this report. Value for females is somewhat higher. Representative levels for sera of chicken, rabbit, guinea-pig, rat, mouse, sheep, dog, and monkey are given. Inhibitor is greatly elevated in sera of human females during the third trimester of pregnancy. In a number of selected disease states the inhibitor was found usually to be moderately elevated, although no consistent pattern was noted. The inhibitor was not diminished in sera of patients with arteriosclerosis.

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Received December 29, 1958. P.S.E.B.M., 1959, v101.

Alpha-2 Lipoprotein in Man and Its Relation to Myocardial Infarction.*† (24823)

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In studies on human serum lipoproteins using starch zone electrophoresis, the lipoproteins, as measured by cholesterol distribution, are readily separated into 3 main fractions (1,2). Fig. 1-A shows a cholesterol distribution curve obtained from a normal young male subject together with corresponding protein distribution curve. In healthy elderly individuals a similar curve is obtained as shown in Fig. 1-B, with a decrease in alpha-1 cholesterol percentage of approximately 1/3 and a corresponding increase in beta cholesterol, with no change in alpha-2 cholesterol percentage. Among elderly individuals with moderate or advanced atherosclerosis, a common type of curve is shown in Fig. 1-C, with a higher percentage of cholesterol in the beta fraction. Similar results have been noted by other workers(3,4,5) using paper electrophoresis in which only alpha and beta fractions are usually reported. In 24% of our male subjects there were lipoprotein curves with increased percentage of cholesterol in the alpha-2 fraction. Recently E. B. Smith(6) using paper electrophoresis noted a component which migrated between alpha and beta fractions (designated pre-beta fraction by this author) which appeared associated with presence of recent myocardial infarction in the patient. Schettler and his coworkers(7) using starch electrophoresis also mentioned that changes in the lipoprotein pattern may occur with myocardial infarction. We were therefore interested in determining the incidence of such diseased states among subjects with increased alpha-2 cholesterol.

Methods. Our subjects were patients of one of the authors (WBK). Lipoprotein determinations were made on selected patients visiting the physician for periodic check-ups. Ages varied from 35 to 83 years, most between 50 and 70. Three hundred male patients, taken in order, were used. The subjects were all of better than average economic status and presumably all had adequate dietary intake which was probably relatively high in fats. All blood samples were obtained in the morning with subjects in basal state and lipoprotein determinations carried out by the method used earlier(2).

Results. Patients were divided into groups on the basis of percentage of cholesterol found in the alpha-2 fraction. Thirty-eight, or

* Supported, in part, by funds from Gerontological Research Fn.

† A portion of this material was presented by senior author before First Pan-Amercan Congress of Gerontology, Sept. 22, 1956, Mexico City.

