm), skin fold thickness - provide direct indications of body fat. Body weight and height are two simple measurements that can be used to draw body composition curves (BMI). These curves are universal indicators applicable in all circumstances and widely used by practitioners. Although it is easy to measure waist, hip and limb circumferences, the results obtained are subject to important errors because it is difficult to identify the precise anatomic area to measure and because intra-observer variability is high. For skin fold thickness, a costly, specially designed caliper is needed to acquire quality measurements at one or several sites (tricipital, bicipital, sub or suprascapular). This method is not adapted for severely obese children because it is difficult to correctly measure the thickness of the entire subcutaneous fat layer. Theoretically, skin fold thickness is more appropriate for epidemiological research.

Different methods have been developed to measure body composition. These methods have to be validated in the population to be studied and must demonstrate an adequate degree of precision and sensitivity.

Total body composition can be measured with the hydrostatic method based on the principle of Archimedes. This historical method is not particularly easy to perform in children since the entire body has to be submerged in a cylinder filled with water.

Isotopic dilution methods using deuterium or oxygen-18 or other non-isotopic markers can also be used to assess lean and fat mass. In children, these methods have demonstrated that the increase of the extracellular/intracellular water ratio known to exist in obese adults is also present in children. These methods are considered only research tools.

Imaging techniques have provided most useful information in children. Computed tomography (CT) and nuclear magnetic resonance (NMR) can be used to measure visceral fat since they enable a distinction between the subcutaneous and intra-abdominal layers. The CT scan exposes the child to a low dose of x-rays and the NMR acquisitions are relatively long. Ultrasonography has been used in adults and more recently in Japan to measure subcutaneous fat in children. This technique merits further development.

Dual energy x-ray absorptiometry (DEXA) exposes the child to about one-tenth of the irradiation of a chest x-ray. Although this method cannot distinguish between subcutaneous fat and intravisceral fat, it can differentiate fat mass from lean mass.

Impedancemetry is based on the fact that the speed of conduction of a weak electrical current is different through lean mass and fat mass. The measurement obtained is used to deduce a proportion. Results are however difficult to interpret in children due to physiological changes in body composition during growth and to the expansion of the extracellular compartment in obese children. Impedancemetry can only be used after calibration experiments have validated the method in the population under study.

Measurement of body composition

Technique	Application	Measurement
Double-labeled water	Research	Lean body mass, fat body mass, extracellular compartment
CT scan	Research	Subcutaneous and intra-abdominal visceral fat
NMR	Research	Subcutaneous and intra-abdominal visceral fat
Ultrasonography	Clinical use to be evaluated	Subcutaneous fat
DEXA	Possibly for clinical use	Body composition
Impedancemetry	Clinical use to be evaluated in children	Lean / fat body mass ratio

All of these different methods designed to measure body composition are particularly interesting tools for clinical research in children. However for epidemiology purposes, particular attention must be made when choosing a method since most have been validated in small pediatric populations.

Serum insulin, leptin and free fatty acid levels are high in obese children

In common childhood obesity, hormonal and metabolic anomalies are frequently observed during the early years of excess body weight, but little is known about the “pre-obesity” period. It is not known whether these anomalies are secondary to the development of childhood obesity or exist before its onset.

Obese children have high fasting and post-prandial serum insulin levels (or an abnormal response to a glucose tolerance test). The increase is globally proportional to fat mass with important individual variability. This increase could be the expression of pancreatic adaptation to peripheral demand or reflect a primary hypersecretion in obese children. Studies have to be conducted in children in the pre-obesity period to determine the mechanisms inducing hyperinsulinemia.

Obese children also exhibit hypercortisolism. Here again there is wide individual variability in the high mean level of free cortisol eliminated in the urine over 24 hours.

Serum concentrations of insulin-like growth factor 1 (IGF-1) are high while growth hormone levels are rather low, both in baseline conditions and after stimulation tests (“false” growth hormone deficiency).

Serum levels of leptin, a hormone produced by adipocytes, are higher in obese children, proportionally with excess weight. For the same fat mass, the increase is greater in girls than in boys. Despite the elevated level of serum leptin, known to be a regulator of food intake in rodents and in single-gene human models, certain obese children nevertheless maintain their hyperphagia. The levels of other hormones regulating intermediary metabolism are not affected significantly in obesity.

In vivo physiological investigation methods (glucose clamp, non-radioactive isotopic tracers, controlled hormone infusion) have provided evidence of insulin resistance in liver and muscle tissue. Insulin resistance appears to be a consequence more than a cause of childhood obesity. There is also a marked resistance to the lipolytic effect of catecholamines. It has been hypothesized that leptin resistance could also be present since obese children exhibit high levels of leptin. Although no molecular evidence supporting this hypothesis has been found, it has been postulated that leptin transport to the hypothalamus (capillary endothelium of the blood-brain barrier) could be inhibited.

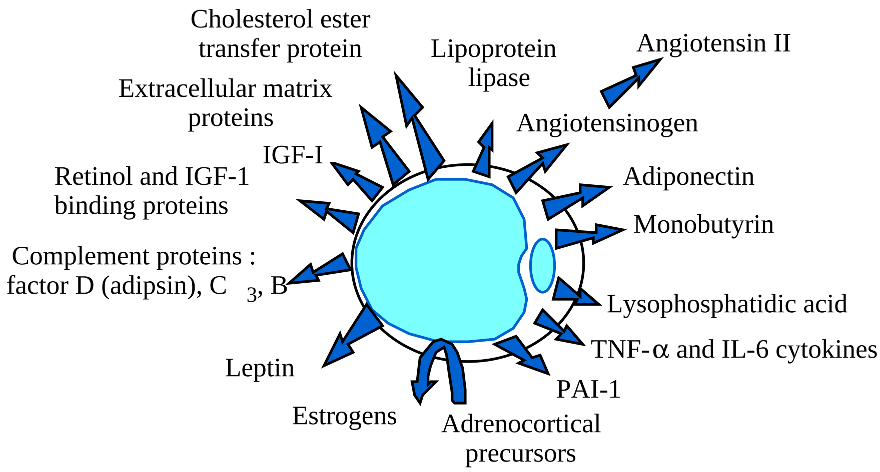
The fasting glucose level is normal in obese children, but a large percentage of them do have true glucose intolerance as demonstrated by oral glucose tolerance tests, potentially heralding later development of type 2 diabetes mellitus. However, to our knowledge, there has not been a single case of diabetes that can be attributed to childhood obesity before the age of 15 years in France. Pathological elevation of cholesterol and triglyceride levels has never been described, but there is a rather loose correlation between the degree of excess weight and the level of circulating lipids. This tendency could be aggravated with increasingly severe and persistent obesity, at least in certain subjects predisposed to obesity.

