Platform

Some ethical problems in Huntington's chorea

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Huntington's chorea occurs in approximately 1 out of every 10 000 persons of European ancestry. Patients are usually ill for 15 to 20 years, most commonly in mid-adult life, with a progressive neurologic and psychiatric illness characterized by involuntary movements, increasing dementia, personality changes and sometimes severe depression or frank psychosis. Some patients manage to go through the entire illness without a great deal of suffering, but for most it is a devastating experience. It is inherited in an autosomal dominant fashion, and in each child of an affected parent there is at birth a 50% chance that the disease will develop. When one includes the close relatives of patients (the unaffected parent and siblings, spouses, and offspring at risk who have not inherited the mutant gene), almost 10 times as many persons suffer chronic anxiety about Huntington's chorea as actually have the disease. Long experience with patients and their families during research on the biochemical basis of Huntington's chorea prompts me to raise some ethical issues that I think merit greater discussion by physicians and other health care professionals who deal with these families.

Need for prevention

Biochemical research during the last decade has shown that several different types of neurons die prematurely in the brains of patients with Huntington's chorea. These include cells whose neurotransmitters are γ-aminobutyric acid (GABA),[1,2] acetylcholine[2] and substance P.[3] The loss of several types of neurons, with resulting imbalances in the brain's content of several neurotransmitters, is likely to make successful drug treatment of this disorder very difficult. The exact mechanism by which the mutant gene causes early neuronal death is still unknown. There is some evidence to suggest that it might involve coding for an abnormal protein in all cell membranes or be due to a defective mechanism for repairing deoxyribonucleic acid (DNA). In either case it is difficult to envisage how the neuronal loss might be avoided and the development of symptoms prevented for long in affected individuals. If this appraisal of Huntington's chorea is not unduly pessimistic, then it would seem of great importance to try to reduce the frequency of the gene and the incidence of the disease in future generations.

There is little evidence that the incidence of Huntington's chorea has been reduced by any preventive measures taken so far. A study in southern Wales, for instance, showed no decrease in the number of observed and projected new cases in persons born in the last 50 years, despite a substantial drop in the birth rate for the general population.[4] This may be due to the fact that accurate information about the disease and systematic genetic counselling have only recently become generally available. I wonder, however, whether the nondirective approach towards genetic counselling that is now fashionable will ever succeed in reducing the incidence of Huntington's chorea. New mutations for this disease are extremely rare. Thus, if genetic counselling resulted in decisions by most persons at risk not to reproduce, the incidence of the disease could be greatly decreased in a few generations.

I suggest that there is nothing inherently unethical in providing *directive* genetic counselling to persons at risk for Huntington's chorea. Directive counselling need not be authoritarian. When asked for an opinion, could one not say that the person at risk would be well advised not to produce children? So long as the genetic counsellor firmly respects the counsellee's democratic right to reject such advice and remains determined to continue friendly professional support even if all advice is ignored, what harm is done? Directive genetic counselling should, of course, include accurate information about the risk of transmitting Huntington's chorea, the course of the disease, possible treatments, and practical advice, when appropriate, regarding contraception, sterilization, artificial insemination and adoption. Such counselling is surely consonant with the clear advice routinely given by doctors to patients regarding the need for elective surgery or the use of an antibiotic for a serious bacterial infection.

In a lecture on medical ethics given shortly before

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he retired as editor of the *New England Journal of Medicine* Dr. Franz Infelfinger[5] had this to say: "A physician who merely spreads an array of vendibles in front of the patient and then says, 'Go ahead and choose, it's your life,' is guilty of shirking his duty, if not of malpractice. The physician, to be sure, should list the alternatives and describe their pros and cons but then, instead of asking the patient to make the choice, the physician should recommend a specific course of action. He must take the responsibility, not shift it onto the shoulders of the patient."

It approaches the point of absurdity if, on the one hand, far-sighted ecologists and some national governments seriously propose zero population growth to the public in efforts to avoid future overcrowding of our planet and the exhaustion of its resources, while, on the other hand, current dogma holds that no such advice should be given to persons at risk for serious genetic disease. I fear that the nondirective genetic counselling now commonly given to persons at risk for Huntington's chorea, often accompanied by well meant but unduly optimistic statements about the advances expected from medical research, will have little effect in reducing suffering from this disease by future generations. The ethical issue here resembles those involved in the careless use of antibiotics in medicine or animal husbandry, which can lead to the development of drug resistance by important pathogens; in the development of nuclear power plants in the absence of safe ways to dispose of nuclear wastes; and in increased military spending in the face of its adverse consequences for our troubled economy and its threat of ultimate nuclear destruction.[6] To what extent is it proper to jeopardize the lives or health of people in future generations in order to satisfy either legitimate or selfish needs of individuals living now?

