APPENDIX-H

Are "Small, Dense LDL Particles" Especially Atherogenic? A Basis for Strong Doubt

• Part 1. Evidence, from the Livermore Study, Which Challenges a Current Hypothesis

During the 1990s, a large literature has accumulated around the hypothesis that the smallest, most dense molecules within the Low-Density class of serum lipoproteins are the key atherogenic species. There is clearly renewed interest in the fact that lipoprotein species WITHIN the Std Sf 0-12 segment of the spectrum differ from each other in density, size, and physical behavior --- a fact solidly demonstrated in the early 1950s (Chapter 44, Part 3f, and Chapter 44, Box 2) but de-emphasized by reliance on LDL-cholesterol measurements.

The purpose of Appendix-H is to present some striking evidence from the Livermore Lipoprotein Study --- evidence which persuades us that the purported high atherogenicity of the "small, dense" LDL molecules reflects, instead, the elevated mean level of the triglyceride-rich Std Sf 20-400 serum lipoproteins in Ischemic Heart Disease.

Some Resources in the Literature

Within the following papers, readers can find the history and details of the Hypothesis of Small, Dense LDL Particles:

- 1994: Ronald M. Krauss, "Heterogeneity of Plasma Low-Density Lipoproteins and Atherosclerosis Risk," (Review), CURRENT OPINION IN LIPIDOLOGY Vol.5: 339-349.

- 1994: A.H. Slyper, "Low-Density Lipoprotein Density and Atherosclerosis: Unraveling the Connection," JOURNAL OF THE AMERICAN MEDICAL ASSN. Vol.272: 305-308.

- 1996: Christopher D. Gardner + Stephen P. Fortmann + Ronald M. Krauss, "Association of Small Low-Density Lipoprotein Particles with the Incidence of Coronary Artery Disease in Men and Women," JOURNAL OF THE AMERICAN MEDICAL ASSN. Vol.276, No.11: 875-881.

- 1996: Meir J. Stampfer + Ronald Krauss + Jing Ma + 4 co-workers, "A Prospective Study of Triglyceride Level, Low-Density Lipoprotein Particle Diameter, and Risk of Myocardial Infarction," JAMA Vol.276, No.11: 882-888.

- 1996: Josef Coresh + Peter O. Kwiterovich, Jr., "Small, Dense Low-Density Lipoprotein Particles and Coronary Heart Disease Risk: A Clear Association with Uncertain Implications," (Editorial), JAMA Vol.276, No.11: 914-915.

- 1997: Benoit Lamarche + Andre Tchernof + Sital Moorjani + 4 co-workers, "Small, Dense Low-Density Lipoprotein Particles as a Predictor of the Risk of Ischemic Heart Disease in Men: Prospective Results from the Quebec CardioVascular Study," CIRCULATION Vol.95, No.1: 69-75.

• Part 2. What Are These "Small, Dense Low-Density Lipoprotein Particles"?

Gardner and colleagues have recently stated (Gardner 1996, p.875):

"LOW-DENSITY lipoprotein (LDL) particles are heterogeneous in size, density and composition. Using different methods, including gradient gel electrophoresis, density gradient ultracentrifugation, and analytical ultracentrifugation, various investigators have identified and defined LDL heterogeneity as consisting of 2 to 15 different fractions, patterns, types, diameter ranges, size intervals, subspecies, or peak flotation rates [references provided]. Despite these multiple approaches for defining LDL subclasses, they all similarly differentiate relatively smaller, denser, and lipid-depleted particles from those that are larger, more buoyant, and lipid enriched."

Appendix-H focuses on evidence concerning one such "small, dense lipoprotein" in the LDL group of lipoproteins of density less than 1.063 gms/ml. That lipoprotein, having a density of 1.05 g/ml, was described as HDL-1 over 40 years ago by DeLalla 1954-b (details in Chapter 44, Part 3e). It was always clear that HDL-1, by its density and ability to float in a salt solution of 1.063 g/ml, is truly a member of the LDL group (Std Sf 0-12 lipoproteins). Indeed, HDL-1 is labeled "low density" in the figure from 1956 which is reproduced in Chapter 44, Box 1. It is the smallest and most dense species which we could identify in the Std Sf 0-12 segment of serum lipoproteins. HDL-1 can be regarded as approximately Sf 0-2, in the Sf 0-12 spectrum. Nonetheless, it acquired the name "HDL-1" at Donner Lab because it proved effective to quantify its concentration during runs made to isolate what we named the HDL-2 class of High-Density Lipoproteins.

