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Observations on Occurrence of Lipemia in Rats with Nephrotoxic Nephritis.

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In previous studies[1,2] on the chemical disturbances occurring in rats with nephritis induced by the injection of nephrotoxic sera, we noted that a gross lipemia was frequent during the first 2 weeks of the disease while the animal exhibited edema, hypoproteinemia, and albuminuria. In the course of other studies some additional observations were made on nephrotoxic rats to determine the uniformity and severity of lipemia in this experimental disease. These are reported here.

Experimental Procedure. Rats with severe acute nephrotoxic nephritis which had been employed as controls in immunological studies, or for titration of nephrotoxic sera,[3] were sacrificed by cardiac puncture 4 to 18 days after receiving the last of a series of several daily injections of anti-rat-kidney serum. The oxalated blood from these animals was centrifuged and the plasma analyzed for lipids by the method of Kirk, Page, and Van Slyke.[4] Whole blood urea nitrogen was determined by a modification of the gasometric hypobromite method of Van Slyke and Kugel.[5]

Results. Blood from each of the rats in the edematous phase of acute nephritis appeared lipemic on inspection and on chemical analysis, the total lipid carbon concentration ranged from 916 mg % to 8660 mg % (see Table 1). Total cholesterol, ranging from 208 mg % to 871 mg %, was regularly elevated in roughly the same proportion as the total lipid carbon. The total lipid phosphorus determined on some of the bloods exhibited a wide range of values. There was no apparent correlation between the total lipid carbon and the degree of renal failure as measured by increase of blood urea nitrogen. Gross lipemia bore some relationship to the intensity of the acute nephritis, however, for it was not observed in non-edematous rats with presumably less severe renal involvement. Total plasma lipid carbon in two normal rats of the same strain averaged 559 mg %. Hansen and Brown[6] using a similar extraction procedure but determining total fatty acids and cholesterol by Bloor's methods found that in their normal rats the total lipid carbon averaged about 300 mg % and the cholesterol about 90 mg %. These values are somewhat below the 2 normal rats we observed and serve to emphasize further the magnitude of the lipemia observed in nephrotoxic nephritis.

Comment. The elevation of plasma lipids in all edematous rats with severe acute nephritis induced by anti-kidney serum indicated that hyperlipemia is a regular feature of an early stage of this experimental disease. Gross lipemia disappeared in the second or third week along with anasarca when the rat survived, but plasma protein values did not rise to a normal range until the fourth or fifth week;[2] furthermore, in our experience terminal chronic nephritis, often characterized by plasma protein levels as low as those encountered in the acute phase, has not been associated with gross lipemia. These findings suggest that the lipemia in nephrotoxic nephritis may be related to some acute tissue injury, either renal

1 Smadel, J. E., and Farr, L. E., *J. Exp. Med.*, 1937, **65**, 507.

2 Farr, L. E., and Smadel, J. E., *J. Exp. Med.*, 1939, **70**, 615.

3 Swift, H. F., and Smadel, J. E., *J. Exp. Med.*, 1937, **65**, 557.

4 Kirk, E., Page, I. H., and Van Slyke, D. D., *J. Biol. Chem.*, 1934, **106**, 203.

5 Van Slyke, D. D., and Kugel, V. H., *J. Biol. Chem.*, 1933, **102**, 489.

6 Hansen, A. E., and Brown, W. R., *J. Nutrition*, 1937, **13**, 351.

TABLE I.
Plasma Lipid Concentration in Nephrotoxic Rats.

Rat No.	Day of disease	Total lipid carbon, mg per 100 cc	Total cholesterol, mg per 100 cc	Total lipid phosphorous, mg per 100 cc	Blood urea nitrogen, mg per 100 cc
1	18	2410	253	23.0	13
2	6	1988	387	5.3	11
3	9	2768	473	29.8	34
4	7	1118	208	5.0	34
5	6	1552	218	—	73
6	7	2385	248	—	25
7	12	6413	856	—	40
8	11	8660	713	—	41
9	7	2384	871	—	64
10	5	4325	779	—	46
11	4	916	223	—	—
12	4	1155	378	—	—

or otherwise, and that it is unlikely to be a compensatory osmotic mechanism for the lowered oncotic pressure due to hypoproteinemia.

Summary. Significant hyperlipemia was regularly encountered in rats with severe acute nephritis induced by anti-kidney serum.

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Significance of Salmonella in Ulcerative Cecitis of Rats.*

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Chronic ulcerative cecitis of rats is an ideal disease for chemotherapeutic and prophylactic tests. Unlike most acute experimental infections of small laboratory animals cecitis progresses gradually over a period of months and affords an opportunity to study the effect of drugs on a chronic low grade infection. It seems important therefore to determine definitely the nature of the agent which causes this disorder. Buchbinder and his associates[1] concluded that cecitis of rats was an enzoötic form of paratyphoid infection. Their view was based on the isolation of *S. enteritidis* from the stools and from the spleen as well as on the presence of agglutinins. They give no details of the cultural reactions of their strains of salmonella, of the agglutinin titers, or of the exact relation of salmonella to the lesions. Nor is it clear whether they dealt with a single specific strain.

While these observations are striking they do not actually prove that salmonella is the primary etiological agent of rat cecitis. Stewart and Jones[2] pointed out, for example, that paratyphoid infection or infestation of both laboratory and wild rats is common and that various strains are encountered. Furthermore, Buchbinder and his group report no observations on the experimental production of cecitis with strains of salmonella, and finally the exquisitely chronic and localized lesions so well described and pictured by Stewart and Jones bear no clinical resemblance to any known paratyphoid infection.

* Supported by a grant from the Rockefeller Fluid Research Fund.

1 Buchbinder, L., Hall, L., Wilens, S. L., and Slanetz, C. A., *Am. J. Hyg.*, 1935, **22**, 199.

2 Stewart, H. L., and Jones, B. F., *Arch. Path.*, 1941, **31**, 37.