Free fatty acids are used by the organism to regulate energy balance, but might intervene in intermediary metabolism via other, poorly understood, mechanisms. In most obese children, the fasting serum level of free fatty acids is about twice the normal level. This might affect the regulation of certain specific pathways involved in the development of insulin resistance (glucose uptake in muscles, perturbed response to insulin) or in the transcriptional regulation of the expression of certain pancreatic or adipocyte genes via an interaction between free fatty acids and peroxysome proliferation activation receptors (PPAR).

In girls, the onset of ovulation at the end of puberty is known to be related to the degree of excess fat mass. Experimental and functional arguments would also suggest an interference of leptin in the biology of puberty and reproduction.

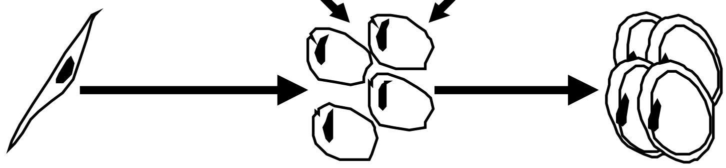
Nutritional factors affecting adipocyte formation, a phenomenon particularly important during early childhood and puberty

The adipose tissue, present in many sites (subcutaneous, abdominal, perirenal), is recognized as an organ with endocrine properties.



Endocrine and paracrine activity of the adipocyte

Adipose tissue, like all other human tissues, develops *in utero*. Adipose tissue first appears during the second trimester of fetal life then develops extensively during the third trimester. Adipocytes stem from precursor cells or preadipocytes and can be formed throughout life. However in both animals and in humans, the capacity of preadipocytes to proliferate then differentiate into adipocytes is much greater during early childhood. This capacity to proliferate appears to decline with age although a second phase of proliferative activity is observed around puberty. Up to the age of 5 to 6 years, the increase in the amount of adipose tissue results more from an increase in the number of adipocytes (hyperplasia) than from an increase in the size of the adipocytes (hypertrophy related to continuous accumulation of neutral lipids or fat in adipocytes). In obese adults, the observed hyperplasia is greater when obesity began during childhood. There are thus two particularly sensitive periods, the post-natal period and puberty. During these periods, nutritional and hormonal stimuli through their intensity and frequency would have an “adipogenic” effect favoring the differentiation of preadipocytes into adipocytes. These adipogenic stimuli in small numbers are well known. In addition to the requirement for glucocorticoids, the other stimuli are modulated by nutrient intake, either directly by fatty acids produced from the breakdown of food fats or indirectly via insulin and IGF-1.



Adipocyte differentiation process

Globally, *in vitro* and *in vivo* work in animal models have demonstrated that all the fatty acids that have a true hormone effect do not have the same "adipogenic" capacity. In the rat, diets enriched with polyunsaturated fatty acids (n-6 or linoleic acid) lead to hyperplasia of adipocytes while diets enriched with saturated fatty acids (lauric, myristic, palmitic acids) lead to hypertrophy of the adipocytes. Unfortunately, once adipocytes have been formed in excess number via a hyperplastic process, they can later undergo hypertrophy if energy intake (high fat diet) exceeds energy expenditure.

The importance of early breast feeding in the prevention of later obesity at the age of 5 to 6 years is quite noteworthy. Mother's milk supplies the infant with a relatively low protein diet, rich in saturated and monounsaturated fatty acids but with a low content in polyunsaturated fats. To date, we have no information on whether or not enrichment of infant formulas with polyunsaturated fats (n-6 or linoleic acid) has an effect on the hyperplastic process.

To summarize, excessive hyperplasia of adipose tissue during the sensitive periods of development, later aggravated by hypertrophy of the adipocytes, could lead to the development of obesity. Nutritional situations that favor the flow of n-6 polyunsaturated fatty acids into infantile adipose tissue (as would be the case with infantformulas) and later would favor circulating and/or local levels of IGF-1 (as in the case of high-protein diets given in addition to formulas) might favor the development of adipocytes by hyperplasia. A diet that is permanently overly rich in lipids and proteins could thus favor the formation of an excessive amount of adipose tissue via the combination of hyperplasia and hypertrophy.

Obesity develops when energy intake exceeds energy expenditure

Nutritional requirements for energy, lipids, carbohydrates and proteins are age dependent. Infants (0 – 2 years) have high energy requirements due to their rapid rate of growth. About half of the energy requirement is supplied by lipids (the brain requires fatty acids for the maturation process which continues during early infancy).

Growth is slower in preschool children. At this age, the child can regulate his/her energy balance over several days. There are few arguments supporting the usefulness of systematic restriction of fat-rich diets. Energy requirements should be covered by a diversified diet.

Comparison between recommended dietary intake (from the Nutrition Committee of the French Society of Pediatrics) and dietary intake measured in French children in 1997 (Boggio et al., 1999)

Age	Protein		Lipids		Carbohydrates		Energy
	(g/kg)	(%)	(g/kg)	(%)	(g/kg)	(%)	(kcal/kg)
			Recommended dietary intake				
0-6 months	2-1.8	7.6-6.6	4-6	34-51	10-15	38-57	110-100
6-12 months	1.5-1.4	6-5.8	4	37	14-15	57-62	95-100
			Real dietary intake				
10-12 months	3.8	16	-	28	-	56	96

For children aged 6 to 12 years, there is a considerable inter- and intra-individual variability in energy requirements for growth and physical activity. During puberty, sufficient nutrient intake (energy, macro- and micro-nutrients) is needed. Severe dietary deficiency can inhibit growth and delay puberty. The maturation phase of growth begins two years earlier in girls than in boys and the peak in the growth curve is more marked in boys, leading to particularly high energy requirements. Consequently, nutritional guidelines designed for adults, particularly those limiting fat intake (≤ 30 or 35%), should be applied progressively, after the peak in growth during adolescence.

