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Abstract

Obesity is often established in adolescence, and advances are being made in identifying its genetic underpinnings. We examine issues related to the eventual likelihood of genetic tests for obesity targeted to adolescents: family involvement; comprehension of the test's meaning; how knowledge of genetic status may affect psychological adaptation; minors' ability to control events; parental/child autonomy; ability to make informed medical decisions; self-esteem; unclear distinctions between early/late onset for this condition; and social stigmatization. The public health arena will be important in educating families about possible future genetic tests for obesity.

Keywords

genetic testing, minors, adolescents, obesity

Comments

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Research Issues in Genetic Testing of Adolescents for Obesity

Mary E. Segal, Ph.D., Pamela Sankar, Ph.D., Danielle R. Reed, Ph.D.

Obesity is often established in adolescence, and advances are being made in identifying its genetic underpinnings. We examine issues related to the eventual likelihood of genetic tests for obesity targeted to adolescents: family involvement; comprehension of the test's meaning; how knowledge of genetic status may affect psychological adaptation; minors' ability to control events; parental/child autonomy; ability to make informed medical decisions; self-esteem; unclear distinctions between early/late onset for this condition; and social stigmatization. The public health arena will be important in educating families about possible future genetic tests for obesity.

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Introduction

Categorizing Obesity as a Biobehavioral Trait

Advances in behavioral genetics point to the importance of biologic inheritance in behavioral traits as well as in medical conditions. Examples of the latter include diseases such as Huntington's disease, cystic fibrosis, Down's syndrome, and many others in which, when known genetic variants are present, it is almost certain that the affected individuals will develop the conditions. Other diseases, including breast and other cancers, are in some individuals the result of genetic variants interacting with environmental factors. This is necessarily a question

of degree: nearly all disease in some sense results from the interaction of genetic variation and the environment.¹

Although individuals affected with these diseases may experience guilt and stigmatization, society does not usually fault them directly for contracting them. It is generally recognized that a person with Huntington's disease does not do anything to acquire the condition—having parents who are carriers is necessary and sufficient. Similarly, breast and other cancers are generally viewed as resulting from either genetic inheritance or external forces, e.g., environmental toxins, outside the individual and largely beyond his or her control (although there are claims that eating this kind of food or avoiding that kind of environment may help to prevent cancer).

These conditions are distinct from those we call “biobehavioral” traits, which are perceived to be under the voluntary control of the individual and include alcohol abuse and addiction; some psychiatric conditions such as depression; obesity; and smoking addiction. Behavior associated with these traits leads to the assumption, in many people's minds, that the affected individuals have personal responsibility for their conditions.² However, recent laboratory advances suggest that biobehavioral traits have a strong genetic substrate.

We are particularly interested in obesity because it is widespread and implicated in many preventable diseases in the United States.³ Adolescence appears to be a critical period in developing obesity, and so obesity genetic testing may be targeted to this age group.

Medical Problems Associated with Obesity

Obesity is a serious and growing health care problem in the United States.^{4,5} We use federal guidelines identifying body mass index (BMI) 25 to <30 as overweight, and ≥ 30 as obese (BMI is calculated as kg/m^2). The condition is a precursor for many health problems, including diabetes,⁶ cardiovascular disease, hypertension, hypercholesterolemia, gallbladder disease, osteoarthritis, some cancers,^{7–10} and stroke.¹¹ As many as one-third of U.S. adults (59 million) are estimated to be overweight or obese,^{12,13} and prevalence is increasing: from 1991 to 1999, it is estimated conservatively that the prevalence of

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obesity in the United States increased by 58%.^{14,15} Prevalence among younger adults 18 to 29 years old is especially notable, increasing 70% from 1991 to 1998, from 7.1% to 12.1%.¹⁴ In youths, the increase in obesity is equally alarming: approximately 11% are seriously overweight and an additional 14% are at risk for overweight.¹⁶ Obesity is now one of the most serious and rapidly worsening health problems of youth in the United States,^{17,18} and obesity-related diseases are increasing in younger people.^{12,19} In long-term follow-up, boys' obesity in adolescence leads to increased mortality in later life relative to lean peers,^{20,21} even if weight at age 50 is statistically controlled.²² Obesity is remarkably resistant to behavioral treatment: up to 90% to 95% of those who lose weight return to their previous obese state.^{23–25} Late adolescence appears to be a critical period in the development of obesity that persists into later life.²⁶

