much larger number of persons will have to be examined before the difference between groups O and A can be accepted as other than fortuitous.

Summary. Persons belonging to blood-group A and those belonging to blood-group O formed protective antibody equally well following ingestion of type 1 pneumococcal vaccine. A somewhat greater percentage of persons in group B responded than in groups O and A but the number of individuals was too small to justify relating the fact to membership in the group.

The author wishes to express his thanks to Dr. Ralph S. Muckenfuss, Director of the Bureau of Laboratories of the Department of Health, for providing the facilities which made it possible to carry out these experiments.

11025

Effect of Desoxycorticosterone Acetate upon Plasma Volume in Patients During Ether Anesthesia and Surgical Operation.

CHARLES RAGAN, JOSEPH W. FERREBEE AND G. W. FISH. (Introduced by W. W. Palmer.)

From the Departments of Medicine, Neurology, and Urology, College of Physicians and Surgeons, Columbia University, and the Presbyterian Hospital, New York.

In recent years, several workers have found that hemoconcentration develops in the course of ether anesthesia. McAllister[1] showed that in dogs there is a drop in plasma volume and a rise in hematocrit. Searles[2] employing an increase in hematocrit, red cell count, and hemoglobin as his criterion for hemoconcentration in dogs came to a similar conclusion. Bollman, *et al.*,[3] also working with dogs, were able to demonstrate a fall in plasma volume and rise in hematocrit in response to ether anesthesia. Gibson and Branch[4] showed that ether anesthesia in man was accompanied by a slight but definite decrease in plasma volume. Stewart and Rourke[5] showed in man

1 McAllister, F., *Am. J. Physiol.*, 1938, **124**, 391.

2 Searles, P. W., *Am. J. Surg.*, 1938, **41**, 399.

3 Bollman, J. L., Svirbely, J. L., and Mann, F. C., *Surgery*, 1938, **4**, 881.

4 Gibson, J. G., 2nd, and Branch, C. D., *Surg. Gyn. and Obst.*, 1937, **65**, 741.

5 Stewart, J. D., and Rourke, G. M., *J. Clin. Invest.*, 1938, **17**, 413.

that surgical procedures are in some instances associated with a fall in plasma volume as determined post-operatively.

Barbour and Bourne[6] felt that the degree of hemoconcentration in dogs brought about by ether anesthesia could be diminished by the preanesthetic injection of fluid. McAllister and Thorn[7] were able to show that the hemoconcentration induced by ether anesthesia in dogs (as evidenced by rise in hematocrit and fall in plasma volume) was overcome by the preanesthetic injection of adrenal cortical hormone. The present work was undertaken in order to determine whether or not adrenal cortical hormone might have a similar effect upon possible changes in plasma volume during ether anesthesia and operation in man.

Plasma volume was determined by the method of Gregersen, Gibson, and Stead.[8-12] Reinjection of the dye at the end of the experiments was not done in this study, as it has been shown (Hamlin and Gregersen,[13] McAllister[8]) that changes in the disappearance curve mirror changes in plasma volume. Hematocrit was determined by using one cc hematocrit tubes spun at a standard rate for a constant length of time employing heparinized blood. Serum protein was measured by means of a Zeiss refractometer. Changes in serum protein were checked in a few instances by the micro-kjeldahl method. Plasma volume was measured one to three hours before operation.*

The patients studied were from the Squier Urological Service. Although an attempt was made to select patients undergoing only minor surgical procedures, this was not at all times feasible, and some of the results are complicated by such factors as blood loss and traction on the kidney pedicle. Anesthesia was administered by the regular anesthetists of the hospital. Preoperative medication consisted of morphine and atropine. In no instance did this medication alone cause a change of plasma volume. Anesthesia was induced in all the patients with nitrous oxide and oxygen and this was followed by the administration of ether. When anesthesia was con-

6 Barbour, H. G., and Bourne, W., *Am. J. Physiol.*, 1923, **67**, 399.

7 McAllister, F., and Thorn, G., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 736.

8 Gregersen, M. I., Gibson, J. G., 2nd, and Stead, E. A., *Am. J. Physiol.*, 1935, **113**, 54.

9 Gregersen, M. I., and Stewart, J. D., *Am. J. Physiol.*, 1939, **125**, 142.

10 Gregersen, M. I., and Schiro, H., *Am. J. Physiol.*, 1938, **121**, 284.

11 Gregersen, M. I., and Gibson, J. G., 2nd, *Am. J. Physiol.*, 1937, **120**, 494.

12 Gregersen, M. I., *J. Lab. and Clin. Med.*, 1938, **23**, 1.

13 Hamlin, E., and Gregersen, M. I., *Am. J. Physiol.*, 1939, **125**, 713.

* We wish to thank Dr. M. I. Gregersen for furnishing us with a supply of the blue dye, "T 1824."

sidered deep enough to permit incision, a blood sample was taken without stasis. Another sample of blood was taken during the operation and a third when the patient returned to the ward. Varying amounts of desoxycorticosterone acetate† were administered subcutaneously for 45 minutes to 8 hours preoperatively, or 20 to 30 cc of cortin† were injected immediately before anesthesia.