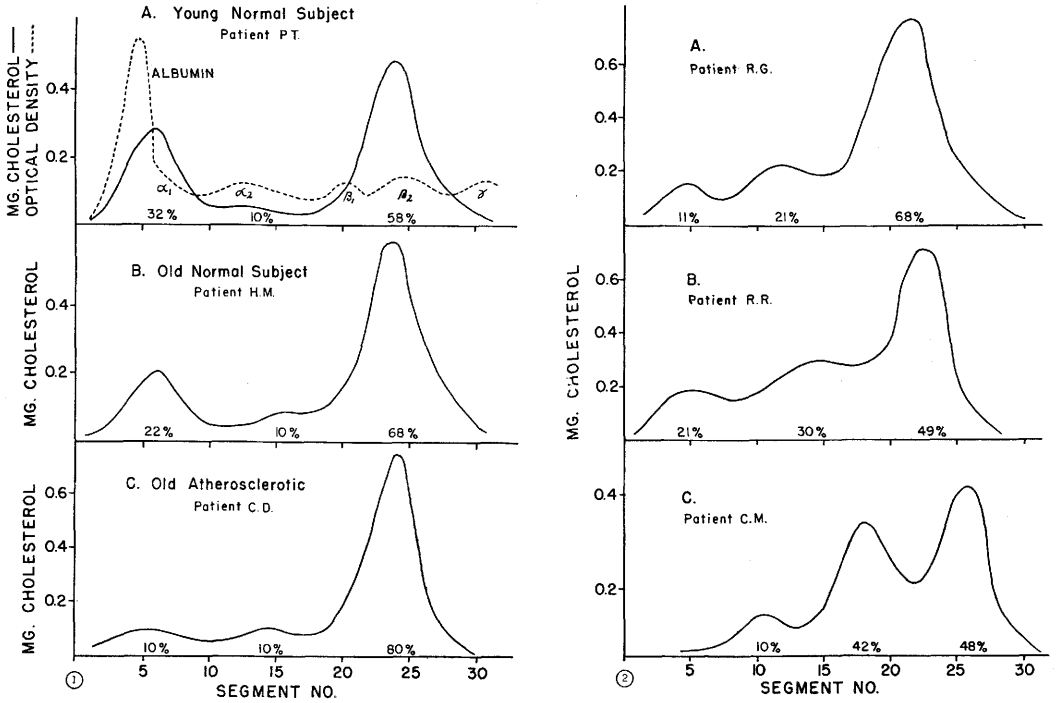

FIG. 1 (left). A. Cholesterol lipoprotein curve and protein curve on a 27-yr-old healthy male subject. B . Cholesterol lipoprotein curve on a 68-yr-old male in good health. C. Cholesterol lipoprotein curve on a 70-yr-old male with advanced atherosclerosis.

FIG. 2 (right). A, B, C. Cholesterol lipoprotein curves on men with elevated alpha-2 fractions and histories of previous myocardial infarctions. Ages of patients are 61, 48 and 52 yr, respectively.

12.6%, had an alpha-2 cholesterol of over 20% (Group I), 34, or 11.3%, had alpha-2 cholesterol of between 16 and 20% inclusive (Group II), and the remaining 228, or 76.0%, had an alpha-2 cholesterol of less than 16% (Group III). After classification on the basis of alpha-2 lipoprotein level, histories were examined for evidence of previous myocardial infarctions or other cardiovascular disease. The results are shown in Table I.

Of those in Group I, 28 had histories of definite myocardial infarcts from 2 months to

TABLE I. Lipoprotein Cholesterol Distribution in Relation to Myocardial Infarction. Average serum cholesterol levels in mg/100 ml and percentage of cholesterol in different fraction. (Figures in parentheses represent range of values. See text for detailed explanation of groupings.)

	No.	Total cholesterol (mg %)	Cholesterol distribution (%) α-1	α-2	β
Group I (avg age 56)					
1. With myocardial infarction	28	306 (205–390)	13 (9–21)	24 (21–49)	62 (41–71)
2. Other disease (see text)	7	375 (305–490)	8 (5–12)	48 (20–69)	44 (25–74)
3. No infarct	3	(165–205)	(15–28)	(21–23)	(50–71)
Group II (avg age 55)					
1. With myocardial infarction	10	304 (225–395)	13 (12–15)	19 (16–20)	68 (65–75)
2. With hypertensive cardiovascular disease	7	280 (230–315)	16 (9–22)	18 (16–20)	66 (63–72)
3. Little detectable cardiac disease	17	225 (195–310)	21 (17–26)	17 (16–20)	62 (57–68)
Group III (Avg age 62)					
"Normal" alpha-2 lipoprotein	228	280 (180–360)	18 (10–25)	12 (8–15)	70 (60–80)

2 years previous, as indicated by clinical evidence and electrocardiographic changes. Typical lipoprotein curves for 3 of these individuals are shown in Fig. 2. Note distinct alpha-2 peak in all instances.

Seven additional patients had very high alpha-2 fractions. All had hyperlipemia, nephrosis, liver disease, or other conditions known to cause a markedly elevated alpha-2 cholesterol(8). Since the elevation due to these causes could completely mask any changes due to possible myocardial infarction, these subjects were not considered further. The 3 remaining patients in Group I showed no positive evidence, clinically or electrocardiographically, of previous myocardial infarction.

Ten of the patients in Group II had a history of previous myocardial infarctions as indicated by clinical symptoms and electrocardiographic changes, 7 more had moderate to severe hypertensive cardiovascular disease, but without any definite evidence of previous infarction, while the remaining one-half had little evidence of cardiovascular disease. Of the 228 remaining patients with normal alpha-2 lipoprotein cholesterol percentage (Group III), only 3 showed any definite clinical or electrocardiographic evidence of infarction in the past.

