

influence. The fact that such a tissue disturbance does exist is shown by the observation that a reduction in the reserve alkali of the blood invariably occurs in the dog during the course of a uranium intoxication.⁶ With this order of reasoning, the suggestion is made that the intravenous use of an alkaline solution: carbonate, bicarbonate or

citrate, exerts its tissue protection not by the neutralization of hydrogen ions in the sense that they are as such responsible for the tissue damage, but by maintaining through such a binding or neutralizing effect an intracellular chemical environment of such an order of balance (acid-base) that various enzymatic systems can operate in an effective manner as life processes.

⁶ MacNider Wm. deB., *J. Exp. Med.*, 1917, **26**, 1.

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Effect of Parabiosis on Experimental Uremia.*

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The purpose of these experiments was to study the efficiency of peritoneal anastomosis in parabiotic rats, one member of the pair being uremic.

Putnam¹ demonstrated in cats that fluids in the peritoneal cavity came into almost complete osmotic equilibrium with the blood plasma. Ganter² first studied peritoneal lavage as a therapeutic measure, noting that the introduction of salt solution into the peritoneal cavity of dogs with bilateral ureteral ligation improved the resulting uremic symptoms. It has been demonstrated that peritoneal lavage can reduce the values of nonprotein nitrogenous constituents of the blood³⁻⁶ and prolong the lives of uremic

dogs^{7,8} and patients.^{9,10} Frank, Seligman and Fine¹¹ eliminated uremia in a patient with acute renal failure by peritoneal irrigation.

A number of investigators¹²⁻¹⁵ have studied renal function by the method of parabiosis. Herrmansdorfer¹² joined pairs of rats in parabiosis with coelioanastomosis and later removed the kidneys of one of the parabionts; he was able to remove 3 kidneys from the 2 rats and maintain life without a rise in non-protein nitrogen, or other constituents of the blood. All of these investigators produced

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¹ Putnam, T. J., *Am. J. Physiol.*, 1923, **63**, 548.

² Ganter, G., *München. med. Wchnschr.*, 1923, **70**, 1478.

³ Landsburg, M., and Groinski, H., *C. R. Soc. de biol.*, 1925, **93**, 787.

⁴ Rosenak, S., and Siwon, P., *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1926, **39**, 391.

⁵ Heusser, II., and Werder, H., *Bruns' Beitr. z. klin. Chir.*, 1927, **141**, 38.

⁶ Curtis, G. M., and Pacheca, G. A., *PROC. SOC. EXP. BIOL. AND MED.*, 1928, **26**, 874.

⁷ Bliss, S., Kastler, A. D., and Nadler, S. B., *PROC. SOC. EXP. BIOL. AND MED.*, 1932, **29**, 1078.

⁸ Jeney, A. von, *Z. f. klin. Med.*, 1932, **122**, 294.

⁹ Balaza, J., and Rosenak, S., *Wien. klin. Wchnschr.*, 1934, **47**, 851.

¹⁰ Wear, J. W., Sisk, I. R., and Trinkle, A. J., *J. Urol.*, 1938, **39**, 53.

¹¹ Frank, H. A., Seligman, A. M., and Fine, J., *J. A. M. A.*, 1946, **130**, 703.

¹² Herrmansdorfer, A., *Deutsche Z. f. Chir.*, 1923, **178**, 289.

¹³ Jeffers, W. A., Lindauer, M. A., Twaddle, P. H., and Wolferth, C. C., *Am. J. M. Sc.*, 1940, **199**, 815.

¹⁴ Grollman, A., and Rule, C., *Am. J. Physiol.*, 1943, **138**, 587.

¹⁵ Dannheisser, F., *Deutsche Z. f. Chir.*, 1931, **232**, 688.

the uremic state at a sufficiently long time after parabiosis for a common circulation to exist, while in the present experiments parabiotic union and uremia were established simultaneously. That an actual anastomosis of the 2 circulations eventually develops has been repeatedly shown by the passage of india ink, bacteria, avian blood cells, and dyes.^{14,16-18} Studies made before the development of vascular communications are few; Spagnol¹⁹ showed that colloidal dyes injected into one member of the pair did not cross to the mate during the first few days after anastomosis.

Experimental. Uremia was produced by bilateral nephrectomy in 8 adult albino rats and these rats died within 72 hours after operation. They became apathetic and later comatose; occasionally there was tetany. Fluid retention with massive edema and pleural fluid occurred. The nonprotein nitrogen of whole blood rose rapidly from the normal of 25 to 45 mg % to about 150 mg % in 24 hours, (Fig. 2) and to about 350 mg % before death.

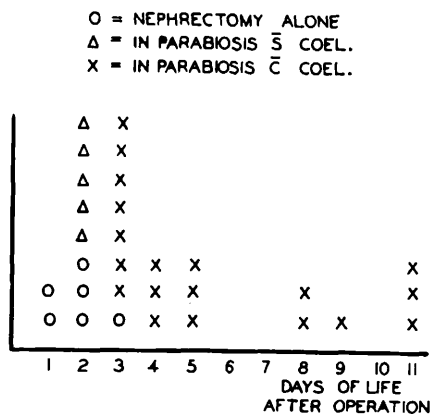


Fig. 1.

The duration of life in nephrectomized rats: after nephrectomy alone, O; nephrectomy in a rat in parabiosis without peritoneal anastomosis, Δ; nephrectomy in one partner in parabiosis with coelio-anastomosis, X.

