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Laboratory Policies and Practices for the Genetic Testing of Children: A Survey of the Helix Network

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Summary

In order to discover whether laboratories have policies regarding the testing of unaffected children, we surveyed all laboratories registered with Helix, a national network of DNA diagnostic laboratories. Of 186 laboratories asked to respond anonymously to a four-page questionnaire, 156 (84%) replied. A screening question removed 51 laboratories that provided no clinical services. Of the remaining 105, 92% said that their requisition forms asked the person's age. Substantial minorities had policies for the testing of minors for late-onset disorders (46%), for carrier status for recessive disorders (33%), or for disorders for which the test offers no medical benefit within 3 years (33%). Most laboratories are responsive to parental requests. For 12 of 13 late-onset disorders, the majority of laboratories that offered testing had had requests to test children. The majority had tested healthy children, <12 years of age, for eight disorders. Approximately 22% had tested children, <12 years of age, for Huntington disease. Majorities had received requests to test healthy children for carrier status for 10 of 15 recessive or X-linked disorders and had tested children, <12 years of age, for 6 of these disorders, including cystic fibrosis, hemophilia A, fragile X syndrome, and Duchenne muscular dystrophy. Approximately 45% of the laboratories occasionally had provided tests directly to consumers. In view of the possibility that the harms of presymptomatic diagnoses of children sometimes may outweigh the benefits, our results suggest a need for consistent laboratory policies designed for the best interests of the child and the family.

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Introduction

The genetic testing of children may have numerous diagnostic and prognostic applications for those who already have symptoms or who may develop them in the near future. However, parental requests for genetic testing of unaffected children and adolescents have raised a number of ethical issues and have led to several statements by professional organizations. In the past several years, the boards of directors of The American Society of Human Genetics (ASHG) and the American College of Medical Genetics (ACMG), the Council on Ethical and Judicial Affairs of the American Medical Association (AMA), and, in Britain, the Clinical Genetics Society (CGS) have published statements on this issue (CGS 1994; AMA 1995; ASHG and ACMG 1995).

The most ethically worrisome situations involve the testing of asymptomatic children for (1) genes for a later-onset disorder, when there is no medical benefit to the child in the near future, and (2) carrier status for a recessive or X-linked disorder, when the information is not immediately useful for the child's reproductive decision making. The statements by the ASHG and ACMG (1995), the AMA (1995), and the CGS (1994) all have expressed caution regarding the testing of minors, in these two situations, especially if the request is from the parents rather than from the child. The International Huntington Association and the World Federation of Neurology have issued a policy statement recommending that minors not be tested for Huntington disease (Bloch and Hayden 1990; Went 1990). Some authors, in both the United States and the United Kingdom, have recommended that testing be performed only if there is a clear benefit for the minor (Harper and Clarke 1990; Institute of Medicine 1994; Clarke and Flinter 1996).

Requests for the presymptomatic and the carrier testing of children are likely to increase. In a recent survey of 1,084 U.S. genetics-services providers, 44% reported that they had had requests to test children for adult-onset disorders (Wertz 1995). Few geneticists reported that they would test for Huntington disease or Alzheimer disease. Although a lesser portion (20%) of 499 U.S. primary-care physicians surveyed reported such requests, the majority thought that parents should be able to have their minor children tested for Huntington dis-

ease (66%) and for Alzheimer disease (58%) (Wertz 1996). In a recent survey of 988 members of the adult general public, conducted by Roper-Starch Worldwide, 53% thought that parents should "be able to have their children under 18 tested for genetic conditions that may appear much later in life," even if the condition was "neither preventable nor treatable" (Wertz 1996), although the question included a statement that the information from the test "might lead to emotional problems or cause people to be prejudiced against the child" (Roper-Starch Worldwide, personal communication) similar pattern appeared in studies performed in the United Kingdom, with nongeneticist physicians more willing to provide testing than were geneticists (CGS 1994).

Except for newborn screening, neither state nor federal law regulates laboratories' practices concerning the testing of children, in routine clinical settings. However, laboratories routinely do provide technical assistance to physicians, concerning the appropriateness of genetic testing in various cases. Laboratories therefore could play an important role in ensuring that genetic tests are applied to minors appropriately.