When obesity develops, the role of food intake can be conceived in terms of two balances regulating body composition : energy balance and macronutrient balance.

When energy intake is greater than energy expenditure, the excess energy is stored in the form of triglycerides in adipose tissue. This dynamic phase of developing obesity can be a slow progressive process when the energy balance is only slightly positive. On the contrary, a rapid gain in weight can be observed in case of hyperphagia. Energy expenditure in obese children is greater than in normal weight children. The weight of the accumulated fat mass is associated with an increased lean mass due to a rise in the basal metabolism, which accounts for nearly two-thirds of the total energy expenditure. Expressed per gram of lean mass, energy expenditure in obese children is the same as in normal weight children. It is important to underline the great inter- and intra-individual variability in energy expenditure in children. Spontaneous or voluntary physical activity varies considerably from one day to another and energy requirements during periods of peak growth can constitute a major part of total energy expenditure.

The macronutrient content of the diet is the second crucial element regulating body composition. If nutrient intake is excessive, carbohydrates and proteins are oxidized and lipids are stored in adipose tissue. Obesity can thus be considered as the consequence of a limited capacity to adapt to a high-fat diet. This capacity depends on genetic factors but also on the level of physical activity and on the amount of muscle mass because at rest muscles use fatty acids as their energy source.

The energy content of food is a major factor regulating food intake. Higher energy foods are more palatable and less satiating. Early in life the infant, via a process of conditioned learning, chooses food to satisfy energy needs. Adaptation potential may be less effective in obese children although the factors involved are very poorly understood. Lipids have a high energy content (9 kcal/g *vs* 4 kcal/g for carbohydrates and proteins), but also have other properties favoring the development of obesity : organoleptic properties and excellent palatability. Energy expenditure for metabolic transformation of lipids is low (< 4% of energy intake). Dietary preference for lipids (it is unknown whether this preference results from genetic or cultural transmission) could be an important element to consider in obese families.

Eating can be considered as a behavioral attitude integrating multiple metabolic, psychological, social, cultural, and more generally environmental factors. The family setting has a certain influence on eating behavior in children (tastes, food choices and preferences). In the current state of our knowledge, no definitive conclusions can be drawn on the influence of changing lifestyle (fast foods, eating outside the home, changing structure of meals). There are no scientific arguments demonstrating an impact of the number of meals per day on obesity. Nevertheless, clinical observations suggest that excess energy intake is often attributed to excessively copious meals or snacking between meals.

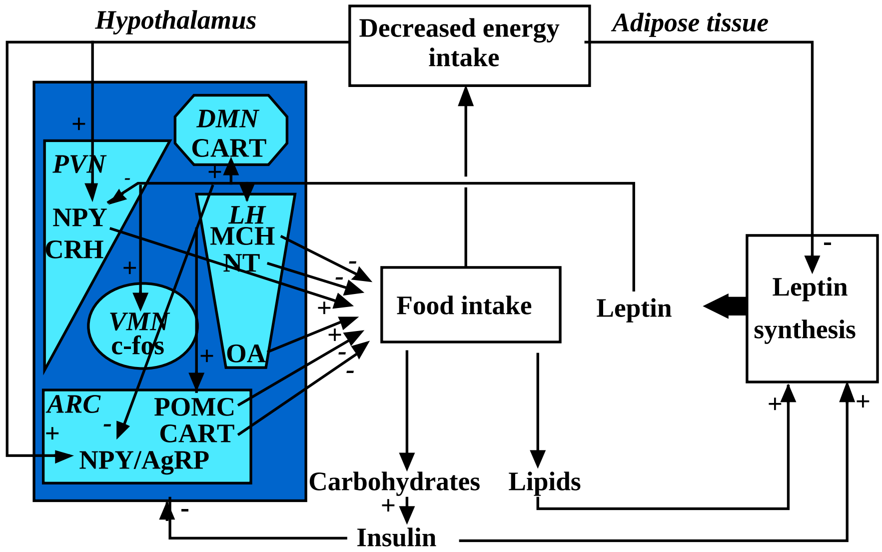
Maternal and post-natal diet influences the early development of systems regulating eating behavior in the animal

The principle data on central regulation of eating behavior have been obtained in normal or obese animal models, mainly in adult animals. Data are sparse in humans for both adults and children because the cerebrospinal fluid, the basic means of obtaining information on the central nervous system and central neuromediators, is not easy to obtain and does not provide an exact picture of events at the tissue level in different areas of the brain.

Many mediators are involved in the regulation of eating behavior. Neuropeptides act via the neuronal networks, particularly in the hypothalamus including the arcuate (ARC), the paraventricular (PVN), the ventromedial (VMN) and the dorsomedial nuclei as well as the lateral hypothalamic nucleus.

Eating behavior results from an equilibrium between stimulating neuropeptides (neuropeptide Y (NPY), galanin, orexins, agouti-related protein…) and inhibitor neuropeptides (corticotropin releasing hormone (CRH), neurotensin, cholecystokinin, type 4 melanocortin receptor agonists…). NPY is currently the only neuropeptide known to induce obesity via its stimulating effect on food intake and its inhibitory effect on energy expenditure. There are strong links between these neuropeptidergic systems and peripheral hormones (leptin, insulin, cortisol).

These neuropeptidergic systems develop early in life and some already have their adult configuration at birth (NPY, somatostatin). Others develop after birth (galanin) and/or continue to evolve into adulthood (galanin, neurotensin…). They are sensitive to nutritional and metabolic conditions early in life (maternal diet during gestation, excessive food intake during the first days of life, insulin deficiency due to diabetes or hyperinsulinism). These different conditions can provoke modifications in body weight at birth which are associated with perturbations of the neuropeptidergic systems (with a particular impact on food preference) and are precursors to the development of obesity.