Progress in Identifying Genetic Underpinnings

The importance of environmental factors in obesity is clear,^{27–29} but the importance of physiologic factors in metabolism has also been confirmed; for example, a recent report showed that obese adolescents consume no more “junk food” than non-obese adolescents.³⁰ Genetic factors are shown in studies of twins, familial aggregation, and adoptees whose weight correlates more closely with their biologic rather than adopted families.^{31,32} Half of the variance in the amount of abdominal visceral fat, which is believed to confer greater health risk than other types of fat, is possibly determined by a single gene in some populations, whereas 21% may be determined by more than one,^{33,34} and 40% to 80% of the variance in body weight is due to genetic factors.^{35,36} Many scientists assert that it is only a matter of time until tests are available for genes that contain DNA sequence variants that predispose people to develop obesity.¹² Five genes responsible for obesity in humans have been described: leptin,³⁷ leptin receptor, prohormone convertase 1 (PC1), and pro-opiomelanocortin (POMC), all of which are associated with hypothalamic and pituitary disorders, and the melanocortin-4 receptor (MC4-R),³⁸ which causes a non-syndromic phenotype of morbid obesity. Recently, another gene has been identified that is associated with a relatively mild obesity.³⁹ A fairly large number of genetic markers are likely involved in most cases, each coding for a specific propensity for a particular metabolic effect.⁴⁰ The implications for genetic testing are clear: “If some environmental variables manifest themselves only on certain genotypes, efforts to prevent obesity at a public health level can be focused on recognition and counseling of susceptible individuals. . . . In addition, appreciating the importance of genetic variation as an underlying cause helps to dispel the notion that obesity represents an individual defect in behavior with no biological basis. . . .”³¹

Genetic Testing of Adolescents for Obesity

We first review the relevant issues in genetic testing generally, followed by genetic testing for minors, and then possible future genetic testing for obesity in minors. We then discuss approaches to future genetic testing for obesity, particularly in minors, suggested by the review.

General issues in genetic testing relevant to adolescents include the involvement of the entire family, difficulty in understanding the meaning of genetic variants and genetic risk, and our incomplete understanding of how knowledge of genetic status affects health behavior and psychological adaptation.

Relevance to Biologic Relatives

A key aspect of genetic testing that is often said to set it apart from other laboratory procedures is that the information an individual receives about a genetic test has implications for biologic relatives, especially close ones. Patients sometimes decide to withhold results from family members.^{41–44} When is it appropriate to notify other family members of results of a genetic test? Is it ever morally defensible, or imperative, *not* to notify members under certain circumstances, e.g., if the family member is emotionally fragile and there is no known treatment or cure? Of course, families are often involved when a member receives any kind of diagnosis or laboratory result, and, even if it does not have direct implications for the physical health of other members, it may well influence their future financial resources and/or their psychological well-being. In the case of genetic tests for obesity, however, which would not signal imminent danger to relatives, there seems to be less reason to reveal test results to other relatives; indeed, it could be seen as a betrayal for a parent to reveal an adolescent's test results to others.

Comprehension of the Meaning of a Genetic Test for Risk

The difficulty of conveying the significance of a genetic test result is particularly acute in the case of polygenic traits of low penetrance, e.g., cancer, in which affected genetic status leads to an increased risk, but far from absolute certainty, that the individual will have the disease. This may well be the situation for obesity. (There are infrequently occurring exceptions—for example, individuals affected with congenital leptin deficiency have a monogenic variation that clearly results in obesity.)

Public understanding of risk and probability statements is limited.^{45,46} Even highly educated adults have difficulty using mathematical operations concerning probabilities,⁴⁷ and scientific illiteracy is widespread.⁴⁸ The concept of lifetime risk is poorly understood, and so is the idea that demographic factors modify average risk.⁴⁹ More research is needed on numeracy and optimal methods for presenting risk estimates.⁵⁰

Subtle language and framing effects often operate, e.g., whether risks are presented as relative or absolute,⁵¹ rates or proportions,⁵² framed as loss or gain,⁵³ or whether subjects are asked whether they would “accept” or “risk” adverse medical situations.⁵⁴ Even after counseling, many patients fail to recall genetic risk figures accurately.^{55–57}

How Knowledge of Genetic Status Affects Health Behavior and Psychological Adaptation

A growing literature documents the public’s attitudes about and perceptions of genetic testing, including tradeoffs in perceived benefits and disadvantages^{58,59} and psychological aspects^{60,61} for adult-onset disorders in general,⁶² and for specific diseases such as breast and ovarian cancer,⁶³ colorectal cancer,^{64,65} prostate cancer,^{66,67} cystic fibrosis,⁶⁸ and Huntington’s disease.⁶⁹ Of course, the applicability of these studies regarding obesity is questionable. Some studies have found psychological effects of reassurance; others of anxiety and depression.⁷⁰ In general, perceived benefits are stress reduction from uncertainty,⁷¹ ability to plan, and relief for those who test negative. Many appreciate the increased knowledge of genetic risk. Disadvantages of a negative result may include a sense of guilt in some members of affected families.⁷² Perceived disadvantages for those who test positive, in addition to the obvious health-related issues, are possible discrimination by employers⁷³ and the inability to obtain life and health insurance.⁷⁴

