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Perhaps test, often explore, always counsel

EDITORIAL

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Patients with serious and potentially hereditary disease and their relatives may benefit from genetic exploration and counselling, even when predictive genetic testing is not available.

In many diseases, such as cancer, cardiovascular disease, Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis (ALS), a small subset of cases are hereditary. A distinction is made between familial and sporadic cases of a disease, the former assumed to have Mendelian inheritance and the latter multifactorial aetiology. Primary diagnosis often depends on clinical diagnostic criteria. The purpose of genetic investigation is first and foremost to identify hereditary cases; in addition to confirming the diagnosis, this can also identify subgroups with specific needs in terms of medical and interdisciplinary follow-up. In hereditary disease, each family has its own disease-causing mutation. Increasingly, this specific mutation can provide information on prognosis and treatment options. Genetic investigation is a textbook example of personalised medicine, defined as prevention, diagnosis, treatment and follow-up that is tailored to the biological makeup of an individual (1).

Only when a disease-causing mutation is identified in a patient can healthy relatives be offered testing for the mutation to gain information about their own risk. In Norway, as in many other European countries, genetic counselling is required by law prior to such predictive genetic testing (2, 3). In some serious hereditary diseases for which there is no effective prevention or treatment, the counselling follows a carefully designed procedure. Research shows that the

majority of healthy individuals who opt for predictive genetic testing after receiving such counselling, cope well with the process – irrespective of the test result (4).

Nakken *et al*. have examined whether clinicians follow, in practice, the international recommendations for genetic investigation of patients with amyotrophic lateral sclerosis (5). The guidelines recommend taking a detailed family history for all patients, but using DNA analysis only in certain cases of familial disease (6). Although testing of certain genes can accelerate the diagnostic process and provide prognostic information, the guidelines recommend that DNA analysis is not conducted in sporadic cases of classical disease.

The latter recommendation is problematic. In the study from Akershus University Hospital, information on family history was absent from the medical records in 38 % of cases (5), indicating that the recommendation to obtain a detailed family history was not followed. Even if a patient is the first known case of the disease in a family, it does not necessarily follow that the disease is sporadic. Due to the reduced penetrance of amyotrophic lateral sclerosis, hereditary disease can go 'under the radar', especially in small families. Autosomal dominant and X-linked hereditary disease may also be the result of *de novo* mutations, which, like other mutations, can be transmitted to descendants. Only after several generations, or when genetic testing has been performed, is it safe to assume that a case was sporadic. Although family history-taking and consent-based retrieval of information is part of the service offered by departments of medical genetics, Norwegian and international studies suggest that neurologists rarely refer ALS patients to such departments. This may be due to lack of knowledge of genetics and genetic services, or to the doctor's views regarding ethical and psychological issues (5, 7).

The recommendation for the limited use of genetic investigation of patients with amyotrophic lateral sclerosis was justified in part by the argument that the patient and his/her relatives have a right not to know whether the disease is hereditary (5). It is unusual for the phrase 'right not to know' to be used about investigating the sick. The term usually refers to the right of healthy persons to not undergo predictive genetic testing. The Norwegian Patient and User Rights Act does indeed state that patients are entitled not to have unwanted information about their illness imposed on them (8), but also states that they have the right to obtain the information necessary to help them understand their health status and the healthcare provision available. Without genetic investigation and counselling, both patient and relatives are also deprived of general information about risk based on mode of inheritance or empirical data, as well as the possibility of deciding whether or not they want to know in cases where relatives can be offered predictive testing.

The conservative guidelines for genetic investigation in cases of amyotrophic lateral sclerosis have been prepared by and discussed in neurological circles, but the same issues also apply to other diseases. There is no evidence that information on genetic heterogeneity or reduced penetrance would lead to increased psychological stress for an individual receiving genetic counselling. Explaining the issues well to the patient and his or her family does, however,

require the specific expertise possessed by genetic counsellors. Patients with amyotrophic lateral sclerosis and their relatives would benefit from genetic investigation and counselling irrespective of the possibility of, or desire for, predictive genetic testing.

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