Results. The results are shown in Fig. 1. Seven patients served as controls. All showed a fall in plasma volume with ether anesthesia alone. The magnitude of this fall as measured by the dye, serum protein, and hematocrit is slight and in all but 2 patients is within the limit of error of the method. However, during the period of operation itself, 5 of the 7 patients showed a fall in plasma volume exceeding the limits of error. In the postoperative period, one of 7 patients showed a lowered plasma volume. In one patient, the drop in

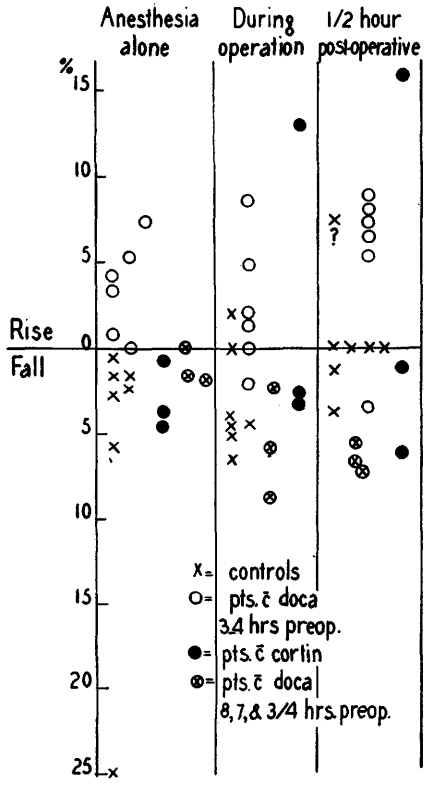

FIG. 1.

Per cent change in plasma volume in operative patients. "Doca" is the term used for desoxycorticosterone acetate.

† Material furnished by Roche-Organon, Inc., Nutley, N. J.

plasma volume as measured by the dye was not confirmed by a drop in plasma volume as measured by the serum protein and hematocrit. In the other 5 patients, there was no change from their preoperative plasma volume.

Nine patients were given between 16 and 20 mg of desoxycorticosterone acetate subcutaneously before operation. In 3 patients in whom the synthetic hormone was given at 8, 7, and ¾ hours respectively preoperatively, there was a fall in plasma volume with ether anesthesia alone of the same order of magnitude as seen in the control group. During the period of the operation, 2 of the 3 showed a significant fall in plasma volume, while in the third the fall was within the error of the method. One-half hour postoperatively, one of the 3 showed a significant fall in plasma volume. In the other 2 patients, the fall in plasma volume as measured by the dye was not supported by the serum protein and hematocrit determinations. In other words, the hormone produced no demonstrable effect in these patients.

In the other 6 patients, the synthetic hormone was given between 3 and 4 hours preoperatively. Three of these 6 showed a measurable increase in plasma volume during the period of ether anesthesia alone. In the other 3, the increase as measured by the dye was either within the limit of error of the method or was not corroborated by a significant increase as measured by the serum protein or hematocrit. During the operative period, one showed a significant increase in plasma volume. In 5, no change was found. Five of the 6 patients showed a significant rise in plasma volume during the postoperative period, while the sixth showed no change. Thus it is apparent in this group that the usual fall in plasma volume was prevented by synthetic hormone given 3 to 4 hours before operation.

Three patients received 20 to 30 cc of cortin intravenously immediately prior to anesthesia. During anesthesia alone, there was the usual insignificant decrease in plasma volume. During the operative period, 2 of the 3 showed a similar insignificant drop and one showed an increase in plasma volume. In the postoperative period, one showed an increased plasma volume, in one there was a minor decrease, and in the third there was a significant fall. In this group, the results are obviously inconclusive.

Summary and Conclusions. (1) Plasma volume was determined in patients undergoing ether anesthesia and surgical operation. Seven patients served as controls, 9 received desoxycorticosterone acetate (subcutaneously) at varying time intervals before operation, and 3 received crude adrenal cortical hormone (intravenously) immediately before the anesthetic. (2) Of the 7 patients serving as con-

trols, 2 showed a significant fall in plasma volume during ether anesthesia alone, 5 during the period of operation, and one, one-half hour postoperatively. In none of these controls was there a significant increase in plasma volume during any of the 3 periods studied. (3) Six patients were given desoxycorticosterone acetate subcutaneously 3 to 4 hours before anesthesia. In this group, 3 patients showed a significant increase in plasma volume during the period of anesthesia alone, one patient during the operation, and 5 patients one-half hour after the operation. There were no patients in this group who showed a significant fall in plasma volume during any of the 3 periods. (4) In this small series of patients who have undergone surgical procedures accompanied by slight blood loss, the decrease in plasma volume associated with ether anesthesia and these surgical procedures is small. This small decrease in plasma volume is not present when patients have been given desoxycorticosterone acetate subcutaneously 3 to 4 hours before operation.

11026 P

Action of Diethyl Ether on Histamine Release in Anaphylaxis.*

G. KATZ, C. T. FREY AND L. IRELAND FREY.

From the Department of Pharmacology, School of Medicine, Tulane University of Louisiana, New Orleans.

Anesthesia is known to lessen the intensity of anaphylactic shock; sensitized guinea pigs, under anesthesia, are more likely to survive the injection of the antigen.[1,2] From experiments in which sensitized guinea pig uteri were suspended in urethane solution and did not contract upon addition of the antigen, Farmer[3] recently concluded that: (a) the anesthetic does not prevent the union between antigen and antibody, since the uteri did not contract either upon readministration of the antigen, when the narcotic had been washed out and the response to histamine was restored, and (b) that the anesthetic inhibits the action of histamine released in shock, while it does not interfere with its release. The following is a report on experi-

* Aided by a grant from the John and Mary R. Markle Foundation.

1 Besredka, A., *Ann. de l'Inst. Pasteur*, 1907, **21**, 957.

2 Farmer, L., *J. Immunol.*, 1937, **32**, 195.

3 Farmer, L., *Ibid.*, 1937, **33**, 9.