associated with a low pH of the vagina, but this effect cannot be ascribed to the inhibition *in vitro* where the secretions were brought to pH 7 prior to testing. The nature of the inhibitory substance has not been determined. It may represent specific antiviral antibody. Polio antibody has been reported to be present in urine of normal human subjects(1). The work of Strauss(2) may be interpreted as meaning that antibody to the typhoid bacillus may not only be found in the mucus of the vagina, but that such antibodies can also be locally formed. The presence of anti-polio and anti-herpes virus substances in the secretions can be explained on the basis of antibody derived from circulation, or in terms of local production of antibody in view of the known occurrence of herpes infection in the vagina and of the close proximity of the vagina to the rectum which may furnish polio antigen from time to time. Yet the lack of correlation between the neutralizing capacity of cervical secretions and corresponding sera coupled with the presence of inhibitory action against RSV (which inhibitor has rarely been found in the human sera) suggests that the substances in question were of a nonspecific or non-antibody nature. It is possible that more than one substance of an inhibitory nature, both antibody-like and nonspecific inhibitor-like, may be present in the secretions.

Summary. A viral inhibitor(s) effective against polio, herpes simplex and Rous sarcoma viruses has been demonstrated in the female genital tract. This may explain why it was not possible to isolate any virus(es) from the vaginal washings and swabbings of 229 volunteers. The nature of this inhibitor has not been determined. Some of the effects described, especially the activity against RSV, suggest that at least part of the inhibitory activity is not due to antibody.

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Production of Fatty Liver in the Rat by Cortisone.* (28790)

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Among other effects of cortisone, there are clearly effects on lipid metabolism. Marked changes in fat distribution occur in humans subjected to excessive doses of cortisone, giving rise to a characteristic body habitus. In addition, some inconstant changes in serum lipids have been reported(1), and it appears that fatty liver may result in some patients (2). Among experimental animals, the rabbit develops gross lipemia and fatty liver when cortisone is administered(3), but this animal is abnormally prone to develop these changes under a variety of relatively minor stimuli. Other animals have not been carefully studied in this regard, although a few undocumented references to the phenomenon exist(4,5). The present communication reports the development of hyperlipemia and lipid deposition in the livers of rats subjected to cortisone administration.

Materials and methods. Animals. Female rats weighing approximately 200 g were obtained from Holtzman Co. After a short period of acclimatization, the rats were di-

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TABLE I. Liquid Diet.

Dextrin	597	g
Corn oil	184	ml
Purified cellulose*	53	g
O and M salt mix	43	g
Vitamin mixture†	11	g
Casein hydrolysate	86	g
Choline chloride	5.2	g
Oleum percomorphum	3	drops

Make up to 2 l with water and mix in Waring blendor. Each rat fed 33 ml per day.

* Alphacel, Nutritional Biochemicals Corp.
† Mixture of water soluble vitamins and dextrin.

vided into equal groups. All rats received tube feedings 3 times daily of a liquid diet (Table I); control rats gained weight satisfactorily on this diet. Experimental rats were also given 6.25 mg cortisone acetate in saline suspension (Merck, Sharp & Dohme) subcutaneously daily. Antibiotics were not found necessary. After 12 hours' starvation pairs of rats were sacrificed, always between 9:00 and 10:00 a.m., by cervical dislocation and decapitation, at varying intervals until a period of 21 days was found to be satisfactory.

Chemical procedures. Small slices of liver (totaling approximately 100 mg) were ground with a Teflon pestle in a Potter-Elvehjem homogenizer in 1 ml physiological saline after being washed in Ringer's and saline. The homogenizer was washed twice with 1 ml saline and the washings added to the homogenate. Protein was determined on a TCA precipitate of the homogenate with the Folin-Ciocalteau reagent(6). One ml of the homogenate was subjected to lipid extraction with chloroform-methanol(7), dried *in vacuo,* and the dried lipid extract taken up in 8 ml of redistilled chloroform. Glycerides were estimated on the lipid extract by the method of Van Handel and Zilversmit(8), and cholesterol by a modification of the Zlatkis-Zak reaction(9). Phospholipids were removed from the lipid extract by layering 1 ml of lipid extract on silicic acid columns (2.5 g activated silicic acid, 11 × 27 mm) and eluting with 30 ml redistilled chloroform; glyceride was determined on the eluate, which contains mono-, di- and triglycerides (10). One hundred per cent recovery of glycerides was readily achieved by eluting the retained phospholipid from the column with chloroform-methanol and pure methanol. All procedures were performed on duplicate samples from the homogenate and each sample was run in triplicate until it became clear that results were reproducible to within 5%.

