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GENERAL PRACTICE & INTERNAL MEDICINE

12 SOUTH JACKSON

PERRYVILLE, MO.

PRIMARY HYPERLIPEMIA

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PRIMARY hyperlipemia is a relatively rare disease. Only 19 cases have been reported in the literature. The first case of primary hyperlipemia was reported by Bürger and Grütz *(2)*. Movitt et al. *(3)* tabulated a total of 14 cases and added 5 cases of their own. Case reports of only 2 other patients with this disorder have been published to our knowledge. One was reported by Koszalka and Levin *(4)* and the other by Dunphy *(5)*. In this condition an excessive amount of fat or lipids are found in the serum and it is recognized by the milky, opaque appearance of the serum *(4)*. Movitt et al. *(3)* stated that primary hyperlipemia is a disorder of fat metabolism characterized by hyperlipemia of the retention type, frequently accompanied by hepatosplenomegaly, eruptive xanthomatosis, and abdominal pain or discomfort. Thannhauser *(6)* reported that the milky appearance of the serum is usually due to an increase in the neutral fat content above 150 percent of the normal value. He also found that an increase of cholesterol or phospholipids without an increase of the neutral fat never causes a milky serum *(7)*. Ahrens and Kunkel *(8)* pointed out that if the amount of phospholipid in plasma is 30 percent or more of the total lipids, the plasma will be clear and appear nonlipemic even at total lipid levels as high as 3,000 mg. per 100 cc.; but if it is less than 30 percent, the plasma will be cloudy and appear

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(1) Reese Air Force Base, Tex., at time of writing.

(2) Bürger, M., and Grütz, O.: Über hepatosplenomegale Lipoidose xanthomatösen Veränderungen im Haut und Schleimhaut. Arch. f. Dermat. u. Syph. 166: 542-575, Oct. 1932.

(3) Movitt, E. R.; Gerstl, B.; Sherwood, F.; and Epstein, C. C.: Essential hyperlipemia. Arch. Int. Med. 87: 79-96, Jan. 1951.

(4) Koszalka, M. F., and Levin, J. J.: Idiopathic hyperlipemia. Ann. Int. Med. 33: 473-480, Aug. 1950.

(5) Dunphy, E. B.: Ocular conditions associated with idiopathic hyperlipemia. Am. J. Ophth. 33: 1579-1586, Oct. 1950.

(6) Thannhauser, S. J.: Lipidoses: diseases of cellular lipid metabolism. In Christian, H. A.: Oxford Medicine. Oxford University Press, New York, N. Y., 1949. Vol. 4, Pt. 2, p. 595.

(7) Thannhauser, S. J.: Medical progress; serum lipids and their value in diagnosis. New England J. Med. 237: 515-522, Oct. 2, 1947.

(8) Ahrens, E. H., and Kunkel, H. G.: Stabilization of serum lipid emulsions by serum phospholipids. J. Exper. Med. 90: 409-424, Nov. 1949.

lipemic even at fairly low levels. Sorenson *(9)* remarked that "the perfect clearness of such liquids as serum and plasma, in spite of their contents of lipoids, is explicable only by assuming linkage between lecithin and sterols on the one hand and the protein on the other." Synonyms for this disorder are idiopathic familial lipemia and essential hyperlipemia *(6)*.

CLASSIFICATION

Koszalka and Levin *(4)* classified hyperlipemia as primary (idiopathic) and secondary. Secondary hyperlipemia may be associated with (1) the ingestion of an excess of fat, (2) von Gierke's disease, (3) starvation, (4) blood dyscrasias, (5) lipoid nephrosis, (6) nephrotic state of chronic glomerulonephritis, (7) hypoproteinemia, (8) obesity due to overnutrition, (9) pregnancy, (10) hypothyroidism, (11) diabetes mellitus, (12) pancreatic disease, (13) liver disease, and (14) the lipoidosis (found in essential xanthomatosis or in Niemann-Pick's disease and in which milky serum is not found as a rule).

To the above list, Movitt et al. *(3)* add as causes of the secondary type, thrombosis of the renal veins, poisoning, and anoxemic and cachectic states. Atlas et al. *(10)* recently reported a case of hyperlipemia associated with primary amyloidosis. Rich et al. *(11)* produced hyperlipemia in rabbits by the administration of cortisone.

ETIOLOGY

The etiology is unknown. The mechanism apparently is similar to a prolonged postprandial hyperlipemia. Fat is absorbed in the usual way but does not go out through the capillaries to the places of metabolism with normal rapidity. The term "retention hyperlipemia" has therefore been coined to describe this condition *(12)*. Thannhauser *(7)* stated that primary idiopathic hyperlipemia may occur as an inherited disorder or it may occasionally be observed with and without secondary eruptions of skin xanthomatoses.