Studies on genetic testing for breast or ovarian cancer⁷⁵ and for Huntington’s disease⁷⁶ suggest that the psychological benefits may outweigh the risks, although there are concerns that genetic information may generate psychological distress.^{77,78} The stigma associated with breast cancer diagnosis has been found to decrease testing interest.⁷⁹ However, obesity is a seriously stigmatizing condition because of its implications about poor personal character, and so the possibility that it is genetically influenced may reassure some people and allay their anxiety. Little is known about how people perceive evidence for a genetic basis for behavioral conditions. For some, a positive genetic test result may be reassuring because it alleviates the burden of individual responsibility, while for others it may be troubling precisely because it seems to diminish their control.

It is also unclear how self-awareness of genetic status might affect health care behavior, e.g., treatment, screening, and prevention efforts. Might patients who discover a genetic propensity feel more motivated to avoid overeating, or might feelings of hopelessness overwhelm them and negatively affect their desire for self-control?⁸⁰

Genetic Testing of Minors

Advantages and Disadvantages Specific to Minors

Adolescents often need to believe that they have explicit control in order to adjust well to life problems.⁸¹ Some children may be aware of problems in families with genetic conditions, including the possibility that they are at risk, but may feel unable to express their anxieties and concerns.⁸² An investigation of Canadian high schoolers’ attitudes towards cystic fibrosis screening found that, given the chance to participate, many viewed the experience positively.⁸³ As for adults, advantages of genetic testing for minor children may include resulting freedom from anxiety and lead to more open discussion of the problem. Also, parents may feel better equipped to take the genetic factors into account as they try to secure the best environment they can for the child and for the whole family.⁸⁴

On the other hand, those opposed to testing children focus on how the genetic testing deprives them of making an informed choice when they reach adulthood about whether they wish to be tested. For some conditions, adults do not wish to be tested, and adolescents tend not to look beyond the immediate situation and not to recognize that their values may change over time.^{85,86} As is the case for adults, there may be negative consequences for a child because of discrimination and stigmatization from others because of the inherited condition.

Perhaps more subtle and more devastating, parents’ expectations of and behavior toward a child with the genetic variant may change for the worse,⁸¹ perhaps even resulting in the parents “scapegoating” the child. The reaction of parents when told the results of their children’s genetic tests, e.g., for early-onset cancer, is instructive: positive tests increased anxiety, and parents of children with negative results were not reassured.⁸⁷

Genetic disease can be a source of “enormous personal and family shame and guilt . . . diminished self-esteem, feelings of deficiency and loss of control following birth of a child with a genetic disorder.”⁸⁸ How could this play out in a condition as different from cancer as obesity? The order of magnitude might of course be different; however, knowledge that a child is a carrier for obesity genes might lead some well-meaning parents to restrict the child’s eating excessively, similar to the harshly restrictive diets that some children found to have above average serum cholesterol have been fed.⁸¹ Children who receive a negative genetic test result for a medical condition may experience survivor guilt,^{82,86} especially if the condition affects siblings. There is the possibility of being socially ostracized because parents and siblings may perceive them as different.^{89,90} In the case of obesity, they may also experience frustration because of the lack of a genetic cause to blame.

Data are limited, but some authors have explored the reactions of children to screening for risk factors. In pediatric screening for a predictor of diabetes, children who tested positive were anxious when first told, but their anxiety returned to normal within 2 to 3 months; apparently, the children minimized the health threat, although relatives did not.⁹¹ Children who learned the results, whether positive or negative, of their genetic testing for hereditary colorectal cancer did not show significant changes in depression or anxiety scores over a several-year period of follow-up,^{92,93} although a subsample of children with mutation-positive siblings had higher, although subclinical, depression scores.⁹³

Should Parents Be Final Arbiters, or Should There Be Some Public Consensus about Genetic Testing of Minors?

