

other known measures, and one has a possible means of stopping the progression of the disease with an agent that has been extensively investigated for 40 years, there appears to be little alternative other than to try it.

Critics of gene therapy seem to forget that, when live viruses are used to immunize against a wide variety of diseases, virus genes are being inserted into man. The use of the Shope virus is different only in that we are taking advantage of this possibility. Another advantage of the Shope preparations used is their purity, unlike most live virus preparations given for immunological purposes. Also, man is continually being exposed and infected by a host of pathogenic and nonpathogenic viruses. This raises the additional question as to what a massive dose of virus is, as the total amount of virus present in the body in an active disease such as measles must be truly large. The Shope virions are known not to be completed to any significant degree in any animal other than the wild cottontail rabbit in Kansas or in the same cottontail rabbit brought to the laboratory and fed food raised in Kansas. It appears, then, to be a rather ideal passenger virus to which desired genetic information may be added in the future for further efforts in gene therapy.

The only other point relating to our work was that tissue cultured cells from the patients should be used to test out the virus in vitro. That arginase was induced with the Shope virus in fibroblasts from an argininemic came as quite a pleasant surprise, as the virus was not known to go in culture. No detectable virions have been produced (5).

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References and Notes

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Largely as a result of the pioneering work of Neufeld and her colleagues, there are now several reports that, in tissue culture cells derived from patients with lysosomal storage dis-

eases, beneficial phenotypic effects can be brought about by means of enzymic factors elaborated by other cells (1) or supplied in culture medium in a partially purified form (2). This important phenomenon of course suggests that similar corrective effects may occur in patients with some lysosomal storage diseases (3). However, we feel that important problems exist in ensuring optimum uptake into cells, such as neurons, where the enzyme is critically needed and not only into macrophages and cells of the reticuloendothelial system; in overcoming the blood-brain barrier where target cells are in the central nervous system; and in eliminating the possibility of immunological reaction to the administered enzyme preparation. We agree that further trials with purified enzyme preparations will be required to evaluate further the potential for enzyme therapy in lysosomal or other disorders.

Rogers indicates the many precautions that were taken before injection of Shope papilloma virus into the hyperargininemic patients. In our article, we did not intend to imply that the virus was administered without precautions. However, we still find ourselves in disagreement with Rogers on several points:

1) We believe that a major premise underlying the scientific rationale for the use of Shope virus, that is, that there is a viral gene which codes for a virus-specific arginase, is still questionable. Rogers cites his new evidence in support of this premise but omits mention of work by Orth and his colleagues (4) which shows that the Shope papilloma arginase has kinetic, molecular, and antigenic properties identical to those of the rabbit liver enzyme.

2) Rogers' comparison of live attenuated virus immunization with virus-mediated gene therapy strikes us as an unfair one. Surely there is a difference between injection of a nononcogenic,

nonintegrating virus with the intent to stimulate a patient's antibody production and injection of a virus which is oncogenic under some conditions, which may be able to integrate its viral DNA into the DNA of the patient's cells, with the intent to alter permanently the patient's genetic constitution, albeit, hopefully, in a beneficial way.

3) The initial injections of the virus in the children were made almost 2 years ago and, at least to our knowledge, there have been no reports published in medical or scientific journals describing criteria for virus therapy, preliminary studies in vitro on the patients' cells, and even biochemical and clinical effects of the therapy. We feel that this kind of information would be helpful in evaluating the use of this agent.

4) Finally, the use by Rogers of the word wart tends to obscure the fact that the Shope virus is indeed an oncogenic virus, and it should be remembered that variable proportions of virus-induced papillomas in both domestic rabbits and cottontail rabbits develop into invasive malignant skin cancers (5).

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2 October 1972

Origin of the Martian Chaotic Terrains

From considerations of atmospheric escape processes, McElroy (1) has estimated the rate of degassing of water from the martian surface relative to that for the earth. If one accepts his data, certain restrictions can be imposed on the theory that the martian "chaotic terrains" (rough, uncratered terrains, apparently caused by vertical subsi-

dence) were produced by withdrawal of permafrost.

McElroy calculated that the ratio of the amount of water that has escaped from Mars over its geologic history to the amount of carbon dioxide currently present in the martian atmosphere is approximately 45 (when the quantities of H₂O and CO₂ are expressed in mole-

cules). This figure is the same as the current H_2O to CO_2 ratio that Rubey (2) estimates for the earth. However, McElroy speculates that as much as half of the martian CO_2 has already escaped to space. If one assumes that the H_2O to CO_2 ratio is indeed the same for Mars as it is for the earth, this would require an amount of water still on Mars equal to the 10^{25} molecules per square centimeter that McElroy has calculated to have escaped over geologic history. This would be enough water to cover the entire planet to a depth of approximately 3 m.