There is no doubt that HDL-1 must constitute a large share of the "small, dense LDL lipoproteins" to which Gardner and others have been referring.

• Part 3. Average LDL Diameters: IHD Cases vs. Controls --- from Gardner, Stampfer

Both Gardner 1996 and Stampfer 1996 report that the average diameter of serum LDL molecules is smaller in patients who have Ischemic Heart Disease (Coronary Artery Disease) than in controls. The mean measurements in Part 3a come from their papers: Gardner's Table 3 (p.878) and Stampfer's Table 1 (p.884).

3a. Differences in Diameter of LDL Molecules, in Nanometers

• Gardner 1996, Cases and Controls.				Difference: Cases minus Controls.	
	No. of Pairs	Cases	Controls		
Men	90	26.05	26.58	-0.52	p value <0.001
Women	34	26.46	26.94	-0.48	p value = 0.06
Both	124	26.17	26.68	-0.51	p value <0.001

• Stampfer 1996.		Difference: Cases minus Controls.	
Men, 266 Cases	25.6 nm		
Men, 308 Controls	25.9 nm	-0.3 nm	p value <0.001

While the statistical significance is high, the differences between cases and controls seem quite small in terms of percentage. For the Gardner report, the difference in average LDL diameters is (0.51/26.68), or 1.9 percent. For the Stampfer report, the difference in LDL diameters is even smaller: (0.3/25.9), or 1.2 percent. We will demonstrate (Part 7b) why such differences can be expected --- wholly aside from any special atherogenicity related to reduced LDL diameters in the small, dense range of LDL.

3b. The Views of Gardner and Co-Workers, 1996

Gardner and colleagues state (1996, p.875):

"A large and growing body of epidemiologic evidence shows a consistent association between small, dense LDL particles and prevalent coronary artery disease (CAD) in case-control studies. In each of these studies, the case-control difference in LDL size or subclass concentration was statistically more significant than the difference in LDL cholesterol (LDC) levels. This epidemiologic evidence is supported by mechanistic evidence from human, animal, and in vitro studies that suggest the smaller, more dense LDL Particles are relatively more atherogenic than larger, more buoyant particles." And later (Gardner 1996, p.880):

"The findings reported herein add to the accumulating evidence that small, dense LDL particles meet many of the criteria for being an important CAD risk factor. Angiography and MI survivor case-control studies have consistently found an association between small, dense LDL and CAD. The

present study and a recent report from the Physicians' Health Study demonstrate that the presence of small LDL particles precedes CAD. Our data suggest that the relationship with CAD is graded. Similar to our own findings, other investigators have reported that the relative risk of CAD among individuals with small LDL particles is strong ... The association between LDL size and CAD thus appears to be consistent, prospective, graded, strong, and biologically plausible."

We think the association has a different explanation. And we do not consider any size-effect to be biologically plausible, for LDL molecules in this part of the lipoprotein spectrum.

• Part 4. The Livermore Study: The "Massive HDL-1 Hyperlipoproteinemia Syndrome"

Long ago, the Donner team found the HDL-1 class to be massively elevated in the blood of (a) Diabetics during acidosis and decontrol (Gofman 1952-d, + Kolb 1955), (b) Persons with Glycogen Storage Disease (Kolb 1955), and (c) Persons with "Essential Hyperlipemia" who have "creamy serum" but have no overt clinical troubles (Gofman 1954-a).

