numbering is not nearly so obvious in the case of genomic sequences as it is in the case of cDNA sequences. Finally, errors are more likely to occur in determining a genomic sequence, because insertion or deletion of a nucleotide does not produce a telltale frameshift. As errors are discovered, numbering needs to be changed, or flawed sequences need to be retained as standards. Moreover, polymorphisms representing different numbers of repeats occur commonly in introns and not in coding regions.

Conclusions.—The advantages and disadvantages of different notations are summarized in table 1. The development of uniform notation for the designation of mutations would be highly desirable. Such a system should be as broadly applicable to mutations as possible. Amino acid–based designation, although commonly used, has relatively little to commend it. The choice would seem to be between systems based on the nucleotide number in a cDNA- and a genomic DNA–based numbering system. Each of these has advantages and disadvantages, and a cDNA-based system probably represents the most acceptable compromise.

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Presymptomatic Testing for Huntington Disease in the United States

To the Editor:

Presymptomatic testing for Huntington disease (HD) by using linkage analysis has been available in the United States on a limited basis since 1986. Guidelines for testing have been published by both the Huntington's Disease Society of America (1989) and the World Federation of Neurology (WFN) Research Group on Huntington's Chorea (Went 1990). Recommended testing protocols include neurological, psychiatric, and psychological screening; pretest counseling; and posttest follow-up.

Unlike Canada and many European countries offering predictive testing, the United States has no central organization to coordinate testing or to gather information on the number of individuals tested and the outcomes of testing. In a meeting held in conjunction with The American Society of Human Genetics annual meeting in 1990, an ad hoc committee was established for the purpose of gathering and disseminating information about testing protocols, results, and outcomes of presymptomatic testing in the United States. The results of two surveys of all the centers offering presymptomatic testing for HD in the United States, conducted in May 1991 and again in May 1992, are presented here.

In May 1991, surveys were mailed to the contact person at each of the 23 sites offering predictive testing, asking their center for information as of December 31, 1990. All 23 centers (100%) replied. A second survey was mailed in May 1992 asking for data as of April 15, 1992. At the time of the second survey, three new centers had begun to offer testing, and two centers that had participated in the original survey were no longer offering this service. Data for this second survey were obtained from all 26 centers.

Results indicate that, after an initial increase, the number of centers offering testing has leveled off. By year, the number of new centers offering testing is as follows: 1986 (2), 1987 (2), 1988 (2), 1989 (8), 1990 (8), 1991 (2), and 1992 (2). Seventeen (65%) of the 26 centers are university based, although in different departments: neurology (3), psychiatry (4), genetics (4), and pediatrics (6). Two are based in health maintenance organizations, three in private genetics clinics, one in a medical center, and two in nonprofit organizations, while one was unspecified. Twelve (46%) of the centers have an HD clinic associated with the program, and 14 do not. Most centers, 19 (73%), have completed fewer than 15 tests.

The testing programs are directed by individuals of various professions and training. These professions include Ph.D. medical geneticist (6), Ph.D. medical geneticist/psychologist (1), Ph.D. psychologist (3), neurologist (2), M.D./Ph.D. medical geneticist (3), genetic counselor (6), M.D. medical geneticist (3), M.D. neuro-

geneticist (1), and Ph.D. biochemical/molecular geneticist (1).

The range of costs for the recommended elements of the testing protocol varies widely among programs, as follows: neurological exam ($90–$285), psychiatric screening ($100–$200), psychological screening ($70–$835, if a full neuropsychological battery is included), and pretest counseling ($55–$75 per session or $100–$500 all inclusive). The number of pretest counseling sessions ranges from 2 to 10, with 3 being the average. The cost for the genetic analysis is $495 per sample or ranges from $1,200 to $2,000 total for an entire family.

Twenty-five of the 26 centers reported having regularly scheduled follow-up, with the duration of follow-up ranging from 3 to 36 mo. For several of these centers, however, follow-up consisted of one or two contacts by telephone. Ten centers reported systematic collection of outcome data after testing.

Eighteen (69%) of the centers reported denying or postponing testing at least once. The most frequently cited reasons for denying or postponing testing were as follows: currently symptomatic with HD, under 18 years of age, request for confirmation of diagnosis of HD, current depression, unstable living situation, recent psychiatric history, unable to give informed consent, request for adoption testing, unwilling to involve family members, and recent diagnosis of HD in the family.