The issue of respect for a child's autonomy versus beneficence for his or her welfare is central to the discussion about parental and child decision-making about genetic testing. There is an increasing emphasis today in the medical profession on patients' decision-making, with information and guidance from their physicians. This emphasis on autonomy has encouraged increasing participation by children as well as adults in health care decisions. Authors in the critical care literature have called for physicians to consider consulting adolescent patients about the direction of their care, rather than relying solely on parents or guardians. This trend is fostered by an increasing respect for the child's capacity to make medical decisions.^{91,94,95} However, in medical issues for children in general, and in genetic issues in particular, an important question concerns the autonomy of the adult (parent) as well as the child.⁸⁶

There appears to be an impasse involving the value judgments at the heart of decisions about testing children for various adult-onset conditions. Some authors believe strongly that these kinds of decisions "should be made by those who care most about the children—the parents,"⁸² and researchers have described parents' frustration when they have been denied breast cancer genetic testing for their minor children.⁹⁶ Indeed, some suggest that if parents are anxious about a child, the reduction of this anxiety through testing may benefit not only themselves but also the entire family, including the tested child and siblings. So this reduction of parental anxiety in itself might be sufficient reason to test the child.

What if parents and minor children disagree? Some believe that both the parents and adolescent must consent to testing if there is no therapeutic intervention that can begin in childhood.⁹⁷ However, there is the potential for undue parental influence over minors in medical decisions.⁹⁸ Others have suggested that in some circumstances, the wishes of an adolescent to participate in or refrain from testing might override parental wishes, e.g.,

for an allele that is a risk factor for the severity of consequences of head trauma that might be sustained during high-contact sports.⁹⁹ This situation seems analogous to obesity in that the adolescent's decisions about present-day behavior might cause later problems. However, some public health experts believe that testing decisions involve values and thus are decisions that concern society as a whole,¹⁰⁰ and not just any single group of stakeholders. Testing minors is potentially dangerous for their social adjustment and access to insurance, and could be an invasion of their privacy.

Furthermore, there is no consensus among professionals about if and when to test minors, so suggestions to leave the decisions to health care providers would not be useful. Geneticists in the United States are less willing to test children than are pediatricians and parents.^{85,86} In one study, half of surveyed geneticists, but three-quarters of pediatricians, would test for a genetic predisposition to alcoholism if such a test existed, although they would not necessarily share results with the children until the age of majority.

Geneticists and pediatricians were also surveyed about whether a 16-year-old should be able to refuse genetic testing in spite of the parent's desire for the child to be tested. If the condition were treatable, only 28% of pediatricians and 22% of geneticists would honor the minor's wishes to refrain. If not treatable, however, more geneticists would wish to withhold the testing.

Existing research has only begun to focus on these issues. Michie and Marteau⁹¹ noted that we need to examine more closely the attitudes of children, parents, and health professionals; the informed consent process and how communication leads to information recall and decision-making; and the psychological consequences of predictive testing in children, particularly when they are members of families at risk.

Should Age or Competency Be the Criterion?

Age

A number of studies have examined how age influences children's development of the kinds of abilities that are required for informed decision-making about genetic testing. Informed consent for research is required for those 18 years and older; children as young as 7 years are sometimes considered capable of assent, defined as "a child's affirmative agreement to participate in research."¹⁰¹ However, there are no clear guidelines for obtaining assent for different ages and abilities of young children.¹⁰²

Piaget's work suggested that children enter the stage of formal operations and abstract thought at about age 12. Although his work has been criticized as insufficiently sensitive to factors such as social class, income, ethnicity, number of children in the family, parents' ages

and education, and other home aspects¹⁰³—all of which can produce variation in the age at which formal operations are undertaken—11 or 12 years is the age when children are considered capable in many religious traditions of major decisions.⁸⁵ Research that compared children's perceptions of their understanding of elements of research consent with their actual measured levels of understanding suggested that those older than 11 years had significantly greater understanding than younger children.¹⁰⁴

Some authors point out that early adolescence is the time at which understanding and maturity begin.¹⁰⁵ Adolescents 12 to 14 years old appear less able to perform the required activities, such as anticipating consequences and recognizing vested interests in communication, than those around the age of 15.¹⁰⁶ The courts have ruled that minors can consent independently to medical treatment at age 15.⁸⁶ While some have suggested that 14-year-olds appear to have levels of mental competence comparable to adults regarding decision-making about medical treatment in general,^{107,108} social concepts and motivational aspects appear somewhat later, in those 15 and older.¹⁰⁶ In a recent study, more than 70% of early-onset breast cancer survivors believed that the appropriate age for informing children about the familial possibility of hereditary breast cancer risk was before 18.¹⁰⁹ When children and adolescents themselves were asked about the age at which they should be allowed to make medical decisions, the average response was in the range of 15 to 16.6 years.^{110,111} But some experts have noted that decisions to test 16-year-olds should take into account issues of personal identity, sexuality, and family relationships that adolescents are dealing with at that age.⁹¹

