

February 1, 1972

Lipid Research Center
Criteria for Hyperlipidemia
(Dr. A. Ostfeld 1/25/72)

Initial screening will be based on NEJM 1967 distributions (attached) and the following criteria, to be reevaluated after new distributions obtained and the first 200 cases identified.

Type IIa LDL cholesterol above 95% level for each decade of age and triglycerides at or below 95% level for age decade. Sex ignored.

Type IIb Same as above and triglycerides above 95% level, assuming floating beta and chylomicrons absent (presumably adequate fasting specimen, etc.)

cc: Dr. A. Ostfeld
Dr. I. Frantz
Dr. H. Taylor

TABLE 3. Plasma Lipid and Lipoprotein Concentrations in Normal Subjects.*

Age	Sex	TOTAL CHOLESTEROL†	TRIGLYCERIDE†	PRE-BETA CHOLESTEROL‡§	BETA CHOLESTEROL‡§	ALPHA CHOLESTEROL†	No. OF SUBJECTS
		mg./100 ml.	mg./100 ml.	mg./100 ml.	mg./100 ml.	mg./100 ml.	
0-19	M	172 ± 34	61 ± 34	9 ± 7	108 ± 33	49 ± 11	43
	F	179 ± 33	73 ± 34	11 ± 8	108 ± 10	53 ± 12	38
20-29	M	183 ± 37	73 ± 32	11 ± 8	111 ± 30	53 ± 11	41
	F	179 ± 35	62 ± 29	12 ± 10	115 ± 31	52 ± 9	37
30-39	M	210 ± 33	78 ± 39	21 ± 13	143 ± 27	48 ± 11	50
	F	204 ± 37	67 ± 48	14 ± 10	119 ± 31	58 ± 13	32
40-49	M	230 ± 55	90 ± 41	21 ± 9	128 ± 28	49 ± 10	67
	F	217 ± 35	80 ± 42	14 ± 9	130 ± 24	62 ± 14	44
50-59	M	240 ± 48	104 ± 45	29 ± 8	152 ± 22	47 ± 15	28
	F	251 ± 49	83 ± 46	23 ± 8	147 ± 36	59 ± 15	41

Age	Suggested "normal limits" §:	
	MALES	FEMALES
0-19	120-230	30-65
20-29	120-240	30-70
30-39	140-270	35-70
40-49	150-310	35-75
50-59	160-330	30-65
		35-80
		40-85
		35-85

* Population sample is derived from subjects with no evidence of metabolic disease or family history of hyperlipoproteinemia whose triglycerides <200 mg./100 ml.; all samples obtained 12-14 hr. after evening meal.

† Mean & standard deviation.

‡ Obtained on smaller no. of patients varying from 13 to 27.

§ Based on 95 per cent fiducial limits calculated for small samples — all values rounded to nearest 5 mg. (it will be noted that, for practical purposes, differences between sexes have been ignored except for alpha-lipoprotein concentrations).

...ined for the 2 sexes even though modest but significant differences actually exist. The sex difference in α -lipoprotein concentrations has been maintained (Table 3) since the lower limits do have value in detecting heterozygotes for Tangier disease.¹⁴⁹ The upper (5 per cent) limits for all the quantities are relatively high because the samples from which they are calculated are rather small. This should bias interpretation of patterns in the direction of mislabeling as "normal" subjects some who have marginal hyperlipoproteinemia.

Age-related changes. Lipid and lipoprotein concentrations do not progress stepwise as suggested by Table 3 but as continuous and nonlinear function of age that is not necessarily identical for males and females.^{64,164-166}

The lowest lipoprotein concentrations are those in cord blood. The mean cholesterol concentration is about 70 mg. per 100 ml.,^{167,168} and the α lipoproteins are about half and the β lipoproteins about a third of the concentrations shown in Table 3 for the youngest age decrement.⁶⁷ At this time there are practically no pre- β lipoproteins. Within the first few hours after birth the infant is forced to call upon the fat reserves that he has accumulated mainly in the last trimester of pregnancy. The initially low concentrations of free fatty acids are doubled, and the respiratory quotient begins to fall.¹⁶⁹ The transport of endogenous glyceride, perhaps required mainly to take care of overshoot in release of free fatty acids, begins in this early period. The mechanisms for transporting exogenous glyceride are also activated with the first feedings. Therefore, the demands upon β and possibly α lipoproteins should increase very early. Indeed, the concentration of β lipoproteins doubles or triples within the first week of life, and lesser but definite increases in α lipo-

proteins also occur.^{170,171} A very slow ascent in lipoprotein and cholesterol concentrations continues until well into the third decade.¹⁷² For practical purposes pediatricians may use the limits in Table 3 for the first two decades without any correction except for the immediate postnatal period.

In the third decade there begins a "third phase" in which concentrations of β and pre- β lipoproteins rise at a new and more perceptible rate.^{164,165} These increases are probably expressions of the change in fuel economy that is taking place at this time. Physical growth is ending, and the subject becomes more sedentary; caloric excess is easier to achieve, and perhaps other environmental and humoral factors come into play.

There is no general agreement about lipoprotein concentrations after about the age of sixty. From the available data it appears that the rise is over, at least for men. One must be very careful not to overinterpret lipoprotein determinations in very old subjects, and this sometimes poses difficulties in kindreds in which a younger propositus has hyperlipoproteinemia.

Naming the Patterns

In Figure 7 the terms "Type I," "Type II" and so forth appeared without comment. These are shorthand designations that were originally used to define different phenotypes of hyperlipoproteinemia because the existing nomenclature for the familial syndromes was inadequate and frequently misleading.^{159,173,174} They have proved to be of such value for ready communication both in the laboratory and in the clinic that they may be used to denote specific lipoprotein patterns whether they are associated with primary or secondary hyperlipoproteinemia. The advantage is one of convenience. The