Schematic representation of the regulation of eating behavior : neuropeptidergic and peripheral signalization pathways

Thus nutrition during fetal life appears to be one of the strong vectors of mother-fetus interactions with the environment. The nutritional factor is particularly interesting because it can be quantified and also because it can be modified and controlled. Ingestion of a poorly balanced diet (carbohydrate-rich diet, fat-rich diet) leads to differences in body weight at birth. It also leads to over expression of neuropeptide Y and galanin at weaning, associated with a long delay in the establishment of food preferences. This qualitative dysregulation can have a long-term impact on body weight. If rats are overfed during the post-natal period, a condition provoked by limiting the number of animals in the litter, they overeat throughout their life and develop obesity associated with modifications in the neuropeptidergic systems. Larger numbers of galanin- and NPY-sensitive neurons are also detected in zones playing a key role in eating behavior regulation (ARC, VMN, PVN). Changes in other neurotransmitters (catecholamines, dopamine) are also observed.

Metabolic disorders in the gestating female rat, such as diabetes or hyperinsulinism, favor the development of obesity in the offspring. Here again, an increase in the number of NPY- and galanin-sensitive neurons is observed in the adult offspring born to mothers with metabolic disorders. These modifications contribute to dysfunctions in eating behavior and weight regulation.

Stress is a difficult parameter to define in terms of neuropeptidergic status and its impact on weight regulation. Corticotropin releasing hormone is the main mediator. Activation of CRH activates the hypothalamo-hypophyseal-adrenal axis (HHAA). The resulting hypercortisolemia is associated with abdominal type obesity. A fat-rich diet in gestating or nursing mothers leads to hypersensitivity to stress in the offspring after weaning. The HHAA is activated during stress leading to elevated ACTH and cortisol secretion inducing greater storage in adipose tissue. In the obese rat model, meal eating also activates the HHAA (but via a pathway independent of CRH) and can be considered as a stressful event leading to the same storage effect.

In humans, certain studies have demonstrated that stress factors specific to childhood (lack of attention from the family, school failure) are associated with increased risk of obesity.

Brown adipose tissue in humans and its role in energy balance : a potential anti-obesity effect ?

Most of the lipid reserves in the human body are stored in adipose tissue widely distributed in subcutaneous and intra-abdominal areas. Adipose tissue is basically composed of triglyceride-containing cells called adipocytes. All the adipocytes are similar in the adult body, but not so in infants. At birth, part of the triglycerides are stored in a special type of adipocytes called brown adipocytes. The other adipocytes are called white adipocytes.

White adipocytes predominate in adults and constitute nearly all of the adipose tissue. White adipocytes are large cells containing a unique vacuole filled with fat (unilocular fat deposit). Brown adipocytes form brown adipose tissue. This tissue is a well-characterized tissue with specific anatomic locations and function in rodents and hibernating animals. The distribution and physiological role of brown fat in the human newborn is poorly understood. Brown adipocytes are however present in the human body and are identical to the brown adipocytes observed in rodents.

Unlike white fat, brown fat deposits have a rich vascular system. In addition, brown adipocytes are directly innervated by orthosympathetic fibers. Brown adipocytes contain several drops of fat (multifocal fat deposits) and most importantly a large number of mitochondria. This simple observation indicates that these cells have a particularly high capacity for oxidation.

Work conducted in rodents exposed to cold, in newborn rabbits and in animals arousing from hibernation has demonstrated that this brown adipose tissue produces heat used to regulate body temperature. It would thus be logical to hypothesize that brown adipose tissue in newborn humans has the same function.

The mechanism of thermogenesis in brown adipocytes in rodents is well known. When rodents are exposed to cold, the brain, particularly the hypothalamus, activates orthosympathetic fibers innervating the brown adipocytes. This activation leads to the release of noradrenaline that binds to the cell's adrenergic receptors. These receptors then immediately induce active lipolysis of the triglyceride droplets releasing free fatty acids. Within less than one minute there is a strong rise in heat production. The heat produced is evacuated towards the brain, heart, and kidney via vessels situated near the brown fat deposits.

Thermogenesis in brown adipocytes stems from regulated respiratory uncoupling. In most of the cells in the human body, the respiration process occurring in the mitochondria is coupled with the phosphorylation of adenosine diphosphate (ADP) producing adenosine triphosphate (ATP). In brown adipocytes, the mitochondria possess a specific mitochondrial transporter that blocks ADP phosphorylation and stimulates substrate oxidation. This situation is defined as uncoupled respiration and is expressed by dissipation of oxidative energy in the form of heat. The protein regulating this respiratory uncoupling in brown adipocytes has been identified and is called the uncoupling protein (UCP). Activation of UCP by free fatty acids induces the thermogenic uncoupling observed in brown adipocytes.

Brown adipose tissue is present in large quantities in the human embryo around the last two months of gestation. It can be easily observed in newborns and infants. White adipose tissue then becomes predominant in humans. Adults only have a few brown adipocytes although large numbers can be detected in selected subjects. UCP, or more recently UCP1, is easily detected in brown adipocytes in babies proving that these adipocytes are equipped with the same thermogenesis system as brown adipocytes in small mammals.

Since the important thermogenic capacity of brown adipose tissue is well-established in rodents, it is reasonable to postulate that brown adipocytes in humans have the same capacity to dissipate energy in the form of heat. It has been observed that babies transferred from an environment at 30°C to an environment at 16°C double their oxygen consumption and greatly increase their thermogenesis. This might be due to brown adipose tissue metabolism. The potential contribution of brown adipose tissue to thermoregulation in the human newborn remains to be studied, but before such study can be undertaken, it will be necessary to identify the anatomic distribution of brown fat deposits in the human baby. Secondly it will be important to measure the contribution of this tissue to thermogenesis. Brown adipose tissue is an organ capable of rapidly burning fat; it can also inhibit fat deposition. Potentially, this tissue could have an anti-obesity effect. Besides the probable role of brown adipose tissue in controlling body temperature and fat degradation, some very recent reports suggest that thermogenesis in brown adipose tissue could induce satiety at the cerebral level, controlling the end and rhythm of feeding in the baby. Further work is needed in this area. If ongoing work confirms current hypotheses, brown adipose tissue may be found to play an important physiological role in the regulation of energy balance in babies.