Discussion. The fact that 28 of 31 patients with more than 20% of cholesterol in the alpha-2 fraction (excluding those with nephrosis, hyperlipemia, etc.) had histories of previous myocardial infarction, is a strong indication of some relationship between lipoprotein distribution and myocardial infarcts. Considering patients listed in Table I (except Group 1-2, all 65 patients with more than 16% of cholesterol in the alpha-2 fraction, 38 have histories of myocardial infarction, 7 have hypertensive cardiovascular disease without definite evidence of myocardial infarct and 20 have little detectable cardiac disease. The difference in alpha-1 cholesterol is also of interest. In 38 patients with infarcts, the average alpha-1 cholesterol was 13%, and in 20 patients without infarcts, the average was 21%. The difference between these averages was significant at the 1% level. In patients with only moderately increased alpha-2 cholesterol, an accompanying lower alpha-1 level is additional indication of a possible previous infarction. If criteria used to divide patients into 2 groups were changed as follows: one group with alpha-2 cholesterol of more than 15% and an accompanying alpha-1 cholesterol numerically at least 3% less (*e.g.*, with alpha-2 cholesterol of say 16% and an alpha-1 cholesterol of 13% or less, or with an alpha-2 cholesterol of say 20% and an alpha-1 cholesterol of 17% or less), and all other patients in a second group, the first group would then contain 38 patients with a history of myocardial infarction and 4 without, while the second group of 255 patients would contain only 3 patients with a history of myocardial infarction. The large differences between these 2 groups would indicate a very definite correlation between abnormal type of lipoprotein curve and history of previous myocardial infarcts. The increased alpha-2 would apparently be the primary determinant and the decreased alpha-1 would be of secondary but adjunctive significance. Of 4 patients in the first group without a definite diagnosis of a myocardial infarct, 3 had moderate to severe hypertensive cardiovascular disease. The fourth patient was a young physician of 35 who had a typically abnormal curve with a cholesterol distribution of 15%, 23% and 62% but who denied any symptoms of even a mild infarction.

When lipoprotein distribution curves were obtained, all subjects with previous myocardial infarcts had made successful recoveries. The data do not tell us whether the abnormal curves existed prior to infarction or how long they had been present. E. B. Smith(6) found that the pre-beta fraction developed within a few days after infarction and disappeared within a few weeks. Because of the difference in technics, comparison with our results is difficult. We have made repeated determinations on some patients with infarctions and in only 2 out of 17 did the distinguishing features of lipoprotein distribution disappear. In one instance the abnormal alpha-2 peak had disappeared when a second determination was made 2 months later. In the second instance the determination was not repeated until 2 years after the initial calculation. With other

patients on whom repeated determinations were made, the character of the curve has remained essentially unchanged over periods as long as 2 years. The time between myocardial infarction and when the initial curve was obtained, also varied from a few months to over a year. The fact that the abnormal features of the lipoprotein curve can disappear might account for the 3 patients (out of 228) with normal curves with a history of previous myocardial infarction. Our observations would therefore indicate that the character of the curves is relatively constant. At present we cannot state whether such curves occur prior to myocardial infarction. Lipoprotein curves were made from 2 elderly patients who died within a few days after a myocardial infarction. The results showed relatively normal curves, suggesting abnormal lipoprotein distribution occurs at some interval after infarction. Our results, however, are based almost entirely on patients who have survived myocardial infarction as compared with those who have not had one.

Summary and conclusions. Data are presented which indicate that an abnormal type of cholesterol lipoprotein curve is associated with a history of recovery from a previous myocardial infarction. The type of curve obtained from a given individual is relatively constant over years. As yet we are unable to say whether the abnormal type of curve develops prior to, or after, initial infarction, or whether degree of abnormality is of any prognostic value. The relationship which exists suggests the need for further studies as to diagnostic and prognostic value of this method in the study of myocardial infarction.

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Received January 12, 1959. P.S.E.B.M., 1959, v101.

Fixation of 5-Hydroxytryptamine by Brain Mitochondria.* (24824)

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In investigating some physical and biochemical properties of brain mitochondria, it seemed desirable to know whether any neurohumoral amines present in the brain were attached to mitochondria and involved in their physiology. There is evidence to suggest that histamine(1), nor-adrenalin(2) and acetylcholine(3) are associated with mitochondria elsewhere in the organism; but no comparable study has been made with brain mitochondria. Since recent interest in possible role of 5-hydroxytryptamine (HT)† in brain function, and an extremely sensitive bioassay was available, such study was undertaken with this neurohumoral amine. Our report deals with localization of HT in rat brain mitochondria and its possible relationship to mitochondrial metabolism. A preliminary account of this work has been presented(4).

Methods. Mitochondria were prepared from whole rat brain by methods comparable to those described previously(4), with special precautions to eliminate blood cells and cellu-

* This research was supported by grants from Dept. of Public Welfare, State of Ill., and with Office of Naval Research.

† The following abbreviation were used: HT, 5-hydroxytryptamine; P/O, oxidative phosphorylation. HT was kindly supplied by Dr. R. K. Richards of Abbott Labs., Chicago.