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# Decreases in Plasma Volume During Electrically Induced Convulsions in Man.

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Electrically induced convulsions as used in the treatment of mental disease consist of a brief period of generalized muscular contractions of maximal vigor; they are associated with marked rises in intrathoracic and intra-abdominal pressures and the development of anoxia. Studies made here on the effects of electroshock therapy have afforded data bearing on problems connected with the physiology of violent physical exercise; it was considered of interest to describe the changes in plasma volume which occur during this type of muscular exertion.

*Material and methods.* Thirteen subjects were studied, 8 of whom were women. Cardiovascular function was normal except for mild hypertension in several. Two of the subjects were studied twice each, the rest being observed in one treatment each. Three of the women (Cases 11, 12, 13) were studied during convulsions moderated as a consequence of the previous intravenous injection of curare (solution Intocostrin or solution d-tubocurarine Squibb); in one of these (Case 11) observations had also been made during a seizure induced without the previous injection of curare.

The plasma volume was measured by the short indirect method of Gibson and Evans,[1] 4 samples of venous blood being taken over a period of 30 to 40 minutes immediately before the induction of the seizure, and another being taken immediately at the end of the convulsion; in 5 instances an additional sample was taken 15 minutes later. The concentration of dye in each sample of plasma was estimated by means of a Coleman Junior Spectrophotometer. The plasma protein concentration was estimated in 5 patients by means of the copper-proteinate method;[2] measurements of plasma protein so made were used to estimate changes in plasma volume using the following formula:

$$\text{plasma volume after seizure} = \frac{\text{plasma volume before} \times \text{plasma protein before}}{\text{plasma protein after}}$$

*Observations.* The plasma volume was diminished at the end of the convulsive seizure in every instance; the decreases ranged between 50 cc and 1040 cc, or 1.7% to 34.7% of the original values (Table I, Fig. 1). In the case of the men, the decreases were between 9.0% and 34.7% of the control levels, the average being 19.4%. The largest decrease occurred in a young muscular athlete in good condition (Case 1), while the smallest decrease in this group was observed in a weak, malnourished, middle-aged individual who had led a sedentary life for several decades (Case 5). One patient, studied twice, showed diminutions in plasma volume of 25.8 and 17.9% on the two occasions. In the uncurarized women, diminution in plasma volume immediately after the convulsion amounted to between 7.3 and 13.7% of the control values; the average was 10.5%. The curarized women showed decreases of 1.7 to 4.7% of the control values for plasma volume, changes which are not significant; the average change was 3.2%. One woman studied twice showed a decrease in plasma volume of 7.3% when not given curare, and of 3.1% when curarized.

Fifteen minutes after the seizure the plasma volume as a rule was partially restored to its original value (Table I).

*Discussion.* Kaltreider and Meneely[3] re-

[1] Gibson, J. G., II, and Evans, W. A., Jr., *J. Clin. Invest.*, 1937, **16**, 301.

[2] Phillips, R. A., Van Slyke, D. D., Dole, V. P., Emerson, K., Jr., Hamilton, P. B., and Archibald, R. M., *Bull. U. S. Army Med. Dept.*, 1943, **71**, 66.

TABLE I.
Changes in Plasma Volume and Plasma Protein Concentration After Convulsions.

| Case | Sex | Plasma volume | | | | Plasma protein, g % | | |
|---|---|---|---|---|---|---|---|---|
| | | Before, cc | After, cc | Difference, % | 15 min. later, cc | Before | After | 15 min. later |
| 1 | M | 3000 | 1960 | 34.7 | 2740 | 6.86 | 8.17 | 7.53 |
| 2a | M | 3000 | 2225 | 25.8 | | | | |
| 2b | M | 2600 | 2135 | 17.9 | | | | |
| 3 | M | 3130 | 2610 | 16.6 | 2900 | 6.69 | 7.29 | 7.08 |
| 4 | M | 3910 | 3430 | 12.3 | 3430 | 5.45 | 6.44 | 6.08 |
| 5 | M | 3050 | 2775 | 9.0 | | | | |
| | Avg—Men | | | 19.4 | | | | |
| 6 | F | 1420 | 1225 | 13.7 | | | | |
| 7 | F | 1750 | 1520 | 13.1 | | | | |
| 8 | F | 2460 | 2190 | 11.0 | | | | |
| 9 | F | 2140 | 1940 | 9.4 | 2210 | 6.27 | 7.16 | 6.49 |
| 10 | F | 2360 | 2160 | 8.5 | | | | |
| 11a | F | 2120 | 1965 | 7.3 | | | | |
| | Avg—Women | | | 10.5 | | | | |
| | Avg—Men and women | | | 14.9 | | | | |
| 11b | F | 2130 | 2065 | 3.1 | | | | |
| 12 | F | 1910 | 1820 | 4.7 | | | | |
| 13 | F | 3010 | 2960 | 1.7 | 2910 | 5.37 | 5.64 | 5.73 |
| | Avg—Curarized women | | | 3.2 | | | | |