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(9) Sorenson, S. P. L.: Constitution of soluble proteins (reversibly dissociable component systems). Compt. rend. d. trav. du lab. Carlsberg 18: 1-124, Apr. 1930. Quoted in Gould, R. G.: Lipid metabolism and atherosclerosis. Am. J. Med. 11: 209-227, Aug. 1951.

(10) Atlas, D. H.; Gaberman, P.; and Stern, K.: Primary amyloidosis associated with hyperlipemia and hypercholesterolemia; report of case. Am. J. Clin. Path. 20: 371-376, Apr. 1950.

(11) Rich, A. R.; Cochran, T. H.; and McGoon, D. C.: Marked lipemia resulting from administration of cortisone. Bull. Johns Hopkins Hosp. 88: 101-109, Jan. 1951.

(12) Block, W. J., Jr.; Mann, F. D.; and Barker, N. W.: Effect of small doses of heparin in increasing translucence of plasma during alimentary lipemia; studies in normal individuals and patients with atherosclerosis. Proc. Staff Meet., Mayo Clin. 26: 246-249, June 20, 1951.

CASE REPORT

A 20-year-old man was admitted on 8 February 1951 with a severe local reaction to a smallpox vaccination on his left arm. On the next day the laboratory reported that a serologic test could not be performed on this patient's serum because it was opaque and milky in character. The patient entered military service on 6 January 1951 and was vaccinated on 11 January. He had not been vaccinated previously. On 13 January blood was drawn from his arm for a serologic test. He was not notified of any abnormality at this time. Eleven days after vaccination he reported on sick call complaining of swelling, redness, and tenderness about the site of vaccination. He received several injections of penicillin at this time.

On admission, there was an ulcer, 2 cm. in diameter and 1 cm. deep, filled with black necrotic tissue, on the lateral aspect of the left arm. It was surrounded by a large area of induration and redness. There were several tender, walnut-sized lymph nodes in his left axilla. His temperature was normal. Repeated examinations of the eyegrounds failed to reveal evidence of lipemia retinalis, but the vascular light reflexes of the retinal arterioles had greater breadth than is usually seen in a person 20 years of age. The other 2 ocular manifestations of hyperlipemia *(5)* (lipid interstitial keratitis and xanthomas of the eyelids) were not present. The patient's stay in the hospital was uneventful. Antibiotics and soaks controlled his infection and the ulcer of the arm was eventually replaced by firm scar tissue.

The results of the lipid tests are shown in table 1. The amount of total lipids on admission was more than 6 times the upper limit of normal. Neutral fat was not determined as such. Two types of therapy were tried. A low-fat diet of 2 weeks' duration resulted in a normal-appearing blood serum. The total lipid content at this time (800 mg. per 100 cc.) was not far above the upper limit of normal. Desiccated thyroid, up to 0.2 gram per day, was then given empirically while the patient was on a normal diet. The serum was milky in appearance before and after this trial. BMR's before thyroid therapy were +13, +16, and +24. After 10 days of thyroid therapy the rate was +30.

Block et al. *(12)* recently found that small doses of heparin given intravenously to normal persons with alimentary hyperlipemia caused an increase in the translucency of the serum within 15 minutes. Accordingly, 20 mg. of heparin was given intravenously to this patient but no decrease in the milkiness of the serum was noted in 15 minutes. On 2 August the cholesterol protein conjugate (12-20 Svedberg flotation units) was 0 mg. per 100 cc. (fig. 1). The electrophoretic serum partition showed:

TABLE 1. *Blood lipid studies (in mg. per 100 cc.)*

	Normal	On admission (9 Feb.)	Before low-fat diet (19 Apr.)	After low-fat diet (26 Apr.)	After thyroid therapy (2 May)	On ordinary diet (3 Oct.)
Total lipids	450-650	4,020.0	1,320.0	800.0	1,110.0	3,300
Fatty acids	310-460	3,597.6	1,093.0	617.2	927.0	2,997
Lipid phosphorus	10-14	21.9	—	7.7	2.2	9.76
Total cholesterol	150-250	248.8	226.2	182.8	183.0	303
Cholesterol esters	80-180	38.2	100	71.8	61.9	65.1
Lecithin	78	—	452.5	—	—	—

albumin, 53 percent; alpha 1 globulin, 3 percent; alpha 2 globulin, 10 percent; beta globulin, 13 percent; gamma globulin, 21 percent; A/G ratio, 1.1; and total proteins, 7.56 grams per 100 cc.