Serum lipids were determined on carotid artery blood collected at time of sacrifice from half the rats. Lipid extraction was performed as above on 0.5 ml serum, and other chemical methods were the same as those used for liver extracts.

Histology. Tissues were fixed in formalin for hematoxylin and eosin staining. Frozen sections of formalin fixed tissue were stained with flaming red and Sudan black B.

Results. Control animals had gained to between 240 and 255 g (average 247 g) at time of sacrifice, while the pair-fed experimental animals weighed between 175 and 234 g (average 210 g).

Table II gives values for serum and hepatic lipids. All cortisone-treated animals exhibited an elevation of total serum glycerides and cholesterol. The rise in glycerides was due in approximately equal parts to a rise in both phospholipid and non-phospholipid components.

A rise in hepatic total and non-phospholipid fractions is clearly demonstrated in the cortisone-treated animals. The phospholipids vary only slightly if at all. Cholesterol values showed no significant differences between control and treated rats.

The elevation of hepatic lipid was reflected in the histologic and histochemical appearance. The liver cells were vacuolated, particularly the cells of the periportal regions, and considerable quantities of fat were demonstrated (Fig. 1). Fat emboli, found frequently in rabbits treated with cortisone(3), were present in the lungs of these rats, but were not a prominent part of the picture.

Discussion. That adrenal cortical hormones have at least a permissive role in the development of fatty liver under some circumstances seems clear(11–13) and under other conditions they may have a primary importance(2,3). The biochemical sequence is by no means clear. Felt *et al* state that the effects they measured in the rabbit given cortisone, namely increase in serum triglycer-

TABLE II. Effect of Cortisone Treatment on Serum and Hepatic Lipids of Rats.

	Serum			Liver		
	Total glyceride*	Non-phospholipid glyceride*	Cholesterol†	Total glyceride‡	Non-phospholipid glyceride‡	Cholesterol§
Untreated controls	1.81 ±.28	1.04 ±.17	156 ± 28	.274 ±.028	.163 ±.018	91 ± 14
Cortisone-treated, pair-fed	3.09 ±.40	1.87 ±.45	252 ± 34	.530 ±.18	.390 ±.058	102 ± 36

All figures are given ± one S.D. Liver lipids result from 13 rats and 13 pair-fed controls; serum lipids from 6 pairs.

* mmoles/l of serum. † mg/100 ml of serum. ‡ mmoles/g of liver protein. § mg/g of liver protein.

ide, serum phospholipid and hepatic neutral lipid levels, and in hepatic phospholipid turnover, could all be duplicated by a simple triglyceride infusion, implying that the important mechanism was fat mobilization(17). There is no question that cortisone mobilizes lipids in many experimental animals, but the fact that hydrocortisone causes lipid accumulation in fibroblasts in culture in the absence of added lipid in the medium(18) suggests that at least one additional mechanism is at work.

Under many conditions in which protein synthesis is depressed, lipid accumulates in the cell(19), and among other effects of cortisone there is an initial rise, then a fall in ability of rat hepatic cells and fractions to incorporate amino acids into protein(14–16). The mechanisms by which depression of protein synthesis affects lipid metabolism in cortisone-treated rats are being studied.

