

# AMMONIA INTOXICATION FROM BANK BLOOD IN PATIENTS WITH CIRRHOSIS OF THE LIVER

## A Clinical Note

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**S**TUDIES<sup>1-3</sup> of ammonia intoxication in patients with cirrhosis of the liver have shown that the administration of drugs such as chlorothiazide,\* acetazolamide,† and ammonium chloride, which have been used commonly in patients with ascites, may cause ammonia intoxication or may increase its severity if it exists. The increased ammonia content of stored blood has been reported,<sup>4-7</sup> and in most clinical conditions is harmless. However, in the cirrhotic patient with hemorrhage that requires massive transfusion, the use of stored blood may precipitate coma because of its high ammonia concentration.

This study was undertaken to determine the rate of increase in ammonia nitrogen in stored blood for the purpose of predicting the ammonia content of blood administered in emergency situations, and for considering means of compensating for this difficulty.

Forty-two samples of whole blood, collected in 500-ml. containers‡ were stored at from 4 to 10° C. as long as 31 days. Analyses for ammonia nitrogen were made through the courtesy of W. R. Faulkner, Ph.D., of the Department of Clinical Pathology, whose modifications of the Conway technic were employed.

There was an average linear increase of 20  $\mu$ g. per 100 ml. per day in the amount of ammonia nitrogen in stored blood (*Fig. 1*). In an attempt to explain the unusual values obtained for particular samples, the ease and rapidity of bleeding the donor were evaluated. Easy, rapid bleeding was associated with low values for ammonia; whereas, difficulties with venipuncture and stasis below a tourniquet were correlated with higher values.

### Comment

Theoretically, if a patient (weighing 70 kg.) with cirrhosis and bleeding varices had lost 20 per cent of the blood volume, and he was transfused rapidly with 10 units of blood stored for 10 days, the ammonia concentration in the peripheral blood would be increased approximately 100  $\mu$ g. per 100 ml. Although rarely would blood be administered rapidly enough to produce such a calculated increase, this increment added to that formed in increasing amounts in the gastrointestinal tract might be critical in producing ammonia intoxication and deepening coma.

This complication of transfusion can be controlled at present by three methods.

\* *Diuril (chlorothiazide), Merck Sharp & Dohme.*

† *Diamox (acetazolamide), Lederle Laboratories.*

‡ *Silicone-coated, nonvacuum containers with A-C-D solution, manufactured by Abbott Laboratories.*

The first is that of using only fresh blood, if adequate amounts are available. The second method is an ingenious adaptation of the cation-exchange resin principle as reported by Schechter, Nealon, and Gibbon.<sup>8,9</sup> These authors used a resin exchange column through which blood from the donor bottle passed before it was administered to the patient. Effective extraction of ammonia and potassium from stored blood occurred at rates of drip as fast as 50 ml. per minute. Unavailability of the necessary equipment is at present a deterrent to the use of this method. A practical, clinical objection is that sodium is the cation exchanged for ammonia and potassium. Sodium thus released and given to the patient may precipitate or increase ascites.

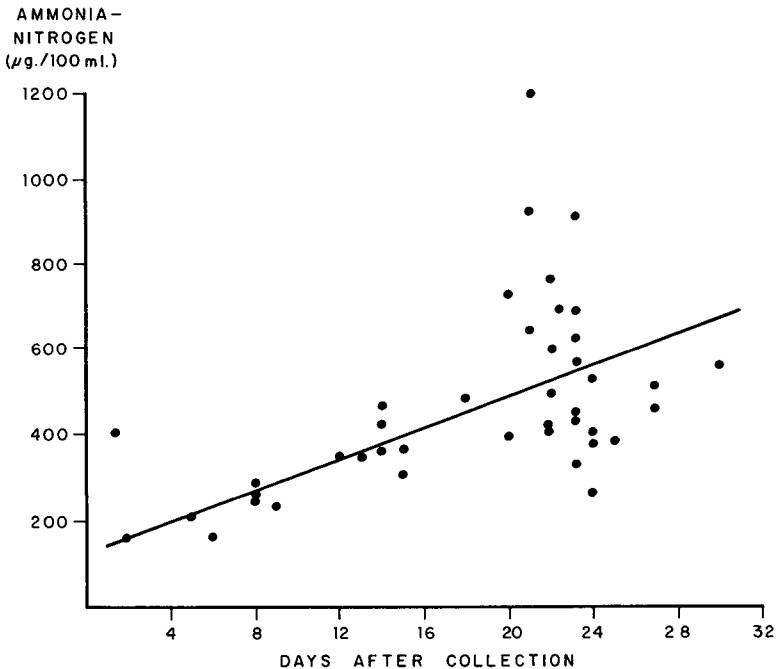


Fig. 1. Graph showing increase of concentration of ammonia-nitrogen in stored blood.

The third and most practical method of controlling the effect of ammonia in stored blood is the simultaneous administration intravenously of arginine.<sup>10</sup> Arginine combines with ammonia in the liver to form urea; this reaction occurs rapidly and continues even in terminal hepatic disease. Arginine monohydrochloride may be simply prepared by adding 25 gm. of analytically pure arginine monohydrochloride to 400 ml. of distilled pyrogen-free water, adding 240 mg. of potassium metabisulfite as an antifungal preservative, autoclaving the solution for 15 minutes at 20 pounds of pressure, and storing it at room temperature. One hundred milli-

liters of 50 per cent dextrose solution may be added prior to use to provide additional calories. Arginine is also available commercially as L-arginine L-glutamate.\*

Arginine injected intravenously has been nontoxic in amounts up to 200 gm. per day. Twenty-five grams given every four hours during massive transfusion is sufficient to prevent any potential toxicity due to increased ammonia content of stored blood.

### Summary

Ammonia in stored blood increases at an average rate of 20  $\mu$ g. per 100 ml. per day. Three clinical methods are useful for reducing or controlling ammonia intoxication that may result from massive transfusion in a cirrhotic patient. The most practical method at present is to administer intravenously arginine monohydrochloride simultaneously with the blood as described.

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\* *Modumate (L-arginine L-glutamate)*, Abbott Laboratories.