Because of the unpublished observations of Harvill, adenosine-5-monophosphate was administered to determine whether it would lower the blood cholesterol level. Beginning on 2 August, 1 cc. of this drug was injected intramuscularly every 2 days for 3 doses. On 7 September this was repeated.

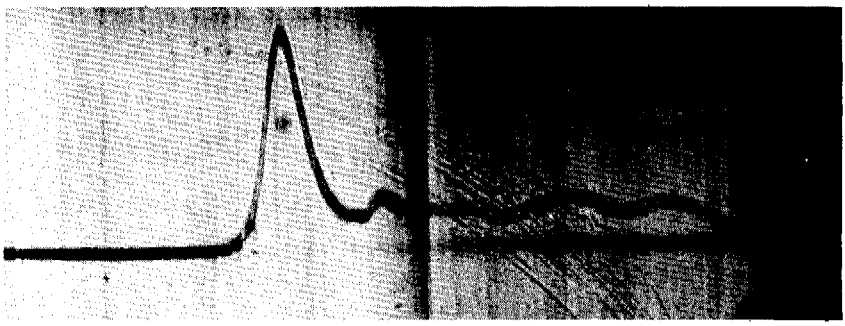

Figure 1.

Before administration of adenosine-5-monophosphate in August there were 2,624 mg. of cholesterol per 100 cc. of mixed blood serum (209 in the clear portion of the serum) and after administration of the drug there were 740 mg of cholesterol per 100 cc. of mixed blood serum (175 in the clear portion). In September there were 478 mg. of cholesterol per 100 cc. of serum before administration of the drug and 374 after.

On admission the erythrocyte count was 5,430,000 with 15.85 grams of hemoglobin. The leukocyte count was 8,500 with 68 percent neutrophils, 26 percent lymphocytes, and 6 percent monocytes. Subsequent blood counts showed no essential change. The platelet count was 300,000. The bleeding time was 1 minute. The blood coagulation time was 6½ minutes.

The nonprotein nitrogen was 47; serum lipase, 0.3 cc.; alkaline phosphatase, 3.34 Bodansky units; acid phosphatase, 2.32 Bodansky units; serum phosphorus, 5.6 mg. per 100 cc.; and serum amylase, 8 units. The total protein on admission was 9.6 grams per 100 cc. The A/G ratio was reversed at this time; albumin, 3.5 grams per 100 cc. and globulin, 6.1 grams per 100 cc. Serial blood protein studies during convalescence from the infected vaccination showed reversion to normal values 3 weeks after admission. Five minutes after injection of bromsulphalein, 82 percent was still present in the blood and at the end of 30 minutes, 4.5 percent was present. The prothrombin

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time was 100 percent. Four hours after the oral administration of 6 grams of sodium benzoate, a total of 3.9 grams of hippuric acid was recovered from the urine.

COMMENT

This patient has been followed for 6 months since his hyperlipemia was discovered. There has been no change in the milky appearance of blood serum in that time. The only factor which decreases the amount of fat in his blood is a low-fat diet. This is in accordance with the experience of other authors. The cholesterol level in mixed serum is much higher than that in clear serum. The significance of the low percentage of esters as compared to total cholesterol is unknown. In this patient, the total cholesterol level was not much above normal when the clear portion of the blood serum was analyzed. When the mixed milky serum was analyzed, there was a marked increase in the cholesterol level. The only known treatment of this condition is a low-fat diet. The prognosis is considered to be good and premature arteriosclerosis probably does not develop in these patients *(12)*. When last seen this patient was performing his military duties in a satisfactory manner.

BOOK REVIEW

Practical Pharmacology, by *J. H. Burn,* Professor of Pharmacology, University of Oxford, Illustrations by *E. M. Vaughan Williams.* 72 pages; illustrated. Blackwell Scientific Publications, Oxford, England, publisher, 1952. Published simultaneously in the United States by Charles C Thomas, Publisher, Springfield, Ill., 1952. Price $3.25.

This book presents 21 groups of experiments, designed to be performed before a class, and represents the work of several people who have had a share in developing the present course in practical pharmacology offered at the University of Oxford. The work is presented in a clear, easily assimilated form and the illustrations are well prepared and helpful. It is interesting and useful as a reference book and is fairly comprehensive, but its value as a text in the United States would be doubtful, because some of the methods described are not used in this country.

—*Commander R. L. Taylor, MSC, U. S. N.*