

human beings who were receiving relatively large amounts of an antigenic foreign protein, were made available to us at intervals during the course of their therapeutic programs.\* These sera were tested for specific antibody content by the conventional precipitation test and by the bacterial agglutination (B.A.) technic herein described. A comparison of the results obtained by the 2 methods of antibody determination indicates that the B.A. method when also applied to the serum of man serves to detect antibody earlier and that significant titers persist longer than is observed with the conventional precipitation test.

It seems likely, therefore, that the B.A. method of antibody detection possesses certain advantages over the conventional precipitin test as made by the antigen dilution method. While the B.A. method may not be more sensitive than the collodion particle agglutinative method as described by Freund,<sup>4</sup> by Cannon and Marshall,<sup>3</sup> and others, we have found, however, that it is more convenient and that the bacteria employed exhibit greater suspension stability than collodion particles.

Since the B.A. method is capable of detecting extremely small quantities of antibody in serum it is conceivable that it may be advantageously applied to various immunological problems, *e. g.*, allergic states, virus diseases and other conditions wherein very small amounts of circulating antibody may be involved in the mechanism of the disorder. Our current studies involving the use of this newly devised technic in a virus disease (encephalitis of the St. Louis type) will be reported subsequently, wherein it will be shown that the sera of convalescent patients agglutinate bacterial cells treated with mouse brain virus antigen.

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#### Paradoxical Blood Concentrating Effect of Intravenous Four Normal Plasma Injections.

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If plasma is injected intravenously, one would expect the blood to become diluted. If concentrated plasma is similarly injected, be-

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\* These sera were supplied by Dr. R. O. Muether and the precipitation tests were made by Miss Ruth Kettler.

<sup>4</sup> Freund, J., *Am. Rev. Tbc.*, 1925, **12**, 124.

cause of osmotic attraction of fluid from the tissues, one would expect the blood to become even more diluted than following the intravenous injection of normal plasma.

These theoretical expectations outlined in the previous paragraph were not supported by our experiments, which gave exactly the opposite results. Experiments were performed on healthy dogs under nembutal anesthesia. Large doses of reconstituted 4 normal dried dog or human plasma (prepared by the method of Hartman<sup>1</sup>) were rapidly injected intravenously and numerous blood samples were taken from an ear artery for hematocrit and hemoglobin estimations. An immediate paradoxical blood concentration occurred which lasted for about 30 minutes and was not followed by any secondary blood dilution.

Similar experiments were performed using 4 x normal glucose solution (20%). The results were the exact opposite of the plasma injections and revealed a marked immediate dilution as would be expected. Typical curves are shown in Fig. 1.

Calculations can be made assuming the vascular tree of the recipient dogs to be a closed system, thus:

*A. Glucose injection*

Dog wt—12.0 kg  
Calc. blood vol.—920 cc ( $\frac{1}{13}$  body wt)  
Control hematocrit—44  
Calc. control erythron—405 cc.  
Calc. control plasma vol.—515 cc  
Add 120 cc 20% glucose  
Final erythron still—405 cc  
Final plasma vol. now—635 cc  
Final calc. hematocrit—39  
(Final observed hematocrit—33)

*B. Concentrated plasma injection*

Dog wt—9.7 kg  
Calc. blood vol.—745 cc ( $\frac{1}{13}$  body wt)  
Control hematocrit—38  
Calc. control erythron—285 cc  
Calc. control plasma vol.—460 cc  
Add 100 cc 4 x normal plasma  
Final erythron still—285 cc  
Final plasma vol. now—560 cc  
Final calc. hematocrit—34  
(Final observed hematocrit—45)

From these calculations it is seen that glucose produces more of a blood dilution than would be expected (decrease of 11 in the hematocrit instead of 5), while plasma causes the reverse effect (increase of 7 instead of the calculated decrease of 4 in the hematocrit). The excess dilution produced by glucose may be caused by an immediate inflow of tissue fluids into the blood stream, while there is no evidence for such a response to concentrated plasma injections.

A search of the literature revealed only two articles bearing on our results. Brennan<sup>2</sup> noted an increase in the red blood count in acutely anemic neurosurgical patients following the injection of half-normal plasma. He also noted a decrease in the mean corpuscular volume, which did not occur in our experiments, since the alterations in the hemoglobin paralleled those of the hematocrit.

<sup>1</sup> Hartman, F. W., and Hartman, F. W., Jr., *J. A. M. A.*, 1940, **115**, 1989.

<sup>2</sup> Brennan, H. J., *Brit. M. J.*, 1940, **1**, 1047.

## 16 PARADOXICAL HEMOCONCENTRATING EFFECT OF PLASMA

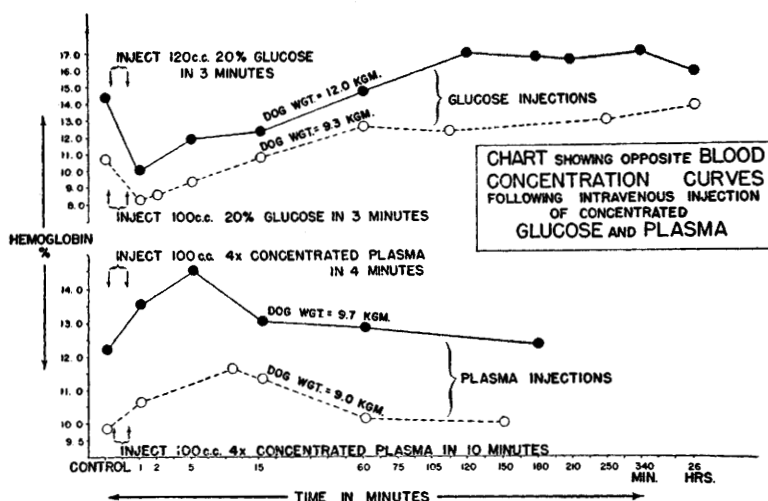


Fig. 1.

Keeley, Gibson and Pijoan<sup>3</sup> found that following burns, there was an increase in circulating erythrocytes in normal animals, but a decrease in splenectomized animals. This latter paper suggested the possibility that in our experiments the blood concentration resulted from splenic contractions. One splenectomized dog so far studied showed a blood dilution following 4 normal plasma injections, rather than the usual paradoxical blood concentration.

**Conclusions.** (1) The intravenous injection of concentrated glucose solution causes an immediate blood dilution. This dilution is greater than would be expected if the vascular tree were a closed system. (2) The intravenous injection of concentrated dog and human plasma under similar conditions not only causes no dilution, but a paradoxical blood concentration.

<sup>3</sup> Keeley, J. L., Gibson, J. G., 2nd, and Pijoan, M., *Surgery*, 1939, 5, 872.