Competency

Development of criteria for informed decision-making by adolescents may be approached by focusing not on the age at which certain competencies appear, which must be variable, but on the sources of such cognitive, psychological, and social variability. Each case could then be specifically evaluated for these competencies. Competency has been defined as understanding relevant information, having the wisdom or discretion to evaluate it in light of one's best interests, and having the confidence to act with some independence and to take responsibility and accept blame. Assessment of competency will be difficult without clearly agreed upon methods.¹¹²

Because few adults have these capacities, authors have pointed out that higher standards should not be expected of children.¹¹² Processes used by adults fall far short of normative rational decision-making, and are subject to the kinds of biases found in situations marked by uncertainty.^{111,113} Thus, adolescents' processes may not be noticeably worse than those of adults. However, a

recent review of the relatively few studies available suggested that adolescents' decision-making competence in general may be less than adults in some areas, such as advice-seeking and goal setting, but similar to adults in other areas, such as response to moderating factors.¹¹⁴ Children age 10 to 17 who were interviewed about participating in research involving genetic testing for breast cancer and heart disease initially viewed the research as low risk before they received counseling about the hazards,¹¹⁵ yet adults often have similar reactions. Variables that should be taken into account in describing these processes include¹¹²:

- *Knowledge of relevant condition based on personal experience.* Children who have lived with a relative who has the medical condition may have a better grasp of the issues than children who may be cognitively more advanced but cannot personalize the information to the same extent.¹¹²
- *Family pressure applied to the child regarding testing.*¹¹⁶ Pressure from parents or other family members may compromise a child's ability to look at the cognitive issues clearly. Also, such pressure may come from the same families that afford the most knowledge of the relevant conditions, mentioned above, because of daily pressure of living with a loved one affected with the condition. Nevertheless, it seems unreasonable to expect complete freedom from family pressure¹¹²; indeed, adults often feel family pressure regarding the decision to get genetic testing. However, it is likely more serious in a minor because of his or her dependent relationship upon the parents.
- *Children's understanding of inheritance and kinship.* Richards¹¹⁷ points out that inheritance and kinship should not be equated with Mendelian genetics, but with lay concepts of kinship and children's understanding of the relationships and responsibilities among their family members. He found that evidence of children's beliefs about kinship is lacking in the literature, but would be important in assessing competence in decision-making about genetic testing.
- *The more general educational context.* The context in which explanations are given to the children also affects their ability to make informed decisions, e.g., how well the experts explaining the facts to them understand the condition and testing/treatment, and how new and risky the treatment.¹¹²

Psychological Adaptation: Adolescence, Self-esteem, and Future Protective Barriers

Adolescence is a critical time for the formation of the concepts of social identity, self-esteem, and personal worth. Concerns have been raised that knowing a posi-

tive test result for a future debilitating condition might well interfere with these natural processes. However, these concerns need to be balanced against positive results relevant to the adolescents' future that have sometimes been found: in some situations, when individuals are told about a condition such as Huntington's disease during adolescence, they appear more able to deal with it later during their lives than those told during adulthood.¹¹⁸ While of course we do not equate Huntington's disease with obesity, adolescence may be an important formative period, and knowledge obtained then may facilitate development of autonomy¹¹⁹ and buffer individuals in their later accommodation to their situation.¹²⁰ This trade-off between adolescents' developing self-esteem and future protection requires further research. Some authors believe that decisions about some genetic testing, e.g., for hereditary breast cancer, should be made by all "psychologically normal" adolescents, because respect for their autonomous choices has such positive consequences for their self-esteem.¹²¹

Other attributes of adolescents relate to the way that self-esteem develops during this period and how this may influence their ability to participate in decisions about genetic testing. These include pressure to conform to peer group norms at all costs (although parents often remain more influential regarding key values)¹⁰⁶ and adolescents' perceptions of an external locus of control, which may make them less likely to question received health-related information.⁸⁵

Issues Specific to Genetic Testing of Minors for Obesity

Distinction between Early and Late Onset Is Frequently Made but Not Simple to Apply

The National Human Genome Research Institute's Task Force on Genetic Testing 1997 report, "Promoting Safe and Effective Genetic Testing in the United States," recommended that children not be tested for adult-onset genetic conditions unless medical interventions existed that could benefit the children directly.¹²² Similarly, a 2001 policy statement by the American Academy of Pediatrics stated that "genetic testing of children and adolescents to predict late-onset disorders is inappropriate when the genetic information has not been shown to reduce morbidity and mortality through interventions initiated in childhood."¹²³ While the distinction between early- and late-onset diseases may be useful in evaluating genetic testing of children for many conditions, obesity is not so easily categorized. Except for some rare childhood-onset conditions, obesity may be either a youth- or an adult-onset disease, with gradual onset of symptoms. However, the actual medical conditions that require treatment (e.g., diabetes or heart disease) are less likely to occur in youth (although this is changing somewhat).