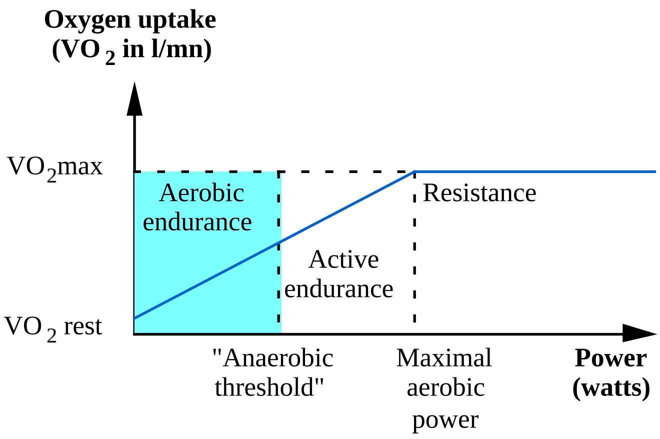
Regular physical activity induces reduced fat mass and improves metabolic anomalies in obese children

Despite disagreement on the best way to assess physical activity in children, many studies report an association between increased prevalence of childhood obesity and the current trend towards more sedentary lifestyle in children. Although much attention has recently been focused on the energy expenditure induced by fidgeting, a possible explanation of the observed differences in individual weight gain, it is clear that the most important factor favoring weight gain is the general reduction in overall physical activity among children who spend much time watching television or playing video games. The impact of this reduction in physical activity would be particularly important in young girls during the critical prepubertal period.

This trend must be taken into account when developing programs designed to reduce the incidence of obesity. It must also be acknowledged that the prescription of physical activity in obese children is not necessarily followed by the expected results. As for adults, physical training has little effect on weight. It does increase total energy expenditure but apparently has only a relatively small effect on resting energy expenditure, both in the short and long term. There are mainly two reasons underlying these apparently disappointing results.

The first explanation is probably the difficulty encountered in assessing the optimal level of physical activity and in the participant adherence to the program.

Physical activity is often defined with low precision in terms of type of activity, intensity, and duration, although it is known that the respective expenditure of fat and carbohydrate energy is directly related to the relative intensity of exercise. The level of physical exercise can be expressed as a percentage of maximal aerobic power, providing a simple definition of the notions of endurance and resistance. The problem thus is to define for a given child the level of exercise allowing maximal use of fat over carbohydrates while keeping in mind that exercise level also determines how long such activity can be maintained. This level could be considered as an “anaerobic threshold”.



Evaluation curve for physical aptitude

Like adults, children have a hard time adhering to regular training programs maintained over a long period. Recent studies have developed different approaches aimed at improving adherence, sometimes using methods some might consider to be overly directive.

The second reason behind the disappointing results of training programs in obese subjects is probably related to inadequate assessment criteria. Measuring weight loss is insufficient. The efficacy of a physical activity program should be assessed by measuring changes in body fat mass or improvement in metabolic anomalies associated with obesity. An illustration is the fact that many of the French finalists in the latest rugby world cup would have to be considered as obese on the basis of weight or BMI measurements Actually, studies conducted in obese children do generally demonstrate a marked effect of regular physical activity on the percentage of fat mass and on improvement in associated metabolic anomalies.

Several mechanisms are involved, but it is clear that the effect of physical activity on fat mass is related to adipocyte lipolysis. Visceral or subcutaneous adipose tissue stores fat in the form of triglycerides and releases free fatty acids by lipolysis. Lipolysis is regulated by a number of mediators, particularly catecholamines (adrenaline and noradrenaline). These two hormones bind to specific membrane receptors present in two forms, α and ß receptors, with opposing effects on lypolysis. Stimulation of the ß receptors (three types of ß receptors, ß1, ß2 and ß3 are recognized in humans) generates a cascade of events leading to activation of hormone sensitive lipase that releases free fatty acids and glycerol from triglyceride degradation. Inversely, stimulation of α receptors (here the α subtype) inhibits this cascade of events and thus has an antilipolytic effect. The distribution of these two types of receptors and their relative affinity for catecholamines differ for different types of adipose tissue (subcutaneous or deep adipose tissue); localization of the subcutaneous adipose tissue (abdominal or gluteofemoral), gender and age also affect receptor distribution and catecholamine affinity. These notions are helpful in understanding the difficulty encountered in mobilizing certain fat deposits compared with others, particularly in children where very little data is available on the relative distribution of adipose tissue in the body.

Until the development of more pertinent tools, the analysis of adipocyte lipolysis in humans is limited to measurements of changes in plasma concentrations of glycerol and fatty acids after exercise and/or training. Subcutaneous adipose tissue can now be studied by taking biopsies, allowing *in vitro* studies of the response of isolated adipocytes to catecholamines and other lipolytic agonists or antagonists such as insulin. Comparisons can thus be made between obese and normal weight subjects when they participate in acute exercise or endurance training programs. More recently, microdialysis techniques have been adapted to the study of human subcutaneous adipose tissue to enable *in vivo* or *in situ* analysis. With these techniques, lipolysis and its mechanisms can be studied during a given exercise session to examine the effect of calorie restriction or inversely the effect of macronutrient intake. This is a safe minimally aggressive method particularly adapted to future research in children.

The favorable effect of endurance training on lipolysis in subcutaneous adipose tissue has been demonstrated in adults. During exercise, fatty acid release is significantly higher in endurance trained subjects than in obese subjects. This better release is associated with lower antilipolytic ($\alpha 2$) activity in trained subjects. The fatty acid concentration in the blood stream is higher in obese subjects not only because of the importance of the fat mass that counterbalances a weaker response, but also because of the reduced use of these fatty acids. This points out the fact that training not only improves fat mobilization but also improves use of fatty acids in lean muscle tissue.

Endurance training, both in normal weight and obese subjects, improves adrenergic lipolysis in the adipocytes via a double mechanism : improved efficacy of the ß lipolytic pathway and reduced activity of the antilipolytic α pathway. Most of these effects have been demonstrated in abdominal subcutaneous tissue that is easily accessible for study in humans. A remaining question is whether these results obtained in adults can be extrapolated to children. Well-conducted longitudinal studies will be necessary to answer this question.

