cance of urinary hydroxyproline in osteoporosis. *Panminerva Med.* 5:155, 1963.
4. Benoit, F. L., Theil, G. B., and Watten, R. H. Hydroxyproline excretion in endocrine disease. *Metabolism* 12:1072, 1963.
5. Klein, L., Lafferty, F. W., Pearson, O. H., and Curtiss, P. H., Jr. Correlation of urinary hydroxyproline, serum alkaline phosphatase, and skeletal calcium turnover. *Metabolism* 13:272, 1964.
6. Hosley, H. F., Taft, E., Olson, K. B., Cates, S., and Beebe, R. T. Hydroxyproline excretion in malignant neoplastic disease *Arch. Int. Med.* (in press).

HEMOLYSIS ATTRIBUTED TO MEDICATION

To the Editor: The August 4 issue of the *Journal* carried the article, "Hemolytic-Uremic Syndrome," in which the authors state that the medications used by the patients have not been implicated in causing hemolytic anemia, with the exception of hemolytic episodes secondary to penicillin administration. However, 1 of their patients did receive acetaminophen (Tylenol), an aniline derivative, which does (according to Goodman and Gilman in *The Pharmacological Basis of Therapeutics*, third edition, page 334) occasionally cause a hemolytic anemia, in even small amounts. They further state that this hemolysis may result from 1 of 3 different processes: glucose-6-phosphate dehydrogenase deficiency; an autoimmune process with the drug acting as a hapten adsorbed onto the surface of the red cell; or oxidization of hemoglobin and glutathione and other sulfhydryl groups in the red cell. It is further stated in relation to this last mechanism that "In normal individuals taking large doses of either phenacetin or acetaminophen, the erythrocyte life span is not greatly shortened, but it is significantly shortened in patients with renal insufficiency; this might be due to the fact that uremia as well as the drugs reduce the glutathione content of the red blood cells."

STANLEY C. DERESINSKI
Student
University of Illinois
College of Medicine
Chicago, Illinois

Mr. Deresinski's letter was referred to the authors of the paper in question, one of whom offers the following reply:

To the Editor: Mr. Deresinski is quite correct in his comment that acetoaminophen has been implicated in acute hemolytic anemia and renal failure. Our opinion was founded upon a search of the literature concerning nephrotoxins and adverse hematologic reactions. No specific reference to acetoaminophen as a cause of acute hemolytic anemia or acute renal shutdown was encountered. Articles in the literature concerning the hematologic and nephrotoxic effects of phenacetin, however, often include closely related acetoaminophen and, therefore, the latter drug seems to have developed guilt by association.

In the series reported only 1 patient (Case II) received the drug. At no time was she anuric. Of interest is the fact that the indirect Coombs test was negative, the measurement of glucose-6-phosphate dehydrogenase was normal and the renal-biopsy findings were *not* those of acute tubular necrosis or of interstitial nephritis.

ELLIN LIEBERMAN, M.D.
Assistant Professor of Pediatrics
University of Southern California and Childrens Hospital of Los Angeles
Los Angeles, California

POKEBERRY POISONING

To the Editor: Children and adults sustaining systemic exposure to pokeweed (*Phytolacca americana*) by berry ingestion or even only contact with skin abrasions develop plasmacytosis and other changes (such as mitosis) in peripheral blood cells in vivo.[1,2] The "poke cells" that appear under such circumstances resemble peripheral blood lymphocytes that have undergone "blastogenesis" in vitro in response to phytohemagglutinin or pokeweed mitogen.[3] We are presently engaged in collaborative efforts to elucidate short-term physiologic effects and long-term clinical implications of the in vivo phenomenon. We should appreciate any opportunity to study patients encountered this year in the New England area who have sustained proved pokeweed poisoning.