4a. A Search for HLD-1 "Out-Liers" in the Livermore Lipoprotein Study

In 1993, we examined the records of the 2,297 participants in the Livermore Lipoprotein Study, whose database of clinically healthy adults is described in Appendix-E, Part 12c. During this examination, we searched for persons with serum HDL-1 levels equal to or greater than 100 mg/dl. A level of "only" 100 mg/dl would represent Massive HDL-1 Hyperlipoproteinemia, since it would be some four times above the mean and median HDL-1 levels in the overall database (approximately 6 Standard Scores above the mean). Such persons would be real HDL-1 "out-liers." We found twelve persons in the entire database with this syndrome --- half of one percent. The frequencies, by age and gender, are indicated below:

Males (ages)	Total Persons	HDL-1 "Outliers"	Females Age Band	Total Persons	HDL-1 "Outliers"
17-29	585	ZERO	17-29	190	ZERO
30-39	834	8	30-39	99	ZERO
40-49	399	3	40-49	37	ZERO
50-65	143	1	50-65	10	ZERO

Male frequency = (12/1961) = 0.006. The absence of such cases in the 17-29 year-old males suggests that this is an inherited abnormality which becomes expressed after age 30 in persons who appear to be "normal" before age 30. The absence of any such persons among the females may just mean that the Livermore population sample of females, age 30 and older, is too small.

4b. What ELSE Is Characteristic of Massive HDL-1 Hyperlipoproteinemia?

For the 12 men identified with Massive HDL-1 Hyperlipoproteinemia, the tabulation below shows age at entry (which is the same as age at measurement) and the measured levels in mg/dl of

Case	Age at Entry	HDL-1	Std Sf 0-12	Std Sf 12-20	Std Sf 20-100	Std Sf 100-400	HDL-2	HDL-3
1	32	126	227	76	314	415	19	185
2	33	195	349	101	417	237	22	223
3	36	186	338	67	231	320	0	201
4	37	167	310	38	297	116	42	187
5	38	111	208	76	332	215	13	235
6	38	149	318	43	217	320	24	179
7	38	216	296	92	327	379	16	205
8	39	147	336	65	235	264	10	184
9	41	219	293	47	222	412	10	184
10	44	156	172	47	383	1030	64	205
11	49	117	166	56	177	90	0	139
12	54	264	311	74	367	562	10	221
Averages	39.9	171	277	65	293	363	19	196

HDL-1 and other serum lipoproteins. These measurements were made, ultracentrifugally, in 1954-1957. The AVERAGE values, for this group of 12 men, are shown at the tabulation's bottom.

For age, the mean is 39.9 years; for HDL-1, the mean level is 171 mg/dl in these 12 men. By contrast, the mean HDL-1 level is only 24 for the 891 Livermore males in the age-band 30-39 years (shown in Part 5, below). Although the age-match is not perfect, it is close enough to make meaningful comparisons.

How do the non-HDL-1 measurements in the 12 cases of Massive HDL-1 compare with the measurements in the cohort of 891 Livermore males (ages 30-39)? We can make the comparison by taking means, for the cohort of 891 males, from the measurements listed in Appendix-G, Figures G-2 and G-3.

The tabulated comparison, which follows, shows that the 12 males with Massive HDL-1 Hyperlipoproteinemia ALSO have massively elevated levels of the triglyceride-rich Std Sf 20-100 and 100-400 lipoproteins. From here on, our analysis in this Appendix will use the combined Std Sf 20-100 and 100-400 measurements: Std Sf 20-400.

	12 Men w. Massive HDL-1	891 Men, Ages 30-39
Std Sf 0-12 *	277 mg/dl	353 mg/dl
Std Sf 12-20:	65 mg/dl	51 mg/dl
Std Sf 20-100:	293 mg/dl	93 mg/dl
Std Sf 100-400:	363 mg/dl	54 mg/dl

* Note: The Std Sf 0-12 lipoprotein spectrum includes HDL-1, and Std Sf 0-12 measurements include HDL-1. Although the usual 1.063 gm/ml flotation runs recover somewhat less than 100% of the relatively slow-moving HDL-1 into the top fraction of the preparative ultracentrifugal run, those preparative runs do recover a high percentage of the HDL-1. Because the percentage is not 100%, the subsequent analytical runs routinely underestimate the serum concentration of the total Std Sf 0-12 lipoproteins by a small percentage.

• Part 5. The Very Notable Distribution of Elevated HDL-1 among 891 Livermore Males

The next tabulation shows the distribution of mean HDL-1 measurements when the 891 Livermore males, ages 30-39, are sorted by ascending serum levels of Std Sf 20-400 lipoproteins. After the sort, the cohort is divided into deciles, with 89 persons in each of the first nine deciles and 90 persons in the tenth. Column F shows the mean levels of Std Sf 20-400 serum lipoproteins per decile, and Column C shows the corresponding mean levels of HDL-1. Column D shows the number of persons in each decile who have HDL-1 values equal to or greater than 40 mg/dl, and Column E shows the frequency of such persons (HDL-1 => 40 mg/dl) per 1,000 persons. The last part of the tabulation has divided the tenth decile into its lower and upper halves.

