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Effect of Reticulo-Endothelial Blockade on Blood Chemistry.

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The rôle of the reticulo-endothelial system in immunity, antibody formation and anaphylaxis has been the subject of many investigations. Apart from its place in blood pigment and cholesterol metabolism, however, there have been relatively few and somewhat contradictory reports on the metabolic function of this group of cells. A hypocholesterolemia was observed by Leites¹ and by Goebel and Gnoinski.² Gnoinski³ found a hyperglycemia, Demont⁴ observed a hypoglycemia. Sterken and Kerner-Pashenyan⁵ saw no change in the blood sugar level following colloidal injections. DuBois⁶ observed a drop in albumin and total nitrogen but no constant change in the non-protein nitrogen and we⁷ have previously shown a rise in the blood uric acid level following reticulo-endothelial blockade.

This diversity depends upon a variety of factors, the species of animal used, the amount and character of material injected, and the length of time allowed to elapse following injections. The most important factor, however, in the interpretation of results is whether the reticulo-endothelial cells are stimulated or depressed by the injections. Whether they can be completely blocked is still open to question. Jaffe⁸ believes that a temporary functional depression is possible, and is most marked during intracellular segregation of the electro-negative colloid. Small amounts of colloidal material are supposed to stimulate and large amounts to depress but it is not clearly known what may be considered a small or a large amount.

We have conducted many experiments on rabbits and dogs using India ink and sacharrated iron oxide as blocking agents and believe the former to give better results. Here we report experiments with India ink into dogs.

An 8% suspension of India ink and normal saline was continu-

¹ Leites, *Biochem. Z.*, 1927, **186**, 391.

² Goebel and Gnoinski, *Compt. Rend. Soc. de Biol.*, 1927, **96**, 1483.

³ Gnoinski, *Compt. Rend. Soc. de Biol.*, 1928, **98**, 72.

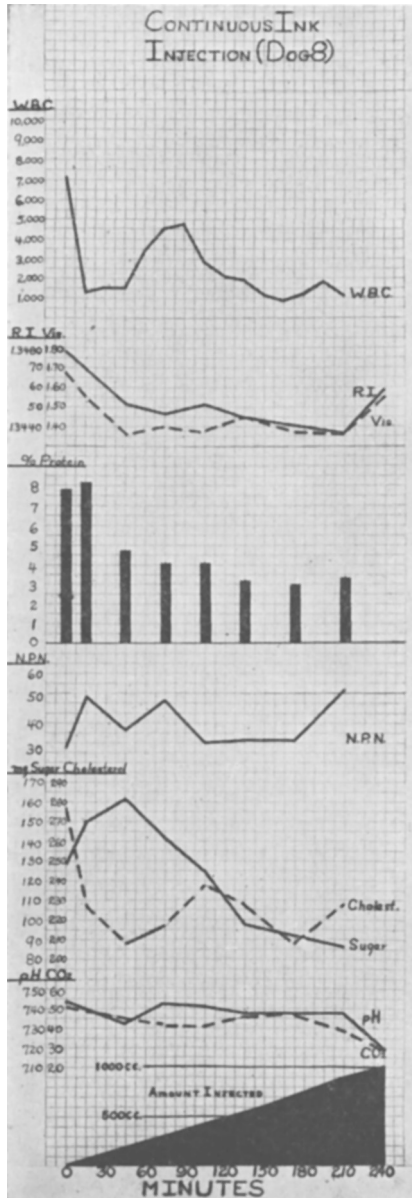
⁴ Demont, *Compt. Rend. Soc. de Biol.*, 1926, **95**, 916.

⁵ Sterken and Kerner-Pashenyan, *Zhur. Exptl. Biol. Med.*, 1929, **10**, 431.

⁶ DuBois, *Compt. Rend. Soc. de Biol.*, 1931, **108**, 637.

⁷ Klein and Levinson, *Proc. Soc. Exp. Biol. and Med.*, 1932, **29**, 885.

⁸ Jaffe, *Physiol. Rev.*, 1931, **11**, 277.



ously injected into the femoral vein of a dog. White blood counts were made and blood drawn before the injection and at various intervals during the injection. The total non-protein nitrogen, cholesterol and sugar, the plasma pH, CO₂, and total proteins and

the refractive index and viscosity of the serum were determined. All of the animals showed similar results as Dog 8.

The immediate response to injection is a sharp drop in the white blood count and cholesterol and a rise in the sugar. The pH, CO₂, and refractive index and viscosity fall more slowly. There is a noticeable peripheral vaso-constriction and increased splanchnic activity due, no doubt, to the reticulo-endothelial stimulation. In 45 minutes, however, we see a definite attempt at re-establishment of equilibrium. The white blood count tends to return to normal, the drop in refractive index, viscosity, protein and cholesterol is arrested. The pH returns to its previous level. The blood sugar which had increased now begins to fall. This is due, in all probability, to the exhaustion of the available supply of glycogen. This period, we believe, is one of attempted re-establishment of equilibrium as the organism brings all of its histiocytic elements into play.

The continuous injection, however, overcomes the attempts of the organism to cope with the constant stimulation and fatigue and functional paralysis with ultimate death follows. This is reflected in the secondary fall in the white blood count, final rise in non-protein nitrogen and the terminal acidosis. These results are strikingly similar to those obtained by Petersen and his associates⁹ during the continuous intravenous injection into dogs of a suspension of *B. coli* and leads us to believe that such changes can be due to the effect on the reticulo-endothelial system alone. It must not be forgotten, however, that India ink contains a protein which we have been able to detect by the biuret test and which may play a rôle.

Summary. The continuous intravenous injection of India ink into dogs over a certain period of time results in a series of changes in the blood and tissues characterized by 3 stages of reaction: (1) an initial period of reticulo-endothelial stimulation and increased splanchnic activity. (2) an attempted re-establishment of equilibrium. (3) reticulo-endothelial exhaustion, the premortal phase.

⁹ Petersen, Mueller and Boikan, *J. Inf. Dis.*, 1927, **41**, 405.