

Asbestos Pad Filtration. Experiments 7 and 8 show that the fever-producing principle in both typhoid broth and the Berkefeld filtrate of typhoid vaccine, is removed by filtration through a Seitz serum No. 3 filter. It may also be mentioned that recent experiments in our laboratory show that another asbestos filter pad, the Ertel No. 0, is equally as efficient in the removal of pyrogen as Seitz. In this respect, too, it reacts similarly to the "pyrogen" in infusion-fluids and inulin.⁸

Conclusions. 1. The fever-producing principle in typhoid vaccine and in broth in which *B. typhosus* has grown for 48 hours is not removed by Berkefeld filtration. The principle is, therefore, not bound to the bacterial bodies.

2. The principle is removed by a 200-second Zsigmondy filter and is, therefore, of approximately the same size as the principle previously found in reactive inulin and infusion-fluids.

3. Like "pyrogen" found in inulin and in infusion-fluids, it is removed by filtration through asbestos pads of the types of Seitz and Ertel.

4. On the basis of the clinical response provoked by intravenous injection, and the filtration characteristics, it is submitted that the fever-producing principle associated with *B. typhosus* and the "pyrogen" found in infusion-fluids and inulin are closely related substances.

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Effect of Electrolyte Disturbance on Resistance to Histamine Poisoning in Rats.

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Following suprarenalecotomy there is a profound disturbance in electrolyte metabolism,^{1, 2, 3} It is possible to reproduce an analogous disturbance in normal animals by introducing large amounts of isotonic glucose intraperitoneally and subsequently withdrawing the fluid.⁴ The effect of this procedure on resistance to histamine was determined.

Method: Twenty cc of isotonic glucose solution was introduced into the peritoneal cavity of each of a number of rats and 4 hours

¹ Marine, D., and Baumann, E. J., *Am. J. Physiol.*, 1927, **81**, 86.

² Loeb, R. F., Atschley, D. W., Benedict, E. M., and Leland, J., *J. Exp. Med.*, 1933, **57**, 775.

³ Zwemer, R. L., and Truszkowski, R., *Science*, 1936, **83**, 558.

⁴ Gilman, A., *Am. J. Physiol.*, 1934, **108**, 662.

TABLE I.
Electrolyte Disturbance Induced in Normal Wistar Rats, by Intraperitoneal Injections of Isotonic Glucose.

| | I. Blood* | | II. Peritoneal Fluid |
|------------------------------|--|---------------------------------|---|
| | (Analysis before injection of glucose mg/100 cc) | 4 hr after injection of glucose | (Analysis 4 hr after injection of 5.4% glucose) |
| Glucose (blood) | 114 | 214 | 1.4% |
| Cl (serum) | 342 | 321 | 292 mg/100 cc |
| Na (serum) | 338 | 265 | 240 " " |
| K (serum) | 22 | 55 | 18 " " |
| Non-protein nitrogen (blood) | 34 | 58 | 32 " " |
| Total protein (serum) | 6.1% | 8% | 0.15% |

*A marked hemoconcentration was observed, the red cell count rising within 4 hr from 9 to 12 or 13 million per mm³.

later the same quantities of fluid were withdrawn. Analyses of the constituents of the blood of such animals with intact suprarenals revealed a fall in the concentration of sodium and of chloride in serum, with a hemoconcentration, a rise in non-protein nitrogen, in total proteins and in the concentration of potassium. The decrease in concentration of serum sodium chloride apparently was due to diffusion of this substance into the peritoneal fluid (Table I). Immediately after withdrawal of the fluid the animals were injected with varying amounts of histamine.

Results: The minimal lethal dose of histamine for rats with intact suprarenals but in which an electrolyte disturbance was induced was 600 to 700 mg per kilo of body weight. Litter mates in which no electrolyte disturbance was induced survived from 1100 to 1200 mg histamine per kilo of body weight. (Table II.)

TABLE II.
Effect of Electrolyte Disturbance on Resistance to Histamine Poisoning in Rats.

| No. rats | Histamine in mg per kg | Survived | Died |
|---|------------------------|----------|------|
| Rats given 20 cc of glucose intraperitoneally. Fluid withdrawn after 4 hours. | | | |
| 2 | 600 | 2 | 0 |
| 9 | 700 | 1 | 8 |
| 5 | 800 | 0 | 5 |
| 8 | 1000 | 0 | 8 |
| Controls* | | | |
| 4 | 1000 | 4 | 0 |
| 2 | 1100 | 0 | 2 |
| 5 | 1200 | 1 | 4 |
| 2 | 1300 | 0 | 2 |
| 2 | 1400 | 0 | 2 |
| 2 | 1600 | 0 | 2 |

*These controls represent only sample experiments from a large experience with the range of tolerance of rats of our stock to histamine.

It would appear that in part the disturbance in resistance following suprarenalectomy may be due to the disturbance in electrolytes resulting from withdrawal of the cortical hormone. However, this is only one factor, for administration of salt to suprarenalectomized rats will raise the resistance slightly but not to a degree comparable to that obtained with injections of suprarenal cortical hormone. Furthermore, suprarenalectomized rats are killed by an amount of histamine (100 to 200 mg per kilo of body weight) approximately one-sixth to one-tenth the M.L.D. for normal rats.

It is of interest to compare these results with the abnormalities which develop in humans suffering from similar electrolyte disturbances, as occurs in Addison's disease, and in heat cramps.⁵

Summary. The production in normal rats of an electrolyte disturbance analogous to that observed after suprarenalectomy is followed by a marked drop in resistance to histamine.

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Adult Phosphatase Levels in Prepubertal Rhesus Prostate Tissue after Testosterone Propionate.

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An "acid" phosphatase with optimum activity at about pH 5 is present in adult human prostate gland and seminal fluid¹ in concentrations greater (500-2,000 units/g fresh prostate tissue, in our series^{2, 3}) than the phosphatase activity of any other human tissue. *Prepubertal* prostate gland, on the other hand, contains less than 5 units of "acid" phosphatase activity per g fresh tissue.^{3, 4} An intermediate value of 73 units was found in the prostate gland of a 13-year-old boy.³

This correlation in man between sexual maturity and the "acid" phosphatase activity of prostate tissue suggested the possibility that stimulation of the prepubertal prostate gland by injection of testo-

⁵ Dill, D. B., *Life, Heat, and Altitude*, Harvard Press, 1938.

¹ Kutscher, W., and Wolbergs, H., *Z. f. physiol. Chem.*, 1935, **236**, 237.

² Gutman, E. B., Sproul, E. E., and Gutman, A. B., *Am. J. Cancer*, 1936, **28**, 485.

³ Gutman, A. B., and Gutman, E. B., *PROC. SOC. EXP. BIOL. AND MED.*, 1938, **39**, 529.

⁴ Moore, R. A., and Hanzel, R. F., *Arch. Path.*, 1936, **22**, 41.