TABLE I.
Agglutinability of Normal and Receptor-Free Erythrocytes Before and After Saponin Lysis.

	Virus dilutions							
	10	100	200	400	800	1600	3200	Saline
Normal, lysed	++*	++	++	++	++	+R	RR	PP
Receptor-free, lysed	PP	PP	PP	PP	PP	PP	PP	PP
Normal, not lysed	++	++	++	++	++	++	PR	PP
Receptor-free, not lysed	PP	PP	PP	PP	PP	PP	PP	PP

* Duplicate tubes.
\+ Complete agglutination.
R—Ring, partial agglutination.
P—Pellet, no agglutination.

agglutinability of saponin-lysed cells by the virus is, in all probability, due to unaltered surface receptors and not to any substance associated with the nucleus. This interpretation is valid, however, only if it can be assumed that virus particles do not penetrate to the interior of the erythrocytes during treatment with the virus. That such a process could occur seems unlikely in view of present knowledge concerning the interaction between red cell and virus.

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The Tinctoral Demonstration of a Glycoprotein in Whipple's Disease. (17388)

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The etiology and pathogenesis of Whipple's Disease (lipodystrophy intestinalis), a clinical syndrome similar to sprue, has been a subject of speculation since its original description.[1] As its synonym implies, it is believed by most observers to represent an obscure disturbance of fat metabolism.

Black-Schaffer, Hendrix and Handler[2] reported a study of 4 cases which led them to the following conclusion: The disease, in contrast to sprue, may be readily recognized, anatomically, by non-lipid macrophagocytosis in the lamina propria of the small intestine and occasionally the proximal colon, lipogranulomatosis of the mesenteric lymph nodes, absence of significant evidence of chylous obstruction; and clinically, poor fat, glucose and probably protein absorption and the absence of macrocytic anemia.

The characteristic intestinal lesion is a crowding of the lamina propria by macrophages containing an isotopic refractile substance which Whipple found unstainable with osmic acid. This observation has been repeatedly overlooked in the literature, almost all authors assuming a lipid nature for this curious substance. The study of Black-Schaffer, Hendrix and Handler confirmed Whipple's observation. In 3 cases* the phagocytosed material did not stain with Sudan IV, and 2† were likewise negative with Nile blue sulphate as well as osmic acid. Chemical analysis of the intestinal mucosa of two cases revealed no increase, over normal controls, of the lipid content.

The characteristic enlarged, cystic, fat-filled mesenteric lymph nodes (lipogranulomatosis) are so prominent that they have dominated the

[1] Whipple, G. H., *Johns Hopkins Hosp. Bull.*, 1907, **18**, 382.

[2] Black-Schaffer, B., Hendrix, J. P., Handler, P., *Am. J. Path.*, 1948, **24**, 677.

* No suitable material was available from one case.

† No suitable material was available from 2 cases.

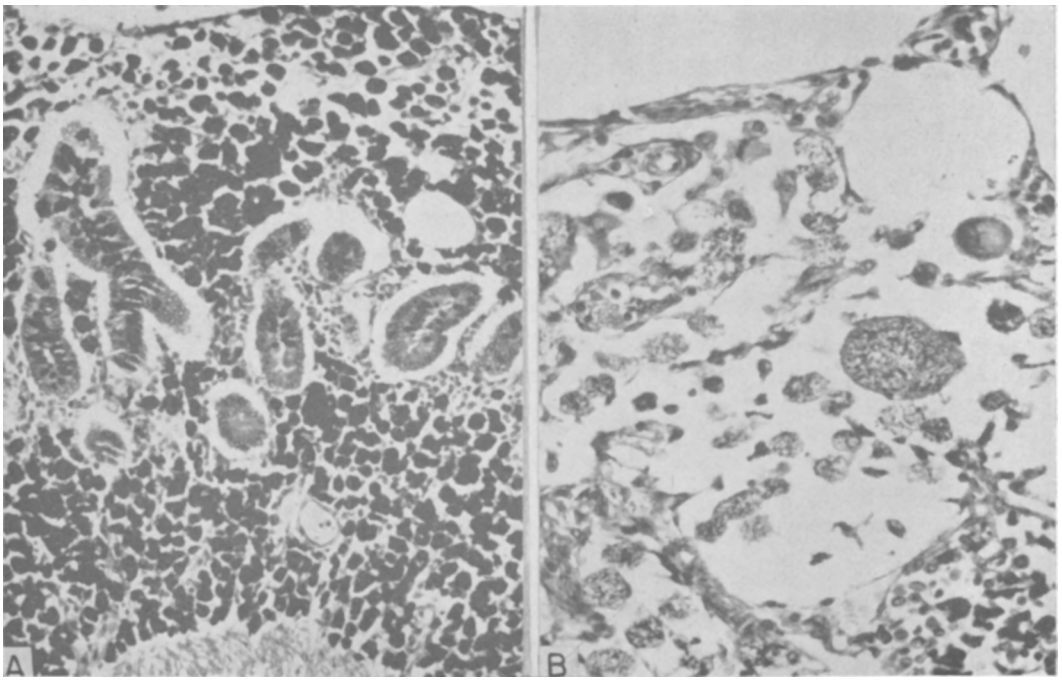

FIG. 1.