viewed the earlier work on the effect of exercise on the plasma volume and added additional data; much of the previous work was fragmentary or carried out by means of methods of doubtful validity. Indeed, the validity of the method of Gibson and Evans[1] used by Kaltreider and Meneely,[3] and also in the present study, has not been established in exercising subjects. In view of the fact that the dye used in that method is attached to albumin,[4] it is clear that if this protein left the vascular bed during exercise the decreases in plasma volume as measured would be smaller than the actual decreases. It appears, therefore, that the decreases in plasma volume which occur during exertion actually are as large as those reported by Kaltreider and Meneely[3] and in the present study, or possibly greater. A criticism of the validity of the method during exertion advanced by Ebert and Stead[5] is more serious; those authors reported a change in optical quality of the serum after exercise, which in 5 of their 6 experiments was large enough to introduce serious errors into the measurement of plasma volume with the dye method. These errors were detected by Ebert and Stead[5] by means of the large discrepancies found when de-

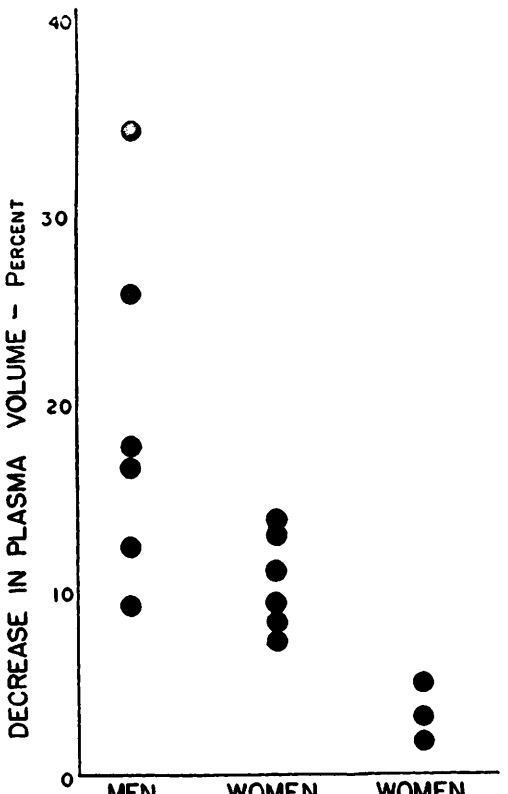

FIG. 1.

[3] Kaltreider, N. L., and Meneely, G. R., *J. Clin. Invest.*, 1940, **19**, 627.

[4] Gregerson, M. I., and Gibson, J. G., *Am. J. Physiol.*, 1937, **120**, 494.

[5] Ebert, R. E., and Stead, E. A., Jr., PROC. SOC. EXP. BIOL. AND MED., 1941, **46**, 139.

TABLE II.
Plasma Volume Immediately After Convulsion.

| Case | Measured by dye method, cc | Calculated from changes in plasma protein, cc | Avg deviation, % |
|---|---|---|---|
| 1 | 1960 | 2480 | ± 11.7 |
| 3 | 2610 | 2870 | ± 4.8 |
| 4 | 3430 | 3310 | ± 1.8 |
| 9 | 1940 | 1870 | ± 1.8 |
| 13 | 2960 | 2870 | ± 1.5 |

TABLE III.
Plasma Volume 15 Minutes After Convulsion.

| Case | Measured by dye method, cc | Calculated from changes in plasma protein, cc | Avg. deviation, % |
|---|---|---|---|
| 1 | 2740 | 2740 | ± 0 |
| 3 | 2900 | 3060 | ± 2.7 |
| 4 | 3430 | 3510 | ± 1.2 |
| 9 | 2210 | 2050 | ± 3.8 |
| 13 | 2910 | 2820 | ± 1.6 |

creases in plasma volume during exercise were, on the one hand, measured by the dye method, and on the other hand, calculated from changes in plasma protein concentration. In the present study, a similar comparison was made in 10 experiments. In 4 of the 5 based on studies made immediately after the convulsion there was satisfactory agreement between the two methods, *i.e.*, the plasma volumes calculated by the two methods agreed with each other within 4.8% of the mean of each pair of values; there was no consistent directional difference between the two (Table II). In one of these 5 experiments agreement was not as good, the two values differing from each other by 11.7% of their mean. In a comparison of data obtained 15 minutes after the convulsion in 5 experiments, good agreement was found between plasma volumes as measured by the dye method and those calculated from changes in plasma protein level (Table III). It is concluded, therefore, that the criticism of the dye method in exercise made by Ebert and Stead[5] is not substantiated by the present data in that whatever changes in optical properties of serum may occur are not significant in measurements of plasma volume by this method; possibly the longer duration of their exercise or the fact that our subjects were fasting may explain the differences found.

