Gene polymorphisms and the risk of myocardial infarction - An emerging relation
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sibility to the idea that the rash predisposes persons to zoster. One could therefore postulate that it is preferable that children not acquire infection with wild-type VZV. The Oka or vaccine strain of VZV rarely causes rash and is associated with less zoster in children with leukemia than the natural infection. There are early indications that zoster may also occur less frequently after immunization of normal children. The choice may be between living with latent wild-type VZV that is prone to give rise to zoster and postherpetic neuralgia and being immunized with the vaccine-type virus that is less likely to give rise to either of these. The obvious preference is for successful vaccination and avoidance of wild-type VZV infection.

In the current report, the authors suggest that the number of primary vaccine failures in previous studies may have been obscured because persons with such failures were excluded from the analysis. The authors go on to comment reasonably that one cannot and should not make policy statements on the basis of a single outbreak and that it will be important to observe the experience of others. Still, this outbreak constitutes a warning signal.

A second dose of varicella vaccine, given routinely, should decrease the number of children who have primary vaccine failure and might also prevent waning immunity, if it does indeed currently occur. The best way to protect children and adults from wild-type VZV might be to give everyone two doses of vaccine; however, formal studies will be required to determine whether this approach works, as well as the cost–benefit ratio. It is noteworthy that it took the routine administration of two doses of measles vaccine to children to control measles in the United States. The time for exploring the possibility of routinely administering two doses of varicella vaccine to children seems to have arrived.

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Today, a person’s genetic background is considered in every aspect of clinical medicine, ranging from susceptibility to diseases, pathogenesis, and clinical outcome to diversity in responses to drug treatment (pharmacogenomics). The new panoramic look at the human genome has stimulated a massive search for clinically relevant genomic information, including single-nucleotide polymorphisms (SNPs), which consist of substitutions of one nucleotide for another in a DNA sequence.

Individual genomes are 99.9 percent identical, with only 0.1 percent of the genome showing polymorphisms. About 2 million or 3 million SNPs have been found in exonic, intronic, regulatory, and intergenic regions. Almost all genes contain SNPs, but only a minority of SNPs result in amino acid variation in proteins. Complexity increases at the protein level, since one human gene may produce up to five different proteins as a result of alternative splicing. Post-translational modifications, such as assembly or glycosylation, further increase the diversity of proteins. Furthermore, polymorphisms in other genes may alter the phenotype that results from genetic abnormalities. Such an effect has recently been found in a family with hypertrophic cardiomyopathy caused by a single mutation in the gene for myosin-binding protein C. SNPs in five components of the renin–angiotensin–aldosterone system were found to determine the degree of left ventricular hypertrophy. As a consequence of these complexities, it is difficult, if not impossible, to predict the biologic or clinical effect of a SNP in a given gene.

Atherosclerotic diseases result from a dynamic, lifelong interaction among genetic, environmental, and behavioral factors. Classic risk factors for myocardial infarction, such as hypertension, diabetes, and dyslip-
The expression of a protein or in its function. Thus, genes, selected on the basis of an expected change in prevalence of 112 polymorphisms in 71 candidate ocardial infarction with the control in terms of the ease. The investigators compared the patients with myocardial infarction and coronary angiography, and from the combined group of inpatients and outpatients, only 27 patients with myocardial infarction per...
center per year were included in the study. Both the use of this definition and the small numbers of patients enrolled may indicate the presence of selection bias, with unknown effects on the results.

Finally, the odds ratios are relatively small, and one cannot rule out the possibility of unintentional bias in the study. With such large numbers of SNPs analyzed, the problems of repetitive testing arise, even with strict criteria for statistical significance. It is noteworthy that the C allele of the C1019T polymorphism in the connexin 37 gene was associated with atherosclerosis in a Taiwanese population\(^2\) and among Swedish men,\(^3\) whereas the T allele was identified as a risk factor for myocardial infarction in men in the present study. With no information on the functional role of the polymorphism, the relevance of these findings is unknown.

In conclusion, the authors are to be commended for a carefully performed study and a huge effort. The findings of the study should be used to initiate further research aimed at replication and at elucidation of the underlying mechanisms of disease. Advice to individual patients or recommendations for primary prevention cannot be based on these findings at present.

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**A Broader Concept of Medical Errors**

**N**o one disputes the goal — a health care system that can reliably provide high-quality care with minimal waste to all in need. Disagreement begins with the question of which problems are most urgent. Some cite inequities in access to care; others emphasize gaps in quality that transcend race, sex, and social class.\(^1\)\(^2\) Employers bemoan the rising costs of health care,\(^4\) whereas the press and health care leaders are appalled by the 44,000 to 98,000 deaths per year that, according to the Institute of Medicine (IOM), may be caused by medical errors.\(^4\)

The accuracy and implications of these estimates are controversial,\(^5\)\(^7\) but the precise number has not been as important as the revelation that preventable deaths occur at all. In response to these estimates and the resulting public attention, high-level positions with titles such as chief safety officer have been created at many institutions. Computerized order-entry systems have been installed at some hospitals and have been the subject of anguished contemplation at the rest. Data on the presence or absence of these and other systems that are believed to reduce medical errors are now available on the Internet (http://www.leapfroggroup.org).

Has all this activity made our health care system better? Probably, but a report by Blendon et al. in this issue of the Journal\(^8\) suggests that two key constituents of the health care system — doctors and patients — have different priorities. Blendon and colleagues found that even though more than a third of their samples of physicians and laypersons reported that there had been errors in their own care or in a family member’s care, neither group considered medical errors among the most urgent problems facing health care today. For both the public and doctors, economic issues such as the cost of care and malpractice insurance were predominant concerns.

A more clinical argument against the focus on patient safety is that medical injuries do not cause nearly as many deaths as errors of omission, such as failure to control blood pressure in most patients with hypertension or to screen for colorectal cancer in about half of patients. As summarized in the second IOM report, our health care system fails with embarrassing frequen-