Col.A Decile	Col.B Number of Men	Col.C Mean HDL-1 (mg/dl)	Col.D Cases w. HDL-1 => 40 mg/dl	Col.E HDL-1 => 40 mg/dl: Rate/1000	Col.F Mean Std Sf 20-400 (mg/dl)
1	89	22.303	1	11.2	30.47
2	89	23.460	1	11.2	54.80
3	89	22.663	1	11.2	72.45
4	89	23.247	2	22.5	89.81
5	89	23.225	2	22.5	106.8
6	89	22.326	0	0.0	126.3
7	89	22.416	2	22.5	154.0
8	89	21.663	1	11.2	186.2
9	89	21.022	0	0.0	236.8
10	90	35.177	10	111.1	415.0
	Avg =	23.750	20 = Sum		Avg = 147.263
Tenth:low half	45	20.511	0	0.0	303.133
Tenth:top half	45	49.844	10	222.2	526.933

Column C makes it obvious that the elevation in average HDL-1 levels occurs in the tenth decile of persons, ranked by ascending levels of the atherogenic triglyceride-rich Std Sf 20-400 serum lipoproteins. Column E confirms that the frequency of persons with HDL-1 elevation (=> 40 mg/dl) is 5-fold to 10-fold higher in the tenth decile (111.1 per 1,000 persons) than in the first nine deciles.

After the tenth decile is split into its lower and upper halves, it becomes clear that the upper FIVE PERCENT of the population, ranked by ascending levels of the atherogenic triglyceride-rich Std Sf 20-400 lipoproteins, account for the real elevation of mean HDL-1 levels (Column C). The top five percent of these 891 men have a frequency of elevated HDL-1 which is 222.2 per 1,000 persons --- a rate ten to twenty times the frequency in the other 95% of the sample (Column E). The same 45 men have a mean concentration of Std Sf 20-400 lipoproteins of 527 mg/dl, compared with a mean value of 147 mg/dl in the 891 men considered as a whole.

The distribution-patterns demonstrated in Parts 4 and 5 are striking --- and important. For reasons set forth in Parts 6 and 7, the distributions explain very nicely why mean LDL particle-size is lower in Cases of Ischemic Heart Disease than in Controls.

• Part 6. Definition and Demonstration of the RATIO Used in Our Analysis

The LDL or Low-Density Lipoprotein spectrum is defined, ultracentrifugally, by flotation rates of Sf 0-12 (Chapter 44, Part 3d). LDL comprises several distinct species, one of which is called High-Density Lipoprotein-1 (HDL-1) --- as discussed in Part 2. HDL-1 is the smallest and most dense Low-Density Lipoprotein which we were able to distinguish ultracentrifugally at Donner Lab. It has the correct properties of size and of density to constitute all, or nearly all, of the "small, dense LDL particles" referred to by Gardner, Stampfer, and others (Part 2). It is correct to say:

LDL = (HDL-1) + (all of the Std Sf 0-12 lipoproteins OTHER THAN HDL-1).

6a. Definition of "the RATIO" Which Is Calculated in Box 1

In Box 1 and in the next two tabulations, we refer to "the RATIO," which is this:

RATIO = (HDL-1 Concentration) / (Std Sf 0-12 Concentration Minus HDL-1 Concentration).

We can characterize the ratio as follows:

$$\text{RATIO} = \frac{\text{The HDL-1 part (small, dense part) of the LDL (Std Sf 0-12) lipoproteins}}{\text{The larger and less-dense part of the LDL (Std Sf 0-12) Lipoproteins}}$$

• The higher this ratio is, the SMALLER will be the AVERAGE size of LDL (Std Sf 0-12) lipoproteins. And:

• The lower this ratio is, the LARGER will be the AVERAGE Size of LDL (Std Sf 0-12) lipoproteins.