Preclinical detection

The recent explosion of research on Huntington's chorea has brought to light many biochemical abnormalities that conceivably may make it possible to detect heterozygosity for the mutant gene long before symptoms first appear. Compared with control fibroblasts, cultured fibroblasts from patients with the disease grow to greater confluent density,[7] show differences with fluorescence spectroscopy after labelling with a fluorescent probe[8] and allegedly are more readily damaged by exposure to high concentrations of glutamate.[9] Erythrocyte membrane ghosts from patients with Huntington's chorea have different electron spin resonance characteristics from erythrocyte ghosts of control subjects.[10] Compared with control lymphocytes, those from patients with Huntington's chorea show decreased capping induced by concanavalin A[11] and increased sensitivity to the lethal effects of x-rays.[12] Finally, concentrations of GABA in the cerebrospinal fluid are reportedly lower in patients with Huntington's chorea than in control subjects.[13]

Although there is some disagreement as to whether all the abnormalities detectable by sophisticated laboratory testing are indeed uniquely characteristic of Huntington's chorea, it seems likely that some of them will be found in carriers of the mutant gene long before symptoms of the disease appear. An accurate preclinical test would be of great value if we had an effective form of therapy for Huntington's chorea, one that worked best when started early in the disease, before significant anatomic damage had occurred in the brain. Since no such therapy is currently available, a reliable preclinical test could become a two-edged sword. It would be rewarding to be able to tell approximately half of the persons at risk that they would never have Huntington's chorea and that they could safely reproduce. But what of the consequences for the unlucky 50% that the test indicated were heterozygotes? What if the bad news led some individuals to abandon plans for their education, to squander their savings or even to commit suicide?

It is also important to emphasize that after using a promising test on a large group of persons at risk for Huntington's chorea it would be wise to wait for at least 20 to 30 years to be sure that all the predictions were accurate. Of 20 individuals at risk for the disease who were given levodopa orally as a predictive test and who failed to have transient chorea as a result (thus appearing not to carry the mutant gene) 1 already had symptoms of Huntington's chorea 8 years later.[14] While reviewing research proposals dealing with predictive tests for Huntington's chorea I have been struck with the cavalier attitudes of some investigators towards the use of the data they hope to generate. I suggest that, pending development of an effective form of treatment, scientists who perform preclinical tests on persons at risk should ensure that the results of individual tests are not made available to those tested.

Improving the quality of life for patients

When we tried experimental treatments with isoniazid[15] and aminooxyacetic acid[16] on patients with Huntington's chorea it became necessary to withdraw the neuroleptic and other tranquillizing drugs that these patients often were receiving. Not infrequently clinical improvement followed. I know of no evidence that giving such patients haloperidol, antipsychotic phenothiazines or tetrabenazine prolongs their lives or slows the progress of their disease. Although such drugs may sometimes decrease choreiform movements or lessen psychotic symptoms, I suspect that in many patients the drugs do more harm than good by dulling intellectual activity and sometimes worsening depression. Is it not important first to ascertain exactly what does bother the patient and the family before resorting to the use of neuroleptic drugs? It is certainly reasonable to use antipsychotic drugs that block dopamine receptors in patients who have periodic outbursts of rage or violent behaviour, or to try a tricyclic antidepressant drug in those who are seriously depressed. However, the knee-jerk response of many physicians to a diagnosis of Huntington's chorea — writing a prescription for haloperidol — surely makes life even worse for many patients.

Provision of better facilities than the typical nursing home or the back ward of a mental hospital could help patients with Huntington's chorea make the most of their remaining years of life. If spouses and other family members were given practical help in caring for patients, as well as regular planned holiday relief, a greater proportion of patients could have the comfort and emotional support of living at home through most of their illness.

In Melbourne, Australia, the Victoria Huntington's Disease Association has recently established a combined residential home and day care centre for patients with Huntington's chorea that is both physically attractive and imaginative in its scope.* Some patients who have no families or who come from distant communities will live there permanently, and others will be accommodated during their family's annual holiday. The majority of patients will be bussed to and from the centre daily, so that spouses can work and children enjoy more normal lives. All these patients will receive the benefits of specialized medical care, occupational and physical therapy, and social work services. Similar centres for patients with Huntington's chorea or other progressive neurologic disorders might usefully be established in Canada.

Ending the stigma

I recall once piously telling a gathering of family members of patients with Huntington's chorea that they should not consider the disorder as deserving any stigma. They responded with a flood of examples of the ways in which patients and persons at risk are, in fact, victimized. In too many communities life insurance is denied to persons at risk, motor vehicle licences are revoked for patients who can still drive safely, and jobs are refused to otherwise qualified applicants. Furthermore, patients are often imprisoned for aberrant behaviour that is not dangerous to others.

Physicians and other health care professionals can lessen the stigma of Huntington's chorea by actively opposing injustices imposed on patients and their families. Genetic registers of patients can be advantageous for medical research and for diagnosis of new cases. However, those who establish such registers must consider the real risks of their abuse by governmental authorities. The excellent lay organizations concerned with Huntington's chorea that are now active in many countries can play an important role in lobbying to change laws that discriminate unfairly against mentally and neurologically handicapped persons.

Finally, one of the most effective measures for decreasing the stigma of Huntington's chorea and for lessening the suffering of patients and their families is to end the isolation surrounding the disease. Physicians can readily help patients by suggesting that they and their families join the local chapter of organizations like the Huntington Society of Canada.† Participation in regular meetings of a group of friendly people with similar troubles eases the misery of Huntington's chorea and helps families to adopt more constructive solutions to their problems. The effectiveness of chapters can also be increased by active participation in them by physicians and other health care professionals.

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