Cumulative results of presymptomatic and prenatal testing for HD are presented in tables 1 and 2. Outcome data are limited by the fact that most centers do not systematically collect information after testing. However, data from centers that were able to report this information represent a substantial portion of those tested (N = 232 [78.4%]) and suggest that the occurrence of those life events (i.e., depression, suicide) which were of most concern when testing was first contemplated appears to be low. For the group receiving increased-risk results (N = 60), three people have been hospitalized for reasons related to testing, and four have been treated with antidepressants. For the group receiving decreased-risk results (N = 129), one person has been hospitalized, and one was treated with antidepressants.

Growth in the number of centers offering presymptomatic testing for HD has slowed, and a few centers that previously offered testing no longer provide this service. Centers offering testing are diverse. Despite published guidelines for testing, centers differ widely in their experience with testing, experience with HD, professional training of program directors, testing protocols, and costs associated with testing.

Some professionals feel that predictive testing for HD has left the research phase and has become a standard clinical service (DeGrazia 1991). There is a corresponding call for doing away with many of the procedures established during the initial phase of offering testing, including pretest counseling (Stanley 1992). However, those most experienced in testing for this late-onset incurable disorder feel strongly that these protocols should continue to be followed, including face-to-face counseling and follow-up (Bloch et al. 1992; Huggins et al. 1992; Quaid 1992). In addition,

Table 1

Cumulative Results of Presymptomatic Testing for HD

Presymptomatic Tests	No. (%)	
	December 31, 1990	April 15, 1992
Increased risk	56 (28)	80 (27)
Decreased risk	115 (57)	169 (57)
Uninformative	30 (15)	47 (16)
Not revealed	2	—
Total	203	296

Table 2

Cumulative Results of Prenatal Testing for HD

Prenatal Tests	No.	
	December 31, 1990	April 15, 1992
Nondisclosing tests:		
Increased risk:[a]		
Pregnancies continued	1	2
Pregnancies terminated	10	11
Decreased risk	14	15
Uninformative:		
Pregnancies continued	2	2
Pregnancies terminated	1	1
Subtotal	28	31
Prenatal tests with parental status known:		
Increased risk:		
Pregnancies continued	0	0
Pregnancies terminated	2	3
Decreased risk	2	4
Uninformative	0	0
Subtotal	4	7
Total	32	38

[a] Approximately 50%.

reports of the outcomes of testing suggest that genetic testing centers should continue to offer predictive testing with great caution (Chapman 1992).

The variety of professional expertise needed to follow the recommended protocols, coupled with the relatively small number of individuals at risk choosing to be tested, suggests that few new centers will offer testing in the near future. The uneven distribution of testing centers throughout the country has limited the ability of individuals contemplating testing to compare programs and to select a program that meets their needs. While the recent discovery of the HD gene and the subsequent simplification of direct gene analysis (HD Collaborative Research Group 1993) may mean that more laboratories will consider offering testing, the real question is whether adequate counseling and follow-up will be provided.

The majority of centers has postponed or denied testing at least once. Reasons for this action include inappropriate requests for testing (e.g., to confirm a diagnosis of possible HD), as well as decisions based on personal or situational factors affecting the individual that indicate that more caution should be exercised. The suggestion has been made that to deny or postpone such testing amounts to a violation of both the autonomy of the individual and the concept of nondirective counseling, both long-held tenets of genetic counselors (Pelias 1991). The question of whether such judgments ought to be made in the case of late-onset disorders without any hope of treatment or cure is likely to remain a matter of debate. In the meantime, the professionals actually offering testing appear to believe that these actions are justified.

The fact that the number of individuals tested in the United States remains small may be a consequence of limited accessibility of testing centers as well as fear of a positive or high-risk result, the lack of a cure, and the threat of losing one's health insurance (Quaid and Morris 1993). In addition, few individuals are choosing prenatal testing for this late-onset disorder.

The incidence of serious negative outcomes as a result of testing appears to be low. However, the centers reporting outcome data are those centers with the most experience offering predictive testing and those which most closely follow recommended protocols. The fate of those individuals tested in centers not collecting outcome data is uncertain.

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