6b. The RATIO for Each of 891 Livermore Males (Ages 30-39)

In Part 5, above, we sorted the 891 Livermore males (ages 30-39) by ascending levels of Std Sf 20-400 serum lipoproteins, and divided them into deciles. Here, we are going to calculate the RATIO, as defined in Part 6a, for each individual in each of those same deciles --- 891 separate RATIOS.

Box 1 demonstrates the 89 calculations for Decile 1, and the arrival at the MEAN ratio for Decile 1. The other nine deciles are handled in the same way. The results are tabulated below. From here on, we will refer to this real-world cohort of 891 Livermore males as the "Control Group" or the "Controls." Part 7 explains why.

Tabulation of Mean Values for the Controls

Mean values in Columns A, B, D, and E in this tabulation match Part 5's tabulation. Columns C and F, below, present additional mean values. One purpose of this new tabulation is to ascertain the

single average RATIO for the entire group of 891 controls. It is the last entry in Column G, below:

Col.A Decile	Col.B Number of Men	Col.C Std Sf 0-12	Col.D HDL-1	Col.E Std Sf 20-400	Col.F RATIO	Col.G Cases times RATIO
1	89	308.88	22.303	30.472	0.0815	7.254
2	89	325.27	23.461	54.798	0.0812	7.227
3	89	342.37	22.663	72.449	0.0736	6.550
4	89	362.10	23.247	89.809	0.0722	6.426
5	89	354.07	23.225	106.753	0.0734	6.533
6	89	369.42	22.326	126.337	0.0817	7.271
7	89	367.56	22.416	154.045	0.0669	5.954
8	89	374.73	21.663	186.236	0.0647	5.758
9	89	383.60	21.022	236.832	0.0599	5.331
10	90	343.48	35.177	415.033	0.1968	17.712
					Sum of Col.G =	76.016
				Avg. RATIO = (76.016 / 891) =		0.085

We are now in a position to examine, in Part 7, why Ischemic Heart Disease will have an association with LDL-size.

• Part 7. Results of Our Livermore Analysis, Regarding LDL Diameter and IHD

Suppose that we regard the 891 clinically healthy Livermore males as a Control Group. Appendix-E, Part 12c, describes the nature of this population sample. The mean level of Std Sf 20-400 serum lipoproteins in this Control Group is 147 mg/dl (from above, Part 5, Column F). By contrast, in a matched set of 891 Cases of ISCHEMIC HEART DISEASE, the mean levels of the triglyceride-rich Std Sf 20-400 lipoproteins would be higher than 147 mg/dl --- as demonstrated by the statistically very significant difference (105.9 mg/dl) observed between IHD cases and the baseline population of males aged 30-39 years in the prospective Framingham Study (Gofman 1966, p.683, Table 3).

7a. A Simulated Set of 891 Cases of IHD

For illustrative purposes, we will simulate a set of 891 Cases of IHD, identical with the Control Group in Part 6b except for two modifications. The first modification: We eliminate Decile 1, which is the least likely to contribute any IHD cases. The second modification: We add a duplicate of Decile 10, which is the most likely to contribute IHD cases. These modifications assure that the mean level of Std Sf 20-400 lipoproteins in the Case Group will be greater than in the Control Group. (And this expectation is confirmed: The average of the ten Column-E entries below = 185.7.) In making these two modifications, we re-name old Decile 2 as Decile 1, etc. The new tabulation follows.

Tabulation of Mean Values for the IHD Cases (Simulated Set)

Col.A NEW Decile	Col.B Number of Men	Col.C Std Sf 0-12	Col.D HDL-1	Col.E Std Sf 20-400	Col.F RATIO	Col.G Cases times RATIO
1, new	89	325.27	23.461	54.798	0.0812	7.227
2, new	89	342.37	22.663	72.449	0.0736	6.550
3, new	89	362.10	23.247	89.809	0.0722	6.426
4, new	89	354.07	23.225	106.753	0.0734	6.533
5, new	89	369.42	22.326	126.337	0.0817	7.271
6, new	89	367.56	22.416	154.045	0.0669	5.954
7, new	89	374.73	21.663	186.236	0.0647	5.758
8, new	89	383.60	21.022	236.832	0.0599	5.331
9, new	89	343.48	35.178	415.033	0.1968	17.515
10, new	90	343.48	35.178	415.033	0.1968	17.712
		Average, Col. E->		185.733	Sum, Col.G =	86.278
				Avg. RATIO = (86.278 / 891) =		0.097

Reminder: The Case Group's average RATIO of 0.097 means 97 mg/dl of HDL-1 per 1,000 mg/dl of (the Sf 0-12 lipoproteins minus HDL-1).