The finding in the present study of decreases in plasma volume in uncurarized subjects of 7.3 to 34.7%, averaging 14.9%, is smaller than expected on the basis of comparison with the data of Kaltreider and Meneely.[3] However, conditions in the experiments of these authors were so different from those of the present study as to invalidate direct comparisons. The rises in venous pressure, and presumably also in capillary pressure, were far greater in our experiments than in those of Kaltreider and Meneely;[3] the increases which occur in uncurarized subjects during electrically induced convulsions average 53 cm of water and in curarized subjects average 23 cm of water.[6] However, as Landis[7,8] pointed out, increased filtering pressure accounts for only a small part of the loss of fluid from the circulation during muscular exercise. Moreover, during electrically induced convulsions the rises in venous and capillary pressures which occur do not become increased effective filtering pressures everywhere, because of the simultaneous, approximately equal, rises in intrathoracic,[9] intra-abdominal[9] and cerebrospinal fluid pressures.[10] Accordingly, blood drawn after the end of a seizure, as in the present study, is a mixture of some blood exposed to high filtering pressures and some exposed to normal filtering pressures in the small vessels. Accordingly, little significance can be attached to the fact that the average decrease in plasma volume found here in uncurarized subjects, *i.e.*, 14.9%, is close to that found by Landis *et al.*[11] *i.e.*, 12.0%, when those authors artificially raised venous pressures in the arm to a level comparable to that reached in patients

[6] Altschule, M. D., and Tillotson, K. J., *Arch. Neurol. and Psychiat.*, in press.

[7] Landis, E. M., *Physiol. Rev.*, 1934, **14**, 404.

[8] Landis, E. M., *Ann. New York Acad. Sci.*, 1946, **46**, 713.

[9] Gordh, T., and Silfverskiold, B. P., *Act. Med. Scandinav.*, 1943, **113**, 183.

[10] Marsan, C. A., and Fuortes, M. G. F., *Riv. di Neurol.*, 1947, **17**, 1.

[11] Landis, E. M., Jonas, L., Angevine, M., and Erb, W., *J. Clin. Invest.*, 1932, **11**, 717.

experiencing induced seizures; the similarity of the findings does not constitute an argument for the importance of increases in filtering pressure in causing the changes in plasma volume observed in the present study.

The effects of other factors which operate during induced seizures are similarly impossible to evaluate. These factors include severe anoxia and hypercarbia,[12] muscular hyperemia with consequent increases in filtering surface due to vigorous muscular contractions[13] and increased transudation of fluid, of uncharacterized etiology, from the vessels of exercising limbs.[8] Likewise, it is impossible to establish significance of the osmotic effects of muscle cell metabolites, considered to result in the drawing of water from the small blood vessels during exercise.[7,8] Until the factors which regulate loss of water from the circulation during exercise can be defined precisely, it will not be possible to analyze the mechanisms responsible for the loss of circulating fluid which occurs during the course of electrically induced seizures. Nevertheless, the data of the present study show a parallelism between the violence of the convulsions induced and the decreases in plasma volume which occurred; the average decrease in men was 19.4%, in uncurarized women 10.5% and in curarized women 3.2%.

It is clear from the present study that the losses of fluid from the circulation, and their possible consequences, are not essential for obtaining a satisfactory clinical result in patients given electroshock therapy.

*Summary and conclusions.* Measurements of plasma volume were made 15 times in 13 subjects in whom convulsions were induced electrically for the treatment of mental disease. Decreases in plasma volume were appreciable and varied in amount with the severity of the seizures induced. The previous administration of curare moderated the convulsions and minimized decreases in plasma volume. It is concluded that the method of Gibson and Evans[1] for measuring plasma volume is valid under the conditions of the present study. It is also concluded that the transitory decreases in plasma volume which occur during electrically induced convulsions are a side reaction and are not essential for obtaining a satisfactory clinical result.

[12] Altschule, M. D., Sulzbach, W. M., and Tillotson, K. J., *Am. J. Psychiat.*, 1947, **103**, 680.

[13] Landis, E. M., *Am. J. Physiol.*, 1931, **98**, 704.

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## Urinary Penicillin Excretion in Women.

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The effectiveness of antacids in preventing penicillin destruction by gastric acidity has been measured by studies of the urinary recovery of orally administered penicillin.[1,2] In these investigations, male subjects had to be studied, since reproducible values were not obtainable with female test persons. This report is concerned with the determination of a possible relationship between renal clearance of penicillin and the menstrual cycle.

*Methods.* Three healthy, young, adult women volunteered for these studies. For each test 25,000 units of commercial sodium penicillin were dissolved in 200 cc of an aqueous solution or suspension of 2 g of buffer or antacid and were taken orally 2 hours after a light breakfast consisting of fruit juice, coffee, and a slice of toast. No food was taken in the following 2 hours. The antacids were the same as previously used:[1] sodium

[1] Golden, M. J., and Neumeier, F. M., *Science*, 1946, **104**, 102.

[2] Perlstein, D., Kluener, R. G., and Liebmann, A. J., *Science*, 1945, **102**, 66.