Thus, obesity may not have the same urgency for treatment as other conditions, e.g., phenylketonuria.

Insurance companies and Medicare do not currently cover many forms of obesity treatment because it is usually considered a symptom or precursor to some other disease, and not worth treating by itself. Until very recently, taxpayers have not been able to deduct the costs of weight loss programs as medical expenses unless they were recommended by a doctor to treat a specific disease. Obesity itself was not recognized by the IRS as an ailment that qualified for the weight loss expense deduction afforded to those with pathology that may be associated with obesity. In April 2002, however, the IRS ruled that obesity itself qualifies as a disease for which medical treatment is tax-exempt, and this could pave the way for insurers to cover obesity treatment per se. These policies may lead to greater public recognition that obesity in minors is an early-onset disease. Especially if more successful prevention efforts can be found now than in the past, or if treatments that have broad applicability are discovered, it is likely there will be greater acceptance of testing minor children for obesity. Research with adolescents is lacking, however, about whether knowledge of a genetic test result could itself, at least under some conditions and for some of those affected, be a deterrent to start or an inducement to control overeating.

Obesity May Be Accompanied by Social Stigmatization Not Present in Some Other Genetic Conditions

The obese are severely stigmatized as self-indulgent, without self-discipline, lazy, and unattractive,¹²⁴ and they believe these stereotypes themselves, leading to self-prejudice and erosion of self-esteem with no self-protective strategy to buffer negative feedback.^{125,126} The social stigma of obesity appears to hold as true for youths and adolescents as for adults. In laboratory studies,¹²⁷⁻¹²⁹ obesity in children leads to rejection by peers and is associated with negative characteristics such as laziness and sloppiness.¹³⁰ The evidence in general suggests that overweight children have poorer self-concept than normal-weight children,^{131,132} and girls may show depressive symptoms.¹³³ By adolescence, those who are overweight develop poor self-esteem¹³⁴ and a negative self-image that persists into adulthood¹³⁵; they are also more likely to report victimization by peers,¹³⁶ social isolation,¹³⁷ and serious emotional problems.^{138,139} Both children and adolescents who are obese report lower social functioning and psychosocial functioning scores on health-related quality of life inventories.¹⁴⁰ However, information that shifts the responsibility from the obese and describes them as not responsible for their condition may mitigate this stigma in children as young as elementary school.¹⁴¹ The attenuating effect of the information

regarding causes of obesity on stigmatization is provocative, and will be important to explore in future research: a recent report found that providing information to adults that obesity is mainly due to genetic factors did not lower bias.¹⁴² In one research study, a majority of adults with other stigmatizing conditions, such as bipolar disorder, and their social supporters endorsed genetic testing for children, even in the absence of treatment, perhaps as a way to counter stigma and suggest that the problem is not the fault of affected individuals.¹⁴³

Suggestions for Research about Genetic Testing of Adolescents for Obesity

Difficulties in Policy Development

Many variables must be taken into account in research to develop policy guidelines for genetic testing of adolescents for biobehavioral traits such as obesity. For example, demographic subgroups must be considered, because gender, race/ethnicity, and social class are confounded with prevalence of and attitudes towards obesity and genetic testing.

Sub-group differences: gender. Psychological effects of the highly stigmatizing condition of obesity are moderated by gender: weight and control of eating appear to be more serious issues for women than for men.^{124,144} In children, the psychosocial effects of obesity appear more severe for girls than for boys,¹⁴⁵ who are less likely to try to lose weight and less concerned about their weight.^{146,147} Adolescent obesity in women (but not in men), as distinct from a variety of other physical chronic conditions such as asthma, is associated with lowered social achievement in early adulthood, e.g., income and advanced education, even after controlling for income and education in the family of origin.¹⁴⁸ Gender differences have also been noted in genetic counseling. For example, in cystic fibrosis testing, women said they were happier than men at being non-carriers and unhappier at being carriers.⁶⁸

Sub-group differences: race/ethnicity. The prevalence of obesity in African Americans is higher than in European Americans: in African-American women, prevalence is estimated at around 37%; more than half are overweight.¹⁴⁹ Psychosocial consequences of obesity have been observed in Latino children as well as in African-American and European-American children,^{134,150} and some studies suggest that Latina women are negatively affected by concerns about body image.¹⁵¹ Poor self-esteem is correlated more often with high body weight among European Americans than among African Americans,¹⁵² and obese African-American women appear less preoccupied with their body image^{146,147} and with the social consequences of their obesity.¹⁵³ There may be a lower BMI-associated mortality rate in African Americans relative to European Americans,¹⁵⁴ and some

researchers believe that genetic factors may contribute to observed differences among ethnic groups.^{155,156} Ethnic differences have also been noted in genetic testing. For example, in one study, African-American women given education and counseling planned to be tested for breast cancer genetic mutations with greater frequency than those who received education only, while no differences were observed for Caucasian women.¹⁵⁷