On the 10 percent of the planet's surface that was photographed during the near encounters of Mariners 6 and 7, Sharp *et al.* (3) mapped 1.5×10^6 km² of chaotic terrain. If this proportion holds true for the entire planet, one would expect to find 1.5×10^7 km² of chaotic terrain on the martian surface. If all the water estimated to be present had once occupied the chaotic terrains, they could have been filled to a depth of only 30 m. However, substantial evidence exists that the chaotic terrains occupy elevations that are actually several kilometers below their surroundings. Radar scans by Pettengill *et al.* (4) and by Downs *et al.* (5) across the Pyrrhae Regio region showed that one portion of the chaotic terrain is bordered by scarps 4.5 km high; and Herr *et al.* (6) derived several topographic profiles from Mariners 6 and 7 infrared spectrometer data which showed an excellent correlation between the areas that are one to several kilometers below their surroundings and the areas Sharp mapped as chaotic terrain. If permafrost was once to have occupied this large volume of chaotic terrain, the ratio of H_2O to CO_2 that degassed from Mars would need to be approximately 100 times as great as the ratio for the earth. If this were not so, the chaotic terrains could not have been produced by the withdrawal of H_2O permafrost.

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NEWS AND COMMENT

(Continued from page 598)

RECENT DEATHS

Rebecca Baker, 58; professor of education, Southern Illinois University; 6 September.

Henry J. Bakst, 66; former dean, School of Medicine, Boston University; 28 August.

Roger H. Bray, 73; professor emeritus of soil fertility, University of Illinois; 10 September.

Sam M. Beiser, 49; acting chairman, microbiology department, College of Physicians and Surgeons, Columbia University; 7 September.

Thomas H. Chilton, 73; former visiting professor of chemistry, Georgia Institute of Technology; 14 September.

Edward D. Churchill, 76; former professor of surgery, Harvard University; 28 August.

Howard J. Curtis, 65; former chairman, biology department, Brookhaven National Laboratory; 13 September.

Jess H. Davis, 66; president emeritus, Stevens Institute of Technology; 17 September.

Albert B. F. Duncan, 69; visiting professor, astronomy department, University of Virginia; 29 August.

James W. Egan, 72; former vice president, Georgetown University; 17 August.

Frank A. Forward, 70; former professor of metallurgy, University of British Columbia; 6 August.

Arthur I. Gates, 81; professor emeritus of education, Teachers College, Columbia University; 24 September.

Charles O. Glisson, 74; professor emeritus of engineering, Tennessee Technological University; 15 August.

Roy F. Graesser, 79; professor emeritus of mathematics, University of Arizona; 23 July.

James H. Griffin, 80; former president, Villanova University; 28 July.

Frederick J. Holl, 74; former professor of biology, State University of New York College, Buffalo; 17 August.

May H. James, 83; former professor of social sciences, New Haven State Teachers College; 3 September.

Trois E. Johnson, 59; professor of public health, University of North Carolina; 21 July.

Carol Karp, 46; professor of mathematics, University of Maryland; 19 August.

George V. Kendall, 91; dean emeritus, Wabash College; 9 September.

Daniel S. Lehman, 53; professor of psychology, Rutgers Newark College of Arts and Sciences; 29 August.

Mary S. MacDougall, 89; professor emeritus of zoology, Agnes Scott College; 19 June.

Edward G. McGavran, 70; dean emeritus, School of Public Health, University of North Carolina; 29 August.

Victor E. Monnett, 82; professor emeritus of geology, University of Oklahoma; 18 September.

William A. Mosher, 59; professor of chemistry, University of Delaware; 23 July.

Leonard Paris, 56; associate professor of pathology, State University of New York, Stony Brook; 4 September.

Thomas G. Perry, 53; professor of geology, Indiana University; 21 August.

Isidor S. Ravdin, 77; former vice president for medical affairs, University of Pennsylvania; 27 August.

Robert A. Reicher, 45; chairman, sociology department, Barat College; 14 July.

Hugo R. Rony, 84; former professor of clinical medicine, University of Chicago; 8 September.

Frederick W. Sohon, 78; professor emeritus of seismology and mathematics, Georgetown University; 25 July.

George P. Springer, 53; dean, Graduate School, University of New Mexico; 29 July.

Jacek Szafran, 51; professor of psychology, University of Southern California; 18 April.

Max Theiler, 73; professor emeritus of epidemiology and microbiology, Yale University; 11 August.

Price E. Thomas, 50; chairman, physiology department, Kirksville College of Osteopathic Medicine; 2 September.

Stephen P. Timoshenko, 93; professor emeritus of applied mechanics, Stanford University; 29 May.

Arthur V. Tobolsky, 53; professor of chemistry, Princeton University; 7 September.

Herbert A. Toops, 76; professor emeritus of psychology, Ohio State University; 12 August.

Harry L. Williams, 52; professor of pharmacology, Emory University; 22 July.

Claude V. Winder, 63; physiologist and assistant director of pharmacological research, Parke, Davis & Company; 10 August.