In addition to the rabbit and rat, it seems clear that cortisone may have a similar effect on hepatic lipids in humans(2). Moran states

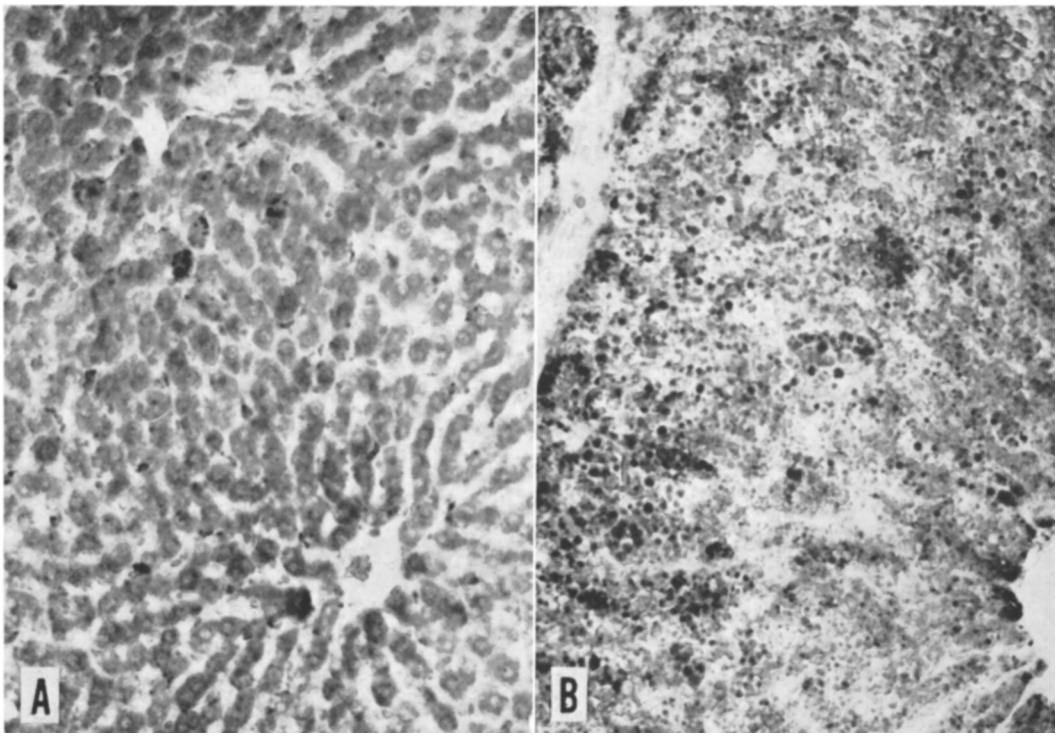

FIG. 1. Photomicrograph of Sudan black B-stained frozen sections of liver. a) Control rat. A few Sudan-positive particles are scattered about. b) Many sudanophilic droplets are present in virtually all cells. × 70.

the "fatty liver was consistently present" in human cases of hypercorticism he reviewed (3); our own experience includes many cases with fatty liver, and many without. Perhaps some other factor added to high cortisone levels, neither of which would produce the fatty liver by itself, is present.

Summary. Cortisone acetate, 6.25 mg/day, consistently produces elevation in rat serum glycerides and cholesterol, and in hepatic lipid glycerides other than phospholipid. Hepatic phospholipid and cholesterol levels are not affected. The question whether this represents a primary effect on the liver or a secondary effect due to mobilization of peripheral fat is discussed.

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Insulin Secretion from the Isolated Pancreas in Absence of Insulinogenesis: Effect of Glucose.* (28791)

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Although glucose stimulates the release of insulin from the islets of the pancreas, it is not clear whether it affects insulinogenesis primarily or acts directly on the secretion mechanism. Humbel *et al*(1) found that glucose-C^{14} can serve as a precursor for synthesis of insulin-C^{14} in fish islets, suggesting that high concentrations of glucose could stimulate insulinogenesis by providing substrate. In addition, Seltzer(2) has explained differences in the patterns of insulin secretion after administration of glucose and tolbutamide in the dog as a result of the stimulation of insulinogenesis by glucose.

On the other hand, an increased secretory process can be visualized(3,4) and depletion of islet cell granules is readily demonstrated after administration of glucose. Although these studies indicate that insulin secretion is accelerated by glucose, they still do not establish whether stimulation of insulin synthesis by glucose was the initial event.

We have previously demonstrated that glucose stimulates the release of immunochemically measurable insulin from the isolated perfused pancreas of the rat and that atten-

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