Sub-group differences: social class and cultural aspects. The variation among different ethnic groups in prevalence of obesity is confounded with social class. A large literature demonstrates the association between lower social class, defined variously as educational status, income, occupational status, or some combination of these, and higher rates of obesity in the United States,^{158–162} Europe,^{163–169} and elsewhere. The effect is widely reported in children and adolescents as well as in adults.

Adults with higher income and educational status are more likely to perceive themselves as overweight, relative to lower-income adults with the same BMI.¹⁴⁷ Also, mothers of low educational status (high school or less) tend to fail to perceive that their young (age 2–5 years) children are overweight, after controlling for child's age, gender, and race.¹⁷⁰ Studies have emphasized the importance of cultural factors in the family, e.g., the amount of physical activity and feeding control patterns on development of obesity.^{166,167,171}

Large Number of Factors

The review above suggests that the following factors will need to be taken into account in research to develop policy and to counsel individual adolescents on obtaining genetic testing for obesity:

- Family demographics,
- Child's age,
- Child's gender,
- Ethnicity,
- Social class (educational status, income), and
- Weight status, e.g., BMI.

In fact, an important question will be whether the adolescent is obese at the time of testing or at risk because of the familial history. For each of the following, both the child's and the family's perceptions should be taken into account:

- Level of stigma experienced for obesity,
- Perceptions of health risks associated with obesity,
- Perceptions of child's ability to control obesity,
- Anticipated changes in self-concept if a genetic test result is positive,
- Attitudes about autonomy of children,
- Anticipated approval or disapproval of the support network,
- Cognitive ability to process the relevant genetic risk information,

- Knowledge of obesity based on personal experience, and
- Understanding of inheritance and kinship.

In most cases, the parents will be the most relevant family members, although siblings, extended family networks, and/or the child's guardian may also be involved.

This is a large number of complex factors. Furthermore, they do not include any of the variables associated with a genetic counselor (e.g., the counselor's beliefs about the family or the trait or the counselor's need for certainty or external/internal locus of control), but surely counselors vary on these, and they will need to be taken into account in any model of shared decision-making between patients and counselors.

Communication, Always Important, Is Critical Here

Many authors have noted the importance of communication in counseling for genetic testing, and have stressed informed consent as a process rather than a single event.¹⁷² This process should involve a transaction between all parties rather than expert advice that flows unidirectionally from counselor to patient, although authors point out the difficulties in applying this to minors.¹⁷³ In this context, tailored print communication, developed especially for an individual on the basis of knowledge about his or her circumstances, may be useful.¹⁷⁴ Audiences appear to interpret the meaning of terms such as "mutation" and "risk" differently from what is meant by authors of these messages, and so it will be very important to pre-test messages; few studies integrate communication research with the genetic context.¹⁷⁵

A good example of ways in which a patient's individual cognitive style may interact with message type is found in Croyle et al.'s 1995 study,¹⁷⁵ which showed an interaction between need for certainty and type of information presented in predicting individuals' interest in genetic testing. People with a high need for certainty were more interested in genetic testing when provided a standard description rather than a more complete description of how to interpret population-based genetic risk for a negative test; those with low need for certainty showed the opposite pattern. Personal perception of the kind of information provided by a test is an important predictor of future use of the test. Effective communication will be very important in dealing with adolescents and biobehavioral traits such as obesity, because of the socially sensitive nature of the behavior, issues of personal responsibility, and the adolescent's stage of development of self-esteem.

The Public Health Arena as a Focus for Educational Efforts

All of the foregoing suggests great complexity in the issues surrounding genetic testing of adolescents for obesity. Will the providers of counseling efforts for genetic testing be ready for this job? Genetic counselors are in short supply, and primary care providers—general practitioners and pediatricians—are currently not well-trained in genetic counseling generally.^{176–179}

Unless the financial regulations change for delivery of genetic counseling services, it seems doubtful that individual counselors will be available, or reimbursed, for in-depth counseling of adolescents and their families on genetic testing for widely prevalent biobehavioral traits such as obesity. Yet these issues will be of serious concern when genetic bases for obesity are identified and tests are available, particularly because tests often emerge into the marketplace before their best use is clearly defined. Schools, workplaces, the mass media, and individualized technologic education programs that use interactive surveys and guidelines all have the potential to be tremendously useful resources that can be efficiently mobilized to help educate consumers about genetic testing of adolescents for obesity.