Recommendations

The important increase in the prevalence of childhood obesity, which has apparently doubled over the last ten years, raises important public health issues that must be addressed by public authorities. This changing situation, together with largely irreversible modifications in lifestyle, points out the importance of searching for risk factors accessible to prevention programs.

Based on a critical analysis of the literature, the group of experts identified several areas where recommendations can be made for clinical screening and prevention of childhood obesity. Studying risk factors for childhood obesity involves a wide range of areas (genetics, nutrition, sedentary lifestyle, stress, social and economic status…). Though incomplete, current data enable the definition of certain groups of children at higher risk of developing obesity. The use of simple tools such as weight and height measurements to monitor growth can help identify obesity early, an important challenge for the health care community in general.

Nutritional factors affecting the development of obesity appear to be particularly important during the early years of life. Coordinated efforts involving the family, the primary care physician, and the public health authorities as well as the food and agriculture industry are needed to determine appropriate preventive actions.

Sedentary lifestyle is a recognized major risk factor of obesity in modern societies where comfortable living conditions and motorized transportation limit physical activity. Actions aimed at counteracting the effects of sedentary lifestyle are difficult to design, involve a large number of participants (community authorities, health care workers, economic agents, consumers, urban designers) and entail complex political issues.

Despite considerable progress made over the last few years in our understanding of the biology of obesity, there remain several areas where reliable data are sparse. The experts emphasize the fact that we still do not have any early marker of obesity and propose a certain number of potential areas for research.

The epidemiological situation merits active surveillance, as well as public health actions and health education programs adapted to the age of the target population and their living conditions. In this light, it is important to focus attention on a certain number of available but often neglected indicators.

Education and training

PROMOTE PHYSICIAN AWARENESS OF OBESITY WITH CONTINUOUS TRAINING PROGRAMS

Obesity is a chronic condition that can begin early in childhood and should be recognized as a fully fledged disease compromising the individual’s physical, psychological and social well being. A better awareness of this disease should be developed among physicians and through medical school training programs. Such programs should review the new pathophysiological data and emphasize the importance of the physical examination, the analysis of risk factors (obese parents, sedentary lifestyle), the analysis of behavior (eating and other behaviors) and the long-term complications. The multifactorial nature of this disease points out that the consultation should not be limited to simple dietary advice. In order to promote active participation of physicians in prevention actions, the medical school curriculum should include a well-rounded training program on nutrition (including dietetics) emphasizing the beneficial effect of physical activity. The group of experts recommends training physicians in applying methods used to evaluate obesity (BMI, growth curves, adiposity rebound) and regularly monitoring growth in children. Physicians should also be trained to assess risk factors of obesity (level of physical activity, eating habits and level of food intake) so they can play their full role as health educators for children and their families. Finally physicians should be trained in recognizing and treating the complications of obesity.

RECOMMENDATIONS FOR PROMOTING MEDICAL MANAGEMENT OF OBESITY

In order to properly assess obesity in children, the physician must devote a considerable amount of time to the consultation with the child and the family to search for all the different aspects of the disease : risk factors, eating habits, physical expenditure, treatments aimed at changing behavior, evaluation of results and search for reasons behind observed failures. During this consultation, the physician should inform the family about the available validated tools for monitoring the child’s growth. The group of experts recommends promoting medical management of obesity by establishing a specific codification for consultations devoted to evaluating obesity and nutritional education.

TRAIN SCHOOL PHYSICIANS AND NURSES ON SCREENING FOR OBESITY AND ITS PREVENTION

School physicians and nurses play an important role in screening for obesity in children. Their training should be in phase with the current knowledge. The group of experts recommends that school physicians and nurses be trained to screen for childhood obesity (calculation of the BMI) so that when they detect obesity they can advise the family to seek medical care.

School physicians and nurses and the physician practicing in Mother and Child Health Prevention Centers should actively participate in prevention programs and in local, regional, or national educational projects. The school physician should play an important role in nutritional education and actively participate in decisions concerning childhood nutrition.

ANTI-DISCRIMINATORY ACTIONS

Studies have demonstrated that obese children are exposed to social discrimination quite early, both from other children and from adults. These children are caught in a vicious circle, integrating the discriminatory attitudes as part of their personal image. This leads to loss of self-esteem, a potential source of failure at school. The group of experts recommends that an information program be developed in the public media. This program should be designed to improve awareness of discrimination against obese children, both in the public opinion and in the educational and medical communities, in order to avoid the isolated situation of the obese children and better fight against discriminatory attitudes.

Screening

CHILDREN SHOULD BE WEIGHED AND MEASURED EVERY YEAR TO MONITOR GROWTH

Obesity is an excess of fat mass that can be estimated indirectly from two easily measured variables : height and weight. The body mass index (BMI) or Quetelet index is the ratio of height (expressed in kg) over the height (expressed in meters) squared. BMI curves, standardized by age and sex, have been printed in the children's health diaries in France since 1995 and are essential tools for monitoring growth in children of all ages. The group of experts recommends that children be weighed and measured at least once a year (family physician, pediatrician, hospital outpatient clinics). These measurements should be recorded in the child's health diary; the BMI should be calculated to draw the BMI curve in addition to the weight and height curves.

For school age children, the group of experts recommends that all children should be weighed and measured every year starting at the age of 6 years as part of the regular school health examinations. The parents should be informed of the results (calculation of the BMI to detect obesity). Before the age of 6 years, children should be followed by a family physician, a pediatrician or a Maternal and Infantile Prevention Center.

IDENTIFY CHILDREN AT RISK OF DEVELOPING OBESITY

The BMI curve takes into account the child's weight, height, and age, providing a means of monitoring changes in body corpulence during growth. Normally, changes in fat mass cause the BMI to rise during the first year of life then to decline up to the age of 6 years, followed later by the adiposity rebound. It is important to monitor the dynamics of the BMI curve in order to identify the beginning phase of obesity. A BMI curve that rises abnormally before the expected adiposity rebound can readily return to the normal range but generally does not if the rise occurs after the adiposity rebound. The group of experts recommends that children whose BMI curve rises to the upper range of the standard curves printed in the health booklet should be considered to be at risk of developing obesity and should benefit from regular medical care. These children and their families should be advised about appropriate nutritional balance and the advantages of physical activity (active games, walk…).