¹⁶ Hill, R. T., *Proc. Soc. Exp. Biol. and Med.*, 1931, **28**, 592.

¹⁷ Hill, R. T., *J. Exp. Zool.*, 1932, **63**, 203.

¹⁸ Hill, R. T., *Proc. Soc. Exp. Biol. and Med.*, 1932, **20**, 922.

¹⁹ Spagnol, G., *Arch. di fisiol.*, 1930, **28**, 157.

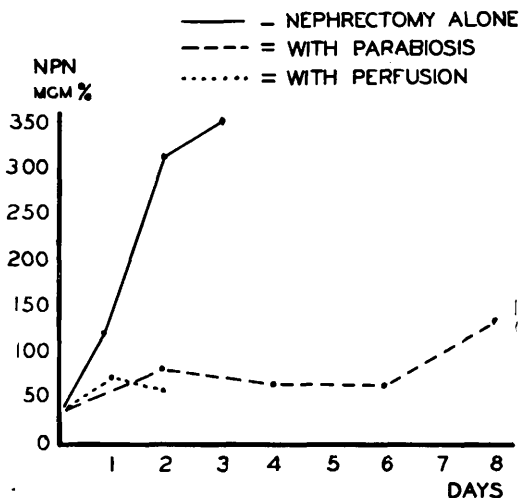


Fig. 2.

Nonprotein nitrogen of whole blood in nephrectomized rats.

The effect of parabiosis of such a nephrectomized rat with a normal rat was tried. A procedure similar to the original method of Sauerbruch and Heyde²⁰ was employed in which the skin of the animals was joined from neck to hip, the scapulæ were sutured together, and a large anastomosis produced between the 2 peritoneal cavities. The type of circulation obtained between the 2 animals was studied. Normal rats, injected intravenously with Evans' blue dye (T-1824) 3 cc of 1% solution, remain blue in color for many months. This amount of Evans' blue was injected intravenously in one rat, and during the first 4 days after parabiosis no transfer to the partner was observed as shown by the unchanged color of the animals and by colorimetric studies on the serum. After 4 days blue coloration was observed to extend into the skin of the uninjected rat for about 1 cm beyond the suture line. On the 6th to the 7th day the dye spread over the entire partner, and studies of the blood serum showed a nearly equal concentration of dye in the serum of both animals. It was therefore concluded that during the first 4 or 5 days the only form of communication was the common peritoneal cavity and the tissue spaces at the anastomosis.

²⁰ Sauerbruch, F., and Heyde, M., *München. med. Wehnschr.*, 1908, **55**, 153.

Bilateral nephrectomy was performed on one of the rats of 22 pairs at the time of parabiosis. The pairs then lived for 3 to 11 days before the nephrectomized rat died. To insure that the coelio-anastomosis was of importance in maintaining life, parabiosis of a nephrectomized rat with a normal mate was done in 6 pairs without communication of the body cavities. All of these pairs died in 3 days or less, as did the single nephrectomized rats (Fig. 1).

Nonprotein nitrogen studies of whole blood showed that coelio-anastomosis was usually effective in maintaining low values, although shortly before death values of 100 to 200 mg % were sometimes reached. The nonprotein nitrogen of the nephrectomized rat usually remained between 75 and 100 mg % (Fig. 2) while that of the normal partner rose to 50 to 75 mg %.

The ability of the partner to excrete phenol red (PSP) injected into the nephrectomized rat was determined. Although there was negligible excretion in the urine when the rats were in parabiosis without coelio-

anastomosis, good values were obtained with peritoneal anastomosis. After 5 mg of PSP were injected intramuscularly 0.1 to 0.2 mg was excreted by the partner in the first 6 hours. The values tended to increase when repeated after 5 days, probably due to the development of an anastomosis of the circulations.

In 15 experiments the peritoneal cavity of a single nephrectomized rat was continuously irrigated with Tyrode's solution. Although the life of the nephrectomized rat was not lengthened over that of the nephrectomized control the nonprotein nitrogen remained at values between 75 and 100 mg %. Absorption of fluid took place and death apparently was due to increased pleural fluid, and pulmonary edema.

Conclusion. These experiments demonstrated the efficiency of the peritoneal membrane as a mode of excretion in renal insufficiency. The effectiveness of the natural dialyzer provided by coelio-anastomosis suggests the feasibility of developing an artificial dialyzing mechanism.

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"Dietary Factor" in Necrotizing Arteritis in Dogs a Lipid Substance.*

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During the past several years arterial lesions affecting principally the large elastic arteries (aorta, pulmonary artery, endocardium of the left auricle, and coronary arteries) have been produced with regularity by controlling 2 factors, diet and renal insufficiency.¹ The arterial lesions have been described and illustrated in previous publications, and the evidence for a dietary

factor has been reviewed in a recent publication.¹

In this paper is presented a summary of the data obtained from systematically testing the ingredients of the "standard diet" which was being fed at the time these unanticipated lesions were first encountered.

Method. The methods have been detailed in a previous publication.¹ Briefly, these consist of feeding a specified diet for a specified period of time (usually 8 weeks or longer), then damaging the kidneys (usually with heavy metal injury), and examining the arterial system both grossly and histologically when the animals die or are sac-

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¹ Holman, R. L., *Am. J. Path.*, 1941, **17**, 359; *Am. J. Path.*, 1943, **19**, 977.