These recommendations assume that general, widely applicable guidelines will be difficult to develop and even more difficult to deliver because:

... each child, and each child-parent relationship, is unique. There is a limit to how helpful general ideas can be when talking with the individual child—so much depends on the specific relationship and on how freely and comfortably the child and adult talk about many other things. It may be assumed that parents should have an orderly plan, gradually unfolding information as the child 'develops,' but life is not like that. Some children understand something long before the textbooks say that they can, others want to talk years after that 'stage'... There are barriers to communication, especially in busy clinics... Communication goes beyond words in tone of voice... facial expression and body language... More important than practical barriers are those of attitudes...¹¹²

This will be very difficult for the genetic counselor to assess in the time available for individual counseling.

Not only children but also adults will need exposure to public education efforts about the basic concepts of genetics, risk, and probability.⁴⁸ Genetic literacy is critical for the coming age of widely available genetic testing. One expert suspects that "as the range of tests that are commercially available continues to grow, within a global economy where information is freely available to those with access to the Web, it is going to

be increasingly difficult to prevent anyone from having tests performed on any DNA sample, whether it comes from an adult or a child.”¹¹⁷

We may infer from the literature on medical decision-making that mid-adolescence may be a time when appropriately educated adolescents can understand the issues involved in such testing and give informed consent, although little work has examined this question directly. With broad media exposure, the public appears to be approaching an understanding that obesity is a disease in its own right that needs to be prevented and/or treated, and that this is a better alternative than waiting until an individual becomes symptomatic for diseases for which obesity is a risk factor. One aspect that will be crucial in future discussions of genetic testing for biobehavioral traits such as obesity is whether effective prevention strategies and behavioral and genetic-based treatments exist. This will have an important effect on the advantages and disadvantages of genetic testing for obesity at specific ages. We cannot predict this in advance, but we can begin to address issues of numeracy and scientific literacy, particularly regarding risk and probability, which have implications not only for genetic testing of obesity, but also for genetic testing in general, as well as understanding the risks of many diseases and treatments. As the consumer decision-making movement continues to grow, this will be extremely important across a wide variety of situations in health care.

We can also begin to understand the best ways to frame the issues in genetic testing for affected youths. Such genetic testing might be widely approved and taken up by parents and affected youths because of the possible relief from stigma and personal responsibility it might provide. Our group is beginning to address these issues systematically with focus groups and in-depth interviews of adults, adolescents, and parents of younger children. We recognize that interest in hypothetical testing has been shown to be a poor predictor of uptake when tests later became available, e.g., for diseases such as Huntington’s disease and breast cancer. However, it is critical not to wait until tests actually become available to formulate the issues and to begin to address them, because experience shows that when a widely desired health care option becomes possible, time is inadequate between its initial availability and subsequent uptake to do the careful research that is required.

Would a positive genetic test result in more responsible health care practices to guard against obesity among affected or at-risk adolescents? At this point, we cannot predict this, as to our knowledge no research has been published with subjects in this age group. However, we can ask adolescents and their parents today to share ideas about this with us. We suspect that such research is likely to be more successful if subjects are asked to

suggest not simply whether they would or would not adhere to improved health regimens, but rather the conditions under which they would or would not, and the reasons why the conditions might yield different results. This approach will yield testable hypotheses at the time that genetic testing becomes available.

Our suggestions that we anticipate using community settings to deliver educational interventions to adolescents and their families regarding genetic testing for obesity, and that we begin to develop interactive, personally tailored mechanisms to do so, are similar to recommendations by Marcus for risk communication for cancer.¹⁸⁰ In this way, we can hope to maximize adolescents’ autonomy within the wider context of the needs of their families for guidance and control. We can help them to obtain tools for understanding and communicating about these sensitive and important issues, and so maximize the usefulness to individuals of the new genetic technologies that will emerge.

Research determining the content of these types of educational strategies is needed. As Marcus has pointed out, “What is not fully understood is the role of socio-cultural norms, and by extension, various significant others (and especially the family) in modifying or mediating risk communication on individual health behavior. . . . Similarly, we lack a basic understanding of how individual risk information might impact the family, including familial relationships and the risk perceptions of other family members.”¹⁸⁰ Research in these areas, with the goal of the eventual development of widely available but personalized public health educational efforts, will be an important start in responsibly addressing the enormous potential of genetic technology for biobehavioral traits such as obesity.

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