Current studies suggest that an early adiposity rebound before the age of six years is predictive of later obesity. The group of experts recommends determining the age of the adiposity rebound using the BMI curves and to consider an early rebound as a risk factor for the development of obesity. A larger scale used for the standard BMI curve printed in the health diary for the 0 to 8 year range would allow a better visualization of the curve during this age range.

IDENTIFY OBESE CHILDREN WHO SHOULD BE GIVEN EARLY MEDICAL CARE

The overweight child can be identified from the BMI curves. A BMI above the 97th percentile is a sign of obesity. However, before the adiposity rebound, i.e. before 6 – 8 years, the BMI is insufficient to diagnose obesity because of physiological changes in body composition. Before this age the diagnosis can only be confirmed if the child has massive obesity and both parents are obese. For these children, the BMI curve should be monitored carefully. The group of experts recommends that all children whose BMI is above the 97th percentile after their adiposity rebound (about 6 years) should be considered as having obesity and given appropriate medical care. If the screening is conducted as part of the school health program, the parents should be invited to consult their family physician or competent health services.

Epidemiology studies have shown that obesity during adolescence increases the risk of morbidity and mortality during adulthood and that most obese adolescents will become obese adults. There is no reason to wait until puberty to give medical care for obesity.

Prevention

PROMOTE BALANCED DIET AND REDUCE THE SEDENTARY BEHAVIOR FOR CHILDREN AT RISK TO PREVENT THE DEVELOPMENT OF CHILDHOODOBESITY

Nutritional requirements for proteins, lipids and carbohydrates evolve with age. A poorly balanced diet early in life can influence later development of obesity. Children under two years of age have a high energy requirement and the balance between fatty acids is important. For children over two years of age, energy requirements should be met by a diversified diet with portions adapted to the child's age. During the rapid growth phase of adolescence, meals should supply sufficient nutrients and energy to avoid between meal snacks, a potential source of excessive calorie intake. The group of experts recommends that family physicians and pediatricians should have appropriate educational material to inform parents about the importance of a balanced diet. Physicians should refer to the propositions of the Nutrition Committee of the French Pediatric Society on nutritional requirements at different ages and recall the importance of eating fruits and vegetables.

Advertisements often incite children to consume high-energy snack foods. The group of experts recommends teaching children how to regulate their intake of high-energy foods both in solid and liquid forms (chocolate bars, biscuits, potato chips, soft drinks…). It is recommended to avoid eating food (both meals and snacks) when watching television.

There is a relation between obesity and sedentary lifestyle, which can be assessed with indices such as the amount of time spent watching television. It is also demonstrated that physical exercise has a beneficial effect on the child's development, corpulence and eating behavior. Thus physical exercise contributes to obesity prevention and reduces cardiovascular risk. The group of experts recommends promoting daily physical exercises for children at risk and varying activities during leisure time.

Obese children are often victims of discrimination at school and consequently want to be exempted from physical education classes. Physical education teachers should be informed about this discriminatory process so they can adapt their teaching methods to these children. If a child requires personal help, physical activities specifically adapted to his/her capacities should be proposed outside the school setting.

PROMOTE PHYSICAL ACTIVITY AS A GOOD HEALTH PRACTICE FOR ALL CHILDREN

The increased prevalence of obesity in children is a general phenomenon involving changing lifestyle and a subsequent decline in energy expenditure during daily life activities. These changes are basically irreversible and should be compensated for by instituting regular physical activities. Different forms of activities can be proposed depending on the age of the child. For infants, physical exercise should be developed mainly as a play activity. Up to the age of 12 years, spontaneous physical activities and leisure activities should be encouraged. In the family setting such activities can also be helpful in tightening family ties. For children over the age of 12 years, these leisure time physical activities should be further developed; sports activities in an organized structure should be encouraged without necessarily favoring competition sports. This implies an appropriate urban environment with sufficient areas for leisure activities and games for children; urban safety is particularly important so children can walk or ride their bicycle without danger.

The school curriculum in France allots a limited time for physical activity. The group of experts recommends that every school day should include at least one hour of organized physical activity under the guidance of a physical education teacher. Acquainting children with diverse physical activities should be helpful for promoting interest in sports activities in adolescents.

Regulations

THE COMPOSITION OF INFANT FORMULAS SHOULD BE BASED ON VALIDATED SCIENTIFIC EVIDENCE

It has been established that nutrition in the early years of life influences growth. The proportions of proteins, lipids and carbohydrates consumed early in life influence the development of obesity later in life. Infant formulas with a high content in polyunsaturated n-6 fatty acid (linoleic acid) can favor the formation of an excessive number of adipose cells. Supplementation of these infant formulas with essential fatty acids should be reexamined in light of recent data on their adipogenic potential. The group of experts recommends that the content of lipid, protein, n-6 and n-3 polyunsaturated fatty acid in infant formulas should match mother's milk as closely as possible. It is recommended that any change in the composition of infant formulas should be based on validated scientific evidence.

PROMOTE COMPREHENSIBLE LABELING OF FOOD PRODUCTS AND CONTROL ADVERTISEMENT MESSAGES

Children are particularly susceptible to advertisements inviting them to consume attractive products. The group of experts recommends that the competent authorities should rigorously control advertisement messages concerning food products and possibly prohibit messages aimed at children. Certain messages announce calorie or nutritional equivalents that are incomplete or equivocal.

In addition, parents should be informed about the nutritional value of food products for children; rigorous comprehensible nutritional labeling is needed. Misleading allegations concerning certain health aspects should not be tolerated. Teaching children to become well-informed critical consumers is an important educational objective for the family, the school and health professionals.