A. The mucosa of the small intestine in Whipple's disease occupied by macrophages filled with glycoprotein, stained by MacManus' modification of Schiff's periodic acid stain. The mucin of the "goblet cells" in the glands shows identical tinctoral properties.

B. Macrophages and giant cells in a mesenteric lymph node of Whipple's disease, revealing the presence of glycoprotein granules (in the photograph black) and lipid (colorless vacuoles). In the lower right corner are macrophages replete with glycoprotein and identical to those pictured in A.

approach to the problem.

Careful examination of the nodes revealed,[2] adjacent to sudanophilic macrophages, others containing sudanophobic substance similar in all respects to that described in the intestine. As a consequence of the pathologic anatomy, the histochemistry and the chemical analyses, a pathogenesis of the lesions was proposed.[2]

The present report is occasioned by the identification of the unknown phagotaxic substance as a glycoprotein. When sections of the intestines of 4 cases were treated with Schiff's periodic acid stain[3,4] the phagocytosed material in the mucosa stained deep scarlet (Fig. 1).

The lymph nodes of 3‡ of the cases confirmed the studies[2] of the fat-stained tissues. Many macrophages, in fact, surprisingly many, color a brilliant scarlet. Most of the giant cells surrounding the large masses of fat contain the same red substance (Fig. 2). Frozen sections treated with periodic acid and Sudan IV demonstrate lipid and polysaccharide side by side within the same macrophages. There is, however, no coalescing of the glycoprotein material to form amorphous masses as does the fat.

The periodic acid stain depends upon the oxidation of a 1-2 glycol bond in a polysaccharide forming polyaldehydes which thereupon take up the fuchsin of Fuelgin's reagent.

The polysaccharide containing material is insoluble in water, being present in apparently undiminished amounts after as long as 13 years in aqueous Kaiserling solution. Best's carmine stain[5] for glycogen is uniformly nega-

[3] McManus, J. F. A., *Stain Technology*, 1948, **23**, 99.

[4] Hotchkiss, R. D., *Arch. Biochem.*, 1948, **16**, 131.

‡ Material is unavailable from one case.

tive. On the other hand the mucicarmine stain[5] for mucus lends a faint tint to the phagocytosed substance. This, plus its insolubility in water—properties akin to those of the glycoprotein mucin which also stains scarlet to red with periodic acid—indicates that the polysaccharide is bound to a protein, thus constituting a glycoprotein.

The diminished fat, glucose, and possibly protein absorption by the small intestine in Whipple's disease indicates that its etiology resides in a disturbance of function of the intestinal epithelium. It is probably this defect which permits absorption of the unusual glycoprotein which may or may not be related to the mucin discharged into the enteric lumen by the intestine itself. At any rate, the presence of this readily demonstrated glycoprotein in the intestinal mucosa and mesenteric lymph nodes, indicates that Whipple's disease is more than an obscure defect in fat metabolism and is certainly not the result, as is commonly suggested, of a block of the mesenteric lymphatics. Thus the name lipodystrophy intestinalis, first proposed by Whipple and currently in use, would seem to be inappropriate. It would appear desirable to return to the eponym "Whipple's disease" until a name denoting the nature, rather than a complication, of the disease is forthcoming.

[5] Mallory, F. B., Pathological Technic, W. B. Saunders Co., Philadelphia, 1938.

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Inhibitory Effect of Cow's Milk on Influenza Virus Hemagglutination.* (17389)

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The development of theories on the mechanism of infection by influenza viruses has received considerable encouragement in the past few years from studies of the interaction between these viruses and inhibitors of virus hemagglutination found in various mammalian and avian fluids.[1-7] For some lines of inquiry it is desirable to compare the properties of several fluids, as well as those of the inhibitors isolated from them. It is of interest, therefore, that cow's milk, a fluid readily available in considerable quantity, exerts an inhibitory effect on virus hemagglutination. Some aspects of this inhibition phenomenon are described in the present report.

Materials and methods. Fresh raw milk was obtained from individual cows or as a pool from a commercial distributor and was skimmed by centrifugation in the cold room in the laboratory. The cream, which carried an insignificant part of the total inhibitory activity, was lifted off with a spatula and discarded. If necessary, the milk was recentrifuged to remove residual cream or sediment. Raw skim milk (RSM), less than one day old, was used for most of the experiments; if intended for use after one day, the milk was preserved with 1:5,000 Merthiolate (Lilly), which was found not to affect the inhibitory activity.

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[1] Burnet, F. M., *Lancet*, 1948, **254**, 7.

[2] Hirst, G. K., *J. Exp. Med.*, 1948, **87**, 301, 315.

[3] Lanni, F., and Beard, J. W., PROC. SOC. EXP. BIOL. AND MED., 1948, **68**, 442.

[4] Anderson, S. G., Burnet, F. M., Fazekas de St. Groth, S., McCrea, J. F., and Stone, J. D., *Austr. J. Exp. Biol. and Med. Sci.*, 1948, **26**, 403.

[5] Svedmyr, A., *Brit. J. Exp. Path.*, 1948, **29**, 295, 309.

[6] Hardy, P. H., Jr., and Horsfall, F. L., Jr., *J. Exp. Med.*, 1948, **88**, 463.

[7] Francis, T., Jr., and Minuse, E., PROC. SOC. EXP. BIOL. AND MED., 1948, **69**, 291.