tuted 60% of the former, but was not present in the latter. 3. Although alkaline phosphatase which migrated with beta-globulin was elevated in both diseases of bone and liver, it is thought to be derived from bone since it had no 5-nucleotidase. 4. Since 5-nucleotidase is not contained in bone and is not elevated in diseases of the bone, it is thought to be derived from the liver.

1. Dixon, T. F., Purdom, M., *J. Clin. Path.*, 1954, v7, 341.

2. Smithies, O., *Biochem. J.*, 1955, v61, 629.

3. Pert, J. H., Sleisenger, M. H., Woods, K. R., Engle, R. L., Jr., *Clin. Res. Proc.*, 1957, v2, 156.

4. Colowick, S. P., Kaplan, N. O., *Methods in Enzymology*, 1955, v2, 1955.

5. Baker, R. W. R., Pellegrino, C., *Scand. J. Clin. and Lab. Invest.*, 1954, v6, 94.

6. Wolfson, W. Q., *Nature*, 1957, v180, 550.

7. Fahey, J. L., McCoy, P. F., Goulian, M., *J. Clin. Invest.*, 1958, v37, 272.

Received November 5, 1958. P.S.E.B.M., 1959, v100.

Effect of Neomycin on Serum Cholesterol Level of Man.* (24569)

PAUL SAMUEL‡ AND ALFRED STEINER (Introduced by David Seegal)

First (Columbia University) Division, Goldwater Memorial Hospital, Dept. of Hospitals and Dept. of Medicine, College of Physicians and Surgeons, Columbia University, N. Y.

During a clinical study of the effect of various dietary fats on the serum lipids of a group of patients with coronary atherosclerosis, it was observed that oral administration of neomycin to a patient with a gastrointestinal infection due to Salmonella Tennessee was associated with a significant fall in serum cholesterol concentration. The decrease in serum cholesterol level occurred at a time when the patient had clinically recovered from the infection although the organism was still present in the stools. To evaluate the significance of this observation, the effect of neomycin administered orally on the serum lipids was studied in 10 additional patients, none of whom were known to have disease of the gastro-intestinal system.

Method. The study group consisted of 6 male and 4 female patients ranging in age from 21 to 72 years. Nine were hospitalized and one was observed as an outpatient. Clinical diagnosis of each subject is listed in the Table. Total serum cholesterol levels were determined twice weekly in each patient by the method of Abell *et al.*(1). The ester fraction was determined by the method of Schoenheimer and Sperry(2); and total serum lipids by a gravimetric procedure(3). Five of the hospitalized individuals were on the regular hospital diet in which 45% of the calories are derived from fat. Of the remaining 5 patients, one (Nas) received a diabetic diet of C 180, P 80, F 80 g without insulin; one (Ber), with familial hypercholesterolemia, was on a low fat diet in which 25% of the calories were derived from fat; 2 patients were maintained on a similar low fat diet after a preliminary period of 6 weeks on the regular hospital diet; and the outpatient ate her usual diet without restriction during the study. Average pretreatment serum lipid values were established during periods of 5 weeks or longer prior to oral administration of neomycin. Neomycin was given as Mycifradin Sulfate®.† This preparation contains 70% neomycin sulfate. The doses of medication in this study represent the weight of Mycifradin Sulfate. Six patients were given 2 g each day. The remaining 4 patients received from 0.5 to 2 g daily. The period of neomycin administration varied from 3 to 16 weeks. If the amount of drug was varied, it was usually done so after 4 week periods at each dose level.

Results. The results of oral administration of neomycin on the serum cholesterol level are

* Aided in part by grants from N. Y. Heart Assn., Albert and Mary Lasker Fn., Thomas Phillips Fund and Revlon Fund.

‡ Present address: Dept. of Med., New York Univ. Med. Center.

† The authors are indebted to Upjohn Co. for generous supply of Mycifradin Sulfate.

TABLE I. Effect of Neomycin on Average Serum Cholesterol Level (mg/100 cc.), in 10 Patients.

Age	Sex	Diagnosis	Regular diet	Low fat diet	Neomycin									
					0.5 g	Wk*	% fall	1 g	Wk*	% fall	1.5 g	Wk*	% fall	2 g	Wk*	% fall
59	♀	Cerebral throm.	233		189	4	19	198	4	15	174	4	25			
58	♂	Hypertensive heart dis.	257		202	6	15	186	10	22						
69	♂	Cerebral throm.	206	194				172	4	11	157	6	19			
50	♂	Rheumatic heart dis., diabetes mel.	241		204	4	14									
52	♀	Fam. hypercholes., coronary art. disease		405										331	10	18
72	♂	Coronary art. disease	262	233										189	4	19
52	♂	Periph. neuritis	266											209	4	21
21	♀	Fam. hypercholes.	366											279	6	24
36	♀	*Idem*	442											367	3	17
64	♂	Coronary art. disease	188											134	3	29

* Weeks on neomycin.

