

concur with the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research in concluding that patients' confidentiality should almost always be respected. The commission states that it is permissible to warn relatives of genetic risks

only if . . . (1) reasonable efforts to elicit voluntary consent to disclosure have failed; (2) there is a high probability both that harm will occur if the information is withheld and that the disclosed information will actually be used to avert harm; (3) the harm that identifiable individuals would suffer is serious; and (4) appropriate precautions are taken to ensure that only the genetic information needed for diagnosis and/or treatment of the disease in question is disclosed.²

Clinicians understandably view the *Safer v. Pack* and *Pate v. Threlkel* cases, which I have argued were wrongly decided,³ as more onerous than Dr. Deftos suggests. Unlike Dr. Deftos, I believe that patients will usually share information, given enough time and support. Finally, if a physician gave the relative of a patient information about a serious but avert-

able risk and that information saved the relative's life, it is hard to believe that a jury would be sympathetic if the relative then sued for invasion of privacy.

The data regarding the incidence of genetic discrimination are not as unequivocal as Dr. Nowlan suggests.⁴ Patients' fear of discrimination dramatically affects their willingness to seek genetic services. Dr. Nowlan is appropriately concerned with genetic exceptionalism. His desire to reexamine "the utility of genetic discrimination as a distinct entity" is consistent with my argument that even when genetic variations do exist, deciding whether they should affect access to social goods inevitably requires competing social values to be weighed.

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Molecular Mechanisms of Amyloidosis

TO THE EDITOR: In the review article by Merlini and Bellotti (Aug. 7 issue),¹ familial Mediterranean fever was listed as one of the common periodic-fever syndromes that may lead to reactive (amyloid protein A, or AA) amyloidosis. However, there is no correlation between the frequency and severity of periodic febrile attacks and AA amyloidosis.² The serum level of amyloid protein A is not constantly elevated. Some patients with frequent periodic febrile attacks are spared from the development of amyloidosis, whereas in other patients there is very early amyloid deposition. The major effect of colchicine seems to be the prevention of the formation and deposition of amyloid A.

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TO THE EDITOR: Merlini and Bellotti highlight AA amyloidosis as a complication of the hereditary periodic fever syndromes (in Table 1 of their article), and they specifically list the hyper-IgD periodic-fever syndrome (HIDS). Although AA amyloidosis is indeed a frequent complication of familial Mediterranean fever (affecting 10 to 37 percent of patients),¹ the tumor necrosis factor receptor-associated periodic syndrome (affecting 14 percent of patients),² and the Muckle-Wells syndrome (affecting 35 percent of patients), it has never been reported in patients with HIDS, nor has it been seen in any of the patients listed in the international Nijmegen HIDS registry. This registry contains clinical data on 195 published and unpublished cases worldwide (information is available at <http://hids.net>).

HIDS is a periodic-fever syndrome caused by a genetic defect in mevalonate kinase.³ Despite a frequent, often persistent,⁴ and vigorous acute-phase response similar to that seen in patients with other periodic-fever syndromes, amyloidosis does not develop in patients with HIDS. This intriguing find-

ing suggests that mevalonate kinase deficiency may provide protection against amyloidosis.

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THE AUTHORS REPLY: Dr. Sungur and Dr. van der Hilst and colleagues highlight the wide variability in the risk of reactive (AA) amyloidosis among patients with hereditary periodic-fever syndromes and note that the severity of familial Mediterranean fever does not fully account for the occurrence of AA amyloidosis. In familial Mediterranean fever, very high concentrations of serum amyloid A (SAA) have been reported at the onset of acute attacks (mean value, approximately 150 times that in a control group),¹ and in most patients, SAA levels are significantly elevated during attack-free periods,² indicating the continuous presence of subclinical inflammation. Increased levels of SAA during asymptomatic periods may contribute to the risk of AA amyloidosis in patients with familial Mediterranean fever. Moreover, variations in the incidence of AA amyloidosis within and among different ethnic groups suggest that there are genetic factors, en-

vironmental factors, or both that modify the risk. The development of renal amyloidosis in patients with familial Mediterranean fever is affected by homozygosity for the M694V allele (although this association may not be significant in Turkish persons), the SAA1 α/α genotype, male sex, and attacks of arthritis.³ How these factors affect SAA levels or the amyloidogenicity of SAA is unknown.

We are grateful to the Nijmegen group for pointing out that amyloidosis has not yet been reported in their registry as a complication of HIDS. HIDS is a heterogeneous disease,⁴ and 24 percent of patients with clinically diagnosed HIDS have normal mevalonate kinase activity (variant-type HIDS),⁵ indicating that other factors, in addition to or rather than mevalonate kinase deficiency, lower the risk of amyloidosis. More data about variations in the HIDS phenotype in ethnic groups other than the Dutch and French will improve our understanding of the molecular mechanisms underlying the reduced susceptibility to amyloidosis in patients with HIDS.

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West Nile Virus

TO THE EDITOR: The Perspective article by Morse (May 29 issue)¹ addresses the transmission of West Nile virus through organ transplantation and blood transfusion. Less than 1 percent of the more than 4000 cases diagnosed in 2002 were attributed to transfusion, with virtually all the rest attributed to mosquito bites.² To reduce the small risk, blood centers, in collaboration with industry, implemented nucleic acid testing for West Nile virus in June and

July and have interdicted hundreds of potentially infectious donations. It is difficult to predict the effect of screening, because we have a limited understanding of the sensitivity of assays and the quantification of viremia in infected persons.

We disagree with the suggestion that leukoreduction be considered as a means of reducing this risk. West Nile virus has been detected in the plasma and serum of patients, blood donors,³ and the im-