B. E. BARKER, PH.D.
P. FARNES, M.D.
P. H. LAMARCHE, M.D.
H. FANGER, M.D.
Departments of Pathology and Pediatrics
Rhode Island Hospital
Providence, Rhode Island

REFERENCES

1. Barker, B. E., Farnes, P., and Fanger, H. Mitogenic activity in *Phytolacca americana*. *Lancet* 1:170, 1965.
2. Barker, B. E., Farnes, P., and LaMarche, P. H. Peripheral blood plasmacytosis following systemic exposure to *Phytolacca americana*. *Pediatrics* (in press).
3. Farnes, P., Barker, B. E., Brownhill, L. E., and Fanger, H. Mitogenic activity in *Phytolacca americana* (pokeweed). *Lancet* 2:741, 1964.

HEPATITIS TRANSMITTED BY ANTIHEMOPHILIC GLOBULIN

To the Editor: The simple, inexpensive and efficient preparation of antihemophilic globulin (AHG, Factor VIII) concentrate by cold precipitation, as described by Pool and Shannon,[1] represents a dramatic advance in the management of classic hemophilia (Factor VIII deficiency). Previous human AHG concentrates have been difficult and expensive to prepare; they have also been known to transmit hepatitis.[2]

We have recently seen a patient with hepatitis presumably transmitted by cold-precipitated AHG concentrate. This thirty-nine-year-old man, who was known to have classic hemophilia, was admitted to the Cleveland Veterans Administration Hospital on July 29, 1966, with a five-day history of jaundice. Sixty days previously he had received a total of 28 units of cold-precipitated AHG concentrate at another hospital at the time of dental extractions. There was no other apparent exposure. Nine months before admission he had been admitted to the same hospital for peripharyngeal bleeding and had received cold-precipitated AHG concentrate and fresh-frozen plasma. Physical examination disclosed obvious jaundice and a tender liver 4 cm. below the right costal margin. The serum total bilirubin was 10.8 mg. per 100 ml., the serum glutamic oxalacetic transaminase 1200 Karmen units, and the alkaline phosphatase 28 King–Armstrong units. After one day of nausea and vomiting rapid clinical improvement ensued, and the liver tests quickly returned toward normal values.

Because hepatitis appears to have been transmitted by the cold-precipitated AHG concentrate in this case, care should be exercised in the selection of donor plasma.

VINCENT DEL DUCA, JR., M.D.
R. BENNETT EPPES, M.D.
Hematology Section
Veterans Administration Hospital
Cleveland, Ohio

REFERENCES

1. Pool, J. G., and Shannon, A. Production of high-potency concen-

trates of antihemophilic globulin in closed-bag system. *New Eng. J. Med.* 273:1443-1447, 1965.
2. Marder, V. A., and Schulman, N. R. Major surgery in classical hemophilia using Fraction I. *Am. J. Med.* 41:56-75, 1966.

The letter printed above was referred to Dr. Pool, who, with a colleague, offers the following reply:

To the Editor: We were interested to learn of the case of probable transmission of hepatitis by Factor VIII cryoprecipitate reported by Drs. Del Duca and Eppes. We are not aware of this complication after the administration of more than 3000 cryoprecipitates in our own institution, but know of no reason why such preparations should be any more free of transmissible hepatitis than other single donor units given in large numbers. We therefore agree that one should be cautious in selection of donors.

JUDITH G. POOL, PH.D.
Senior Research Associate
WILLIAM P. CREGER, M.D.
Associate Professor of Medicine
Head
Division of Hematology
Stanford University School of Medicine
Palo Alto, California

SURGICAL TREATMENT OF MYOCARDIAL ISCHEMIA

To the Editor: We note with interest in the editorial entitled "Revascularization of the Myocardium" commenting on our paper in the same issue of the *Journal* (August 11), the following statement: "unfortunately, they [Gorlin and Taylor] have failed to use the exercise electrocardiogram in the preoperative and late postoperative physiologic evaluation of their series. . .[they] bypass. . .the amazingly accurate and relatively simple test for myocardial ischemia that is afforded by the electrocardiographic comparison of resting with exerted myocardium."

The major reason for *not* presenting such data in postoperative evaluation was given in our original article — namely, that the postoperative pericarditis changed the ST-T segments so much as to render them meaningless. It is an axiom that the exercise electrocardiogram has little meaning if taken in the face of a previously abnormal *resting* electrocardiogram, as was indeed true for all our patients after operation. The exercise electrocardiogram was taken in 10 patients after operation and found not to be subject to interpretation.