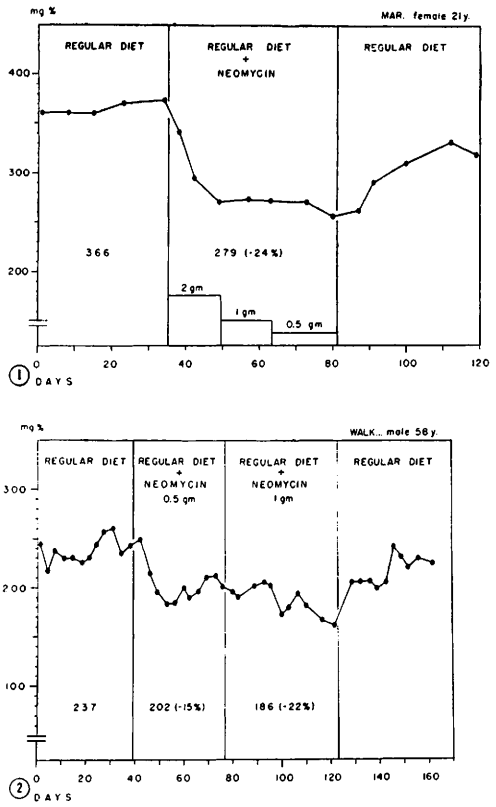

FIG. 1 and 2.

summarized in the Table. In all the patients, the average serum cholesterol level decreased following oral administration of neomycin. The decrease varied from 17 to 29% (average 22%), when 1.5 or 2 g of neomycin was given daily. At the dose level of 0.5 g of neomycin daily, average decrease in serum cholesterol varied from 14 to 19%; at the 1 g dose level average serum cholesterol diminished from 11 to 22%. Two to 3 weeks of oral neomycin administration were required before the level of serum cholesterol decreased to its low point. Increasing the amount of neomycin from 0.5 to 2 g daily resulted in a greater fall in serum cholesterol level. The lowering effect of neomycin could be maintained for the duration of the study, a period as long as 16 weeks, at the dose level of 1.5 to 2 g daily. Serum cholesterol levels returned to control levels within 2 weeks after the medication was discontinued.

Figs. 1 and 2 demonstrate the effect of oral neomycin in 2 patients. In Fig. 1 (Patient

Mar) serum cholesterol level averaged 366 mg % during the pre-treatment period and fell to average 279 mg % while on neomycin. The patient received 2 g of neomycin daily for the first 2 weeks, 1 g daily for the next 2 weeks, and finally 0.5 g daily for 2 weeks. The fall in the serum cholesterol was maintained although amount of medication was reduced. In Fig. 2 (Patient Walk) it can be seen that increasing the amount of neomycin from 0.5 g daily to 1 g daily resulted in a further decrease in serum cholesterol level.

The esterified fraction of serum cholesterol decreased in the serum in proportion to the total serum cholesterol in the 3 patients studied. Total serum lipids decreased in each patient, average fall for the group being 23% during the neomycin period. C/P ratio remained approximately unchanged during the study.

Two patients were subsequently given 60 mg of neomycin intramuscularly daily for 2 weeks without appreciable change in serum cholesterol level. This amount of neomycin was calculated to exceed that proportion of oral neomycin (3%) which is absorbed from the gastrointestinal tract(4).

No significant side effects occurred as the result of oral neomycin but mild transitory diarrhea occurred in 4 of the 10 patients at the 2 g dosage. Otherwise, the patients' clinical status remained unchanged during the period of study. The renal status as measured by urinalysis and blood urea nitrogen determinations and liver function as determined by cephalin flocculation and serum bilirubin tests were unaltered.

Comment. The mechanism of action of neomycin in lowering serum cholesterol concentration is unexplained. It is known that 97% of the orally administered drug is eliminated unchanged in the stool. It is possible that the effect of neomycin on the intestinal bacterial flora or upon certain enzyme systems of the gastro-intestinal tract may be responsible for the decrease in serum cholesterol level. Further studies utilizing antibiotics other than neomycin are in progress.

Summary. Oral administration of neomycin was associated with a significant decrease in serum cholesterol concentration of all of the 10 patients studied. On 1.5 to 2 g of neomycin daily, mean serum cholesterol level in each patient was decreased from 17 to 29%, average fall for the group was 22%. The fall in serum cholesterol level was maintained for the duration of drug administration which varied from 3 to 16 weeks. At a daily dose level of 0.5 to 1 g of neomycin similar but less marked falls in the serum cholesterol level resulted.

1. Abell, L. L., Levy, B. B., Brodie, B. B., Kendall, F. E., *J. Biol. Chem.*, 1952, v195, 357.

2. Schoenheimer, R., Sperry, W. M., *ibid.*, 1934, v106, 745.

3. Fiske, C. H., Subbarow, Y., *ibid.*, 1925, v66, 375.

4. Waksman, S. A., *Neomycin*, Williams & Wilkins Co., Baltimore, 1958.

Received November 5, 1958. P.S.E.B.M., 1959, v100.

Mobilization of Fatty Acids by Epinephrine in Normal and Hypophysectomized Rhesus Monkeys.*† (24570)

H. M. GOODMAN‡ AND E. KNOBIL

Dept. of Physiology, Harvard Medical School, Boston, Mass.

The demonstration by Dole(1), Gordon and Cherkes(2) and others(3) that epinephrine markedly increases the concentration of circulating non-esterified fatty acids

* Supported by grant from Am. Cancer Soc. and U.S.P.H.S.

† Monkey growth hormone used was prepared and generously provided by Dr. A. E. Wilhelmi. Prolactin was a gift of the Endocrinology Study Section, U.S.P.H.S. Technical assistance of Mr. G. R. Best is gratefully acknowledged.

‡ Public Health Service Predoctoral Research Fellow, Nat. Cancer Inst.