Subjects And Methods

In order to discover whether laboratories that offer genetic tests (1) have policies regarding the testing of asymptomatic children and adolescents, (2) have had parental requests to test asymptomatic children for later-onset disorders or for carrier status, (3) have fulfilled such requests, and (4) would honor requests coming directly from adolescents, we surveyed all members of Helix, a national directory of DNA diagnostic laboratories, which is self-described as "a current listing of fee-for-service and research laboratories performing disease-specific testing of heritable disorders" (Helix 1995, p. 1). At the time of the survey, in October 1994, 186 laboratories were listed by individual registrants who were health-care professionals. We sent each registrant a four-page questionnaire regarding the genetic testing of children. There were three waves of mailings. All questionnaires were answered anonymously.

Results

In all, 156 (84%) laboratories returned questionnaires. Of these, 51 reported, in answer to an initial screening question, that they tested for research purposes only and that they offered no clinical testing. They were asked to go no further with the questionnaire. The remaining questions in the survey applied only to testing for clinical purposes. Of the 105 laboratories that offered clinical testing, 92% reported that their requisition forms asked for age, and 55% reported that they had refused to test a minor's sample, on at least one occasion. Almost one-half (46%) reported that they had policies for the testing of children or adolescents for late-onset disorders; but these policies varied widely. Thirty-three percent had policies for testing either for disorders when there is no apparent health benefit in the near future (0–3 years) or for carrier status for recessive disorders. When asked what these policies were, 25 laboratories reported that they do not test unless there is a medical benefit; 11 reported that they decide on a case-by-case basis; 9 reported that they do not test for Huntington disease, including 5 that referred to the guidelines of the ASHG, the Institute of Medicine, the Huntington Disease Society of America, or the Canadian Huntington Disease Collaborative; 8 reported that they test at the parents' request, after counseling; and 7 reported that they do not test for adult-onset disorders but will test for carrier status, at the parents' request. Some laboratories (18%) had been called by physician clients who expressed concern about the ethics of the testing of children or adolescents; reports of physicians' concerns appeared to be distributed equally across the minors' ages.

A minority (26%) of respondents thought that "parents should always have a right to request tests on behalf of their minor (less than 18 years old) children, even if the child objects." When it is assumed that the child does not object, however, 61% of respondents would process a sample for cystic fibrosis carrier testing, for parents who request the testing of a 7-year-old. In all, on some occasions, 45% had "provided testing if requested directly by a consumer rather than a physician."

The questionnaire listed 13 later-onset disorders and asked whether respondents offered clinical tests for these disorders. It was assumed that the responses applied to clinically and analytically validated tests, although validation standards vary among labs. For 12 of the 13 disorders listed, a majority of the laboratories that offered a test had had requests to test *healthy* children or adolescents (table 1). For 8 of the 13 disorders, a majority of the laboratories that offered a test actually had tested healthy children or adolescents (table 1).

With the exception of those testing for Huntington disease, few laboratories reported ever having refused to test on the basis of the age of the patient. For 10 of the 13 disorders, there were no reported refusals. Of those who offered tests, 44% had refused to test children for Huntington disease, 17% had refused to test for familial polyposis coli, and 6% had refused to test for myotonic dystrophy.

The questionnaire listed 15 autosomal recessive or X-linked disorders and asked respondents whether they had ever been requested to perform, and whether they had performed or refused to perform, "tests to determine *carrier status* in healthy unaffected children or adolescents under age 18." The response data appear in table 2. For 11 of the 15 disorders, the majority of the lab-

Table 1

Testing of Asymptomatic Children, for Later-Onset Disorders

Disorder (n)[a]	Percentage of Laboratories That		Percentage of Laboratories That Tested Children of the Ages of		
	Had Requests to Test Children	Tested Children	<12 Years	12–14 Years	15–17 Years
Retinitis pigmentosa (5)	100	80	80	80	80
Spinal muscular atrophy (12)	92	75	67	25	25
Marfan syndrome (8)	75	75	75	88	50
Myotonic dystrophy (32)	84	72	59	38	34
Charcot-Marie-Tooth disease (9)	77	66	44	33	33
Neurofibromatosis (17)	65	65	65	47	29
Hypertrophic obstructive cardiomyopathy (5)	60	60	40	60	60
von Hippel–Lindau disease (7)	86	57	57	43	29
Familial hypercholesterolemia (4)	75	50	50	50	50
Facioscapulohumeral muscular dystrophy (6)	50	50	33	17	33
Familial polyposis coli (12)	58	42	33	25	17
Adult polycystic kidney disease (17)	53	41	35	12	18
Huntington disease (36)	56	28	22	19	17

[a] n = no. of laboratories that offered testing for the disorder.

oratories that offered a test had had requests to test healthy unaffected children or adolescents for carrier status. For 6 of the 15 disorders, including 5 that are X-linked, the majority of the labs that offered a test reported actually having tested healthy girls, <12 years of age, for carrier status. Few laboratories reported ever refusing to test for carrier status on the basis of the age of the patient. For 10 of the 15 disorders, there were no reported refusals. Five percent reported refusing to test for Tay-Sachs disease, fragile X syndrome, and cystic fibrosis, 16% had refused to test for Duchenne muscular dystrophy, and one laboratory (25%) had refused to test for choroideremia.

