

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 contractions¹³ 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 uncured 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 Evans¹ 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.

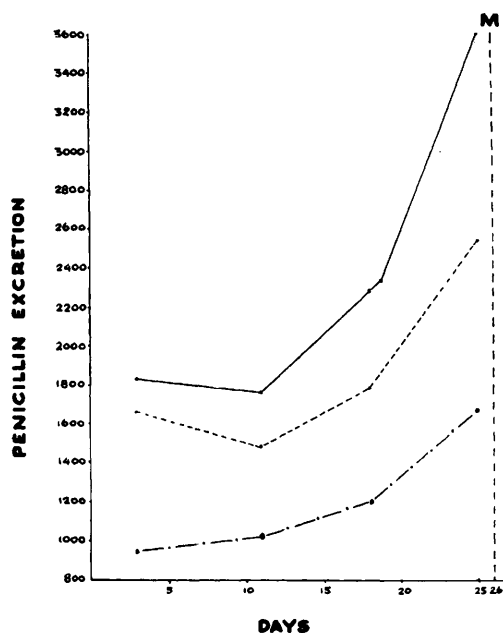


FIG. 1.

Urinary excretion of penicillin in Subject A at various intervals of the menstrual cycle. M signifies the onset of menstruation lasting three days.

— Sodium bicarbonate
 - - - Sodium citrate
 . . . Antacid mixture

bicarbonate U.S.P., sodium citrate U.S.P. and an antacid powder containing sodium bicarbonate, colloidal kaolin, magnesium trisilicate and bismuth subcarbonate. Physiological saline served as control. Urine was collected in sterile glass-stoppered bottles one-half hour after penicillin administration and thereafter at hourly intervals for 6 hours. The volumes of urine were determined, and the samples were assayed, using the FDA cylinder-plate method of January 1945 (*Staphylococcus aureus* FDA No. 209). A standard penicillin assay curve was prepared daily for comparison with the unknowns.

When the frequency and duration of the menstrual periods were established for each subject, identical doses of penicillin plus antacid were given with reasonable spacing from

4 to 6 times during the cycle, excluding actual menstruation. The test was then interrupted for at least one month to avoid any interference with subsequent doses and possible tolerance. A different antacid was then employed in the following month's tests.

Results. Fig 1 is a representative example of the 3 cases studied. It shows penicillin (expressed in Oxford units) recovered from the urine in 6 hours with different buffers at various intervals of the menstrual cycle, plotted against the number of days elapsed since the last day of menstruation. The first one-half hour sample includes the urine already present in the bladder prior to the test. Each point of the graph represents the average of at least 2 determinations.

It is apparent from the data that the recovery of penicillin in the urine is increased just before menstruation. Oral administration of penicillin-saline solutions resulted in small penicillin recovery in the urine, confirming the statement that unbuffered penicillin is absorbed in the intestinal tract to a slight extent.³

Discussion. The increase in urinary penicillin excretion preceding menstruation may be attributed either to an increased absorption or decreased destruction of penicillin from the gastrointestinal tract, or to an increased secretion. The actual mechanism will be investigated further. The data here presented may aid in explaining the discrepant reports on the urinary penicillin recovery in women after the oral administration of buffered penicillin, carried out without regard to the menstrual cycle.^{1,2}

Summary. A marked increase in urinary excretion of orally ingested penicillin has been observed in women immediately preceding menstruation. The physiological mechanism of this phenomenon is under investigation.

³ Rammelkamp, C., and Keefer, C. J., *J. Clin. Invest.*, 1943, **22**, 425.