ation is coordinating efforts with the FDA to establish "equivalence" criteria for substitute materials in shortage areas and to keep critical devices on the market (*1*).

In the short run, the most effective remedy would be to change tort law to bar product liability claims against remote suppliers of "off the shelf" commodity materials and components of devices that have received FDA approval. The entire liability burden would then fall on the device manufacturer, who could decide whether or not to market a device.

Better solutions might be generated through discussion with all involved parties. However, a temporary resolution is urgently needed if we are to avoid a shortage of chronic implants for critically ill patients.

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Cholesterol Vaccines

John Travis's Research News article of 24 December (p. 1974) discusses vaccines to protect against atherosclerosis. Variations of this approach have been tested previously (*1*–*6*). Cholesterol-fed rabbits were protected against atherosclerosis by immunizing them with β-lipoproteins (*1*), and the response of rats to dietary cholesterol was reduced by stimulating the reticuloendothelial (RE) system using zymosan (*2*). In our work, cholesterol-fed rabbits were immunized with synthetic antigens in which cholesterol-esters were covalently linked, as haptens, to various protein carriers (*3*–*7*). Significant reductions in serum cholesterol and up to 90% protection against atherosclerotic plaques were obtained.

In a discussion of the work of the Army group (*8*), the question was raised whether the immune system will develop antibodies to a common constituent such as cholesterol. We found that significant titers were retained against cholesterol after absorption with carrier protein, and extensive cross-reaction was exhibited with cholesterol conjugates of unrelated carrier proteins. This confirmed that antibodies directed specifically against cholesterol could be induced by immunization.

The article also questions how immunization lowers blood cholesterol. We observed increases of greater than 70% in the clearance of ^{14}C-cholesterol-esters from serum of immunized animals (*5*). Significant amounts of cholesterol-antibody complexes were also detected in serum. These observations led to the proposal that the antibodies might label cholesterol-containing lipoproteins for clearance by scavenging macrophages (*6*).

Travis mentions possible long-term adverse effects of the vaccination procedure. In experiments lasting up to 9 months, the hypocholesterolemic effects of immunization persisted, but the protective effects against atherosclerosis gradually declined, despite monthly booster shots. No evidence of autoimmune phenomena or other side effects were noted (*7*).

The cholesterol-fed rabbit may be too severe a test for the cholesterol vaccination procedure. Serum cholesterol in this model frequently exceeds 2000 milligrams per deciliter (mg/dl), whereas the clearance capacity of the RE system is about 300 mg/dl (*7*). The bulk of the public health problem involves cholesterol in the range of 200 to 500 mg/dl. If the procedure can be validated in a more appropriate model, it could become a useful adjunct to diet or drug therapy. However, many technical obstacles would need to be overcome before the scenario of a routine "cholesterol vaccination" could become a reality.

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Fire and Ice . . . and Worms?

May I point out that the "*Würmertod*" referred to in the Vignette from Karl Sigmund's book *Games of Life: Explorations in Ecology, Evolution, and Behaviour* (Oxford Univ. Press, New York, 1993) in the issue of 29 April (Book Reviews, p. 727) means "death of the worms." This is not at all identical with the once-predicted *Wärmetod*, the hypothetical death of a universe coming into perfect thermal equilibrium. It is highly probable that the *Wärmetod* would be preceded by a *Würmertod*, although it must be noted that these hardy animals did manage to survive the *Würm-Eiszeit*.

Lucien F. Trueb
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Corrections and Clarifications

In the Perspective "α-Helical coiled coils: More facts and better predictions" by C. Cohen and D. A. D. Parry (28 Jan., p. 488), the second sentence of the second paragraph of column 1 on page 489 should have read, "The structural motif is indeed a left-handed three-helix bundle with left-handed chain connectivity."

Correction

29 April (p. 734)
and
13 May (p. 911)
issues of

Science

The talk being given by Dr. Harold Varmus at the *Science*/HUGO Human Genome 1994 meeting on Monday, 3 October, in Washington, D.C., is entitled "Manipulating Cancer Genes in the Mouse."