The age of 16 years appears to be the turning point at which many respondents thought "adolescents should be able to request tests on their own." Fifty percent favored the ages of 16–17 years, as compared with 27% who favored the ages of 14–15 years, and 15% thought that adolescents should not be able to request tests until they reach majority. When presented with a hypothetical case, most laboratories reported that they would process a sample for cystic fibrosis carrier testing at the request of a 16-year-old, whether the individual was married (93%) or unmarried (84%).

Discussion

The data suggest that most laboratories had no comprehensive policies. On the other hand, 55% had refused to test a minor on at least one occasion. This suggests that many laboratories were concerned about the possible effects of testing. In the absence of research on children who have been tested and on their families, it is impossible to weigh empirically the balance between the benefits and the harms of testing. In the case of familial polyposis coli, early testing can rule out periodic sigmoidoscopies, for one-half the children, and may help the rest to prepare psychologically for possible surgeries (Peterson 1993). Research on older adolescents tested for Tay-Sachs carrier status has indicated that the majority of those tested showed no measurable psychosocial harms from learning their carrier status (Clow and Scriver 1977*a*, 1977*b*). However, several years later, 19% of the carriers still were worried about this information (Zeesman et al. 1984). We have described elsewhere the possible, but as yet unproved, psychological and familial harms (Wertz et al. 1994).

Professional-society statements and the Task Force on Genetic Testing (in press) have pointed to threats to the child's autonomy. Premature testing forecloses the possibility that the child, when an adult, may not wish to be tested and thus denies the future autonomy of the child, in favor of the present autonomy of the parents.

On the other hand, some consumer groups appear to favor the parents' rights to testing (Genetic Interest Group 1996), on the basis that parents are better able to predict the psychosocial outcomes of testing than are physicians. Parents' groups have differentiated between carrier testing, which they favor, and presymptomatic testing, which they consider to be harmful. They argue that testing for carrier status may be less traumatic in childhood than in adolescence (when the minor may become reproductively active and may seek testing anyway) and that such testing may reduce anxiety and is not stigmatizing if the family is educated sufficiently, through counseling.

The wide variation among laboratories, with regard to the performance of tests and the ages at which tests were performed, suggests the need for a consistent policy

Table 2

Testing of Asymptomatic Children, for Carrier Status for Recessive Disorders

Disorder (n)[a]	Percentage of Laboratories That		Percentage of Laboratories That Tested Children of the Ages of		
	Had Requests to Test Children	Tested Children	<12 Years	12–14 Years	15–17 Years
Fragile X syndrome (64)	84	78	66	63	67
G6PD deficiency (4)	75	75	75	75	75
Duchenne muscular dystrophy (37)	86	68	51	46	51
Cystic fibrosis (47)	81	68	57	53	53
Adrenoleukodystrophy (8)	88	63	63	38	38
Hemophilia A (26)	69	54	58	42	42
Retinitis pigmentosa (6)	83	50	50	50	50
β-Thalassemia (18)	44	44	33	22	17
Fabry disease (7)	86	43	29	43	29
Tay-Sachs disease (19)	53	42	42	32	32
Spinal muscular atrophy (14)	71	36	29	7	7
Sickle-cell anemia (34)	35	29	24	12	15
Choroideremia (4)	25	25	25	25	25
Norrie disease (5)	60	20	20	20	20
α-1-Antitrypsin deficiency (11)	36	9	18	9	9

[a] n = no. of laboratories that offered testing for the disorder.

that takes into account both the best interests of the child and the interests of the family. Although laboratories may not regard themselves as policy makers or as gatekeepers, they are responsible for informing physicians who order tests about the technical appropriateness of a test. Laboratories routinely provide such technical assistance. They can help to educate physicians (including the growing number of primary-care physicians who order genetic tests) about the medical appropriateness of the testing of children of various ages. Sometimes this may mean that the effects of carrier status on health should be explained. For example, some primary-care physicians may believe that a cystic fibrosis carrier test will show the cause of a child's bronchitis. The test is clearly inappropriate for this purpose. However, laboratories are not responsible for educating physicians. If, after receiving information about the appropriateness of a test, the physician still requests the test, the laboratory presumably must comply. Requirements for physician competence, as recommended by the Task Force on Genetic Testing (in press), would help to prevent the ordering of inappropriate tests.