Develop research

STUDY FACTORS HAVING AN EARLY EFFECT ON EATING BEHAVIOR

Central systems regulating food intake and body weight develop during fetal life. This is a critical period of neuron differentiation which, if perturbed, can have an important impact later in life. It is also during this period that adipose tissue develops. Certain events occurring early during gestation remain poorly identified but appear to have a determining effect on later development of obesity. Physiological studies in animal models show that the *in utero* genomic imprint induces the development of several diseases, including obesity.

Certain studies have emphasized the importance of the mother-infant relationship demonstrating a correlation between obesity and lack of attention given to children. Likewise, infants exposed to stressful situations early in life might be more susceptible to obesity. The group of experts recommends studying the impact of nutrition and fetal and post-natal life on the central systems regulating food intake in animals. It would be useful to continue studies on the consequences of maternal obesity, gestational diabetes, and hyperinsulinemia on weight regulation and eating behavior in the offspring.

Very little work has been done on eating behavior in children at different ages, on the learning processes involved in tastes and food preferences, on the impact of stress, on the addictive behavior and on the social and anthropological aspects involved. The group of experts recommends using a multidisciplinary approach to study the regulation of eating behavior in children and its relationship with the development of obesity.

FUNDAMENTAL RESEARCH ON WHITE ADIPOSE TISSUE AND THE ROLE OF BROWN ADIPOSE TISSUE

A non-invasive method for assessing the mass of diverse adipose deposits using imaging techniques would be most useful for studying the development of adipose tissue. Currently, there is no known method that can provide a satisfactory assessment of adipose tissue cellularity, beyond the adipocyte phenotype (size and number), after differentiation has been completed. The group of experts recommends conducting research on molecular characterization of specific markers of adipoblasts in animals and humans. Adipoblasts differentiate into preadipocytes (adipocyte precursors) and could be useful for studying the adipocyte cell differentiation. This research would require using embryonic stem cells in combination with proteome analysis.

To determine the role of brown adipose tissue in the infant, it would be useful to establish the precise anatomic distribution of this tissue in the newborn infant using histological and immunological *in situ* hybridization methods. One hypothesis is that thermogenic activity of brown adipose tissue could be quantified using imaging techniques and indirect calorimetry in babies exposed to ambient temperatures of 30°C, 25°C or 18°C. Finally, a study of the relations between the temperature of body areas rich in brown adipose tissue in the newborn and the frequency and duration of breast feeding should be further developed. The group of experts recommends an investigation of the thermogenic activity of brown tissue in different situations allowing a precise assessment of its potential role in the regulation of food intake.

SEARCH FOR AND VALIDATION OF NEW MARKERS OR PREDICTORS OF OBESITY AND ITS COMPLICATIONS

Reliable methods for direct measurement of fat mass are not currently available for routine practice. It will be important to develop further medical imaging techniques in order to follow the evolution of fat mass/lean mass in children.

Peripheral parameters (hormones or metabolic parameters) reflect the functional status of the central nervous system. For groups at risk, measurements of total cortisol and serum cortisol levels after meals could provide insight into the emotional receptivity of children and their susceptibility to overweight. Measurement of salivary cortisol is a useful non-invasive tool for estimating susceptibility in children. The group of experts recommends studying the validity of certain biological parameters as predictors of obesity. With respect to the links between obesity and physical inactivity, it would be necessary to define a better tool for estimating the level of physical inactivity or sedentary lifestyle. It would be also useful to study the spontaneous activity of very young infants in order to evaluate a potential relationship with later development of obesity.

DEVELOP A LONGITUDINAL STUDY OF THE EFFECTS OF PHYSICAL TRAINING IN CHILDREN AND ADOLESCENTS

Endurance training in normal weight or obese adults improves adipocyte adrenergic lipolysis. This effect has been observed in abdominal subcutaneous tissue. It is not known whether the results obtained in adults can be extrapolated to children. The group of experts recommends initiating a longitudinal study in order to ascertain the adrenergic receptivity of adipose tissue in children and its response to endurance training. One of the objectives could be to demonstrate a critical period for the adipocyte, particularly during puberty, leading to the development of obesity and/or an optimal period when physical exercise is particularly effective.

DEVELOP EPIDEMIOLOGICAL STUDIES TO EVALUATE THE PREVALENCE OF OBESITY AND RISK FACTORS OF OBESITY

In France, few data are available on the trends of theprevalence of childhood obesity. According to a study conducted in the center part of France, the prevalence of obesity has more than doubled since the 1980s. In order to better understand the public health issues, the group of experts recommends establishing the prevalence of obesity in a representative sample of the juvenile population in France and to repeat this study regularly in order to determine the evolution of obesity.

Comparative studies, if possible in different geographical regions where lifestyle is notably different, could be useful to better identify risk factors related to obesity and to open up new avenues of research on the causal mechanisms involved. To better analyze the risk factors, the group of experts recommends the development of questionnaires providing information on nutrition, physical activity and sociological and anthropological data, particularly items that could be used to establish a link between obesity and cognitive dissonance (difference between the social norm and the practical reality). These questionnaires could also be used in consultations and would be helpful to identify the cause and consequences of obesity.

The group of experts repeatedly emphasized the potential role of factors intervening during fetal life or during the first months after birth on later development of adipose tissue. The group of experts recommends the institution of epidemiological studies to register maternal, fetal, and infantile factors that may be linked with the development of obesity and to conduct long-term monitoring of children to further advance our understanding of these relations.

PROMOTE INTERVENTIONAL STUDIES WITH AN EVALUATION OF THE PREVENTIVE ACTIONS AND HEALTH EDUCATION

There have been few interventional studies specifically designed to reduce the prevalence of obesity. Since lifestyle and eating habits vary considerably from one country to another, it will be particularly important to adapt each program to the population involved and to undertake such a study in France. Most of the studies have basically concentrated on nutrition education programs that have not produced any clear effect on body mass index.

Epidemiology studies should be continued on risk factors of obesity in French children in order to better define a prevention strategy. The group of experts recommends initiation or continuation of interventional studies to test the effect of regular physical activity on the reduction of the prevalence of obesity. These studies could compare the efficacy of spontaneous physical activity with that of a structured program in terms of energy expenditure, in the general population, in a group at risk, and in a group of obese subjects.