Finally, we submit that evidence concerning myocardial "nutrient flow" and metabolism after any attempt at revascularization remains the objective type of proof we all need. We, too, wish that a simple test like the exercise electrocardiogram could be useful in postoperative evaluation; unfortunately, it is not.

RICHARD GORLIN, M.D.
WARREN J. TAYLOR, M.D.
Peter Bent Brigham Hospital
Boston

SAFETY OF OXYGEN ATMOSPHERES

To the Editor: Dr. E. M. Roth, in his excellent review article, "Gas Physiology in Space Operations," which appeared in the July 21 issue of the *Journal*, discusses data derived from research done at this laboratory. Although the factual presentation is essentially correct, we disagree with his interpretations.

In rats exposed here to 100 per cent oxygen at 5 psia (5 pounds per square inch absolute) or 258 mm. of mercury for three to ninety days, morphologic changes developed in the liver and kidney mitochondrial structure, but these changes were most impressive at one week and then tended to return toward normal with continued exposure. Subsequent electron-microscopy of tissue from rats, dogs and monkeys exposed to the same environment continuously for two hundred and thirty-six days confirms the impression that the mitochondrial changes are reversible and definitely not progressive with increased duration of exposure. In addition, the significance of these and other ultrastructural changes seen is, as yet, unclear. Although we have demonstrated an uncoupling of oxidative phosphorylation in liver mitochondria after in vivo exposure to 100 per cent oxygen at 15 psi (760 mm of mercury) no abnormalities in mitochondrial function have been found at the 5-psia pressure utilized in space-cabin atmospheres. Whereas initial analysis of data obtained from blood chemical studies of dogs and monkeys exposed to a simulated spacecraft atmosphere continuously for eight months did suggest that there was slight elevation of certain serum enzymes after six months, final analysis of data at eight months failed to confirm this.

By extrapolation from the results of prolonged animal exposures at this laboratory and interpretation of available information on shorter duration human exposures, we believe that the pure oxygen atmosphere at 5 psia is safe for continuous exposures up to six months' duration.

A further elaboration of the findings presented above and a discussion of many of the problems cited by Dr. Roth were presented at the Second Annual Conference on Atmospheric Contamination in Confined Spaces, held in Dayton, Ohio, May, 1966. Proceedings of this conference are currently in press and will be available to interested readers on request.

ANTHONY A. THOMAS, M.D.
KENNETH C. BACK, PH.D.
FARREL R. ROBINSON, MAJOR, USAF, VC
HAROLD P. KAPLAN, CAPTAIN, USAF, MC
Toxic Hazards Division
6570th Aerospace Medical Research Laboratories
Aerospace Medical Division, Air Force Systems Command
Wright-Patterson Air Force Base, Ohio

The letter printed above was referred to Dr. Roth, who offers the following reply:

To the Editor: The data quoted in my review regarding the changes in animals exposed to 5 psia at 100% oxygen for long periods of time were quoted from a preliminary report presented by Dr. Back at the NASA Workshop Conference on Criteria for Selection and Evaluation of Space Mission Atmospheres, Houston, Texas, November 1965. The final report of these data presented by Drs. Thomas, Back, Robinson and Kaplan at the Second Annual Conference on Atmospheric Contamination in Confined Spaces held at Dayton, Ohio, May 1966, does indeed indicate that the findings were only transient.

Since there were residual changes in the electron micrographs, I feel that one must still apply caution in validating pure oxygen atmospheres for human use. The statement that pure oxygen atmosphere at 5 psi is safe for continuous exposure up to 6 months duration should be limited to simulators. I still feel that ground based studies of equal duration should precede the use of any exotic atmosphere in space.

I wish to thank Dr. Thomas et al. for bringing the final findings to my attention.

E. M. ROTH, M.D.
Lovelace Foundation for Medical Education and Research
Albuquerque, New Mexico

RESCISSION OF REVOCATIONS OF LICENSES

To the Editor: This is to inform you that at a meeting of the Board of Registration in Medicine held on September