Some doctors may turn to laboratories for guidance. In our study, 18% of the laboratories reported that physicians had consulted them about ethical issues involved in the testing of children. Although laboratories cannot be expected to provide expertise in bioethics, they could provide sources of information to physicians seeking such guidance.

Approximately one-half (45%) of the laboratories had provided testing directly to consumers, but only five of those providing direct testing reported policies that required pretest counseling, at least in some situations. This is an area in which public health regulation requiring counseling may be appropriate, at least in states that permit consumers to approach laboratories directly. Although adults who have experience with a genetic disorder in a close relative sometimes may wish to avoid what they regard as unnecessary counseling sessions and may prefer to interact directly with a laboratory, children cannot make this kind of choice. The state has a duty to protect children. This duty could be met by the requirement of pretest counseling for the parent and the child, as well as posttest counseling and follow-up if the test is performed, for cases concerning the presymptomatic testing of children when there is no medical benefit expected at age <18 years.

A basic problem is that there are no standards or requirements to be met when new tests are placed into service. The final recommendations of the Task Force on Genetic Testing (submitted for publication May 19, 1997) deal with the issue of technical standards but do not comment in depth on presymptomatic and carrier testing of children, noting only that the "genetic testing of children for adult onset diseases should not be undertaken unless direct medical benefit will accrue to the child, and this benefit would be lost by waiting until the child has reached adulthood" (Task Force on Genetic Testing, in press).

Our survey results suggest a clear need for comprehensive and consistent policies. Although 2 years have elapsed since the survey was conducted, there is, as yet, no evidence of such policies. Most policy on health-care delivery is made at three levels: by law, by regulations issued by governmental agencies, or by professional self-regulation. Laws make the most stringent rules but are

sometimes too inflexible. In medicine, there are always exceptions—for example, the family in which Huntington disease appears in childhood and in which the patient's adolescent siblings desire testing or the family in which the sisters of a boy with fragile X syndrome ask for testing, because they are doing poorly in school. In such situations, the benefits of testing may outweigh the harms, but a law such as that in Norway (1994) would forbid it. There are few regulations regarding genetics, at the state level. Even regulations on newborn screening are uneven; after 35 years of screening, a mature and consistent set of regulations has not emerged. A policy would make little sense if clients could circumvent it by crossing state lines.

For now, we suggest that the appropriate professional organizations, such as the American Academy of Pediatrics and the ACMG, develop detailed guidelines for the genetic testing of children, periodically reevaluate them, and ask laboratories to follow them. Self-regulation by professional societies has the advantage of policy formulation by those most familiar with the needs of parents and children and is also the most flexible approach. One disadvantage is that members of one professional organization may not be aware of or attach weight to the position papers put forward by other organizations.

However, at least some laboratories in our survey paid attention to professional-society statements. The most frequently reported situation for the refusal to test was when testing for Huntington disease was requested, with 44% of the laboratories that offered such tests refusing to test minors. Huntington disease was one of the few disorders for which national and international professional associations had published guidelines, at the time of the survey.

The best way to achieve consistent policies may be to foster consultation among regional genetics groups, geneticists, pediatricians, family practitioners, and their local and national professional societies; state public-health departments; and consumers. Policies could be bolstered by regulations requiring parental informed-consent forms, children's assent forms, and evidence that the family has been offered counseling with a trained professional, before testing.

In view of the limited number of genetics professionals, much genetic testing ultimately will be provided by primary-care physicians. The majority of primary-care physicians believe that parents should be able to have their minor children tested for all genetic disorders, including untreatable adult-onset disorders such as Huntington disease or Alzheimer disease (Wertz 1996). The majority of the U.S. public apparently agrees (Roper-Starch Worldwide, personal communication). As there is more pressure—from primary-care physicians, parents, the health-care system, and, sometimes, adolescents themselves—to test children and adolescents, there will be a growing need for policies that work in the best interests of the child. Laboratories, as potential gatekeepers, could play an essential role in the development of such policies.

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