7b. Meaning of a Higher RATIO in the IHD Cases than in the Controls

We can now compare the average RATIO of the IHD Case Group from Part 7a, with the average RATIO of the Control Group from Part 6b:

- RATIO in IHD Case Group: 0.097
- RATIO in the Control Group: 0.085
- The relative value is (0.097 / 0.085) = 1.14 .

The IHD Cases have an average RATIO which is 14 % higher than the RATIO for the controls.

$$\text{RATIO} = \frac{\text{The HDL-1 part (small, dense part) of the LDL (Std Sf 0-12 lipoproteins)}}{\text{The larger and less-dense part of the LDL (Std Sf 0-12 lipoproteins)}}$$

- The higher this RATIO is, the SMALLER will be the AVERAGE size of LDL particles (Std Sf 0-12 lipoproteins). And:

- The lower this RATIO is, the LARGER will be the AVERAGE size of LDL particles (Std Sf 0-12 lipoproteins).

- It follows, from their higher RATIO, that the cases of Ischemic Heart Disease (Coronary Artery Disease) on the average will be found to have LDL lipoproteins with a SMALLER average size than the LDL lipoproteins in the Controls.

• Part 8. Conclusion

Point 1: There is no doubt that the overall Std Sf 0-12 lipoprotein spectrum is atherogenic. What we do not presently accept is the hypothesis that the smallest, most dense species in the 0-12 spectrum are ESPECIALLY atherogenic.

Point 2: Average LDL diameter has been reported by Stampfer and Gardner to be 1.2% to 1.9% smaller in IHD Cases than in Controls (Part 3a). Our own comparison, of Cases vs. Controls (Parts 7a and 7b), used serum concentrations to establish that a shift toward smaller average LDL diameters in IHD Cases vs. Controls will occur inevitably as the BY-PRODUCT of there being higher mean serum concentrations of triglyceride-rich Std Sf 20-400 lipoproteins in IHD Cases than in Controls. Therefore, the observation of smaller average LDL size, in IHD Cases than in Controls, does not necessarily indicate that the small, dense LDL particles are at all atherogenic.

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Box 1 of Appendix-H

Calculation of the Mean RATIO for Decile 1 of the 891 Livermore Males.

Col.A HDL-1	Col.B STD (Sf 0-12 Minus HDL-1)	Col.C STD (Sf 0-12)	RATIO Col.D HDL-1 / (Sf 0-12 Minus HDL-1)	Continuation of Cols A through D. HDL-1	STD (Sf 0-12 Minus HDL-1)	STD (Sf 0-12)	RATIO HDL-1 / (Sf 0-12 Minus HDL-1)
30	198	228	0.1515	24	316	340	0.0759
27	358	385	0.0754	27	378	405	0.0714
21	248	269	0.0847	18	448	466	0.0402
15	274	289	0.0547	42	193	235	0.2176
12	333	345	0.0360	24	316	340	0.0759
27	172	199	0.1570	21	340	361	0.0618
24	325	349	0.0738	21	225	246	0.0933
24	361	385	0.0665	30	295	325	0.1017
24	265	289	0.0906	18	378	396	0.0476
24	339	363	0.0708	24	265	289	0.0906
24	308	332	0.0779	21	149	170	0.1409
15	191	206	0.0785	12	373	385	0.0322
21	203	224	0.1034	27	240	267	0.1125
34	289	323	0.1176	24	256	280	0.0938
30	281	311	0.1068	9	262	271	0.0344
21	228	249	0.0921	24	316	340	0.0759
36	365	401	0.0986	18	305	323	0.0590
24	252	276	0.0952	26	324	350	0.0802
36	296	332	0.1216	18	246	264	0.0732
18	202	220	0.0891	14	259	273	0.0541
36	399	435	0.0902	18	258	276	0.0698
17	346	363	0.0491	18	347	365	0.0519
18	269	287	0.0669	18	150	168	0.1200
21	198	219	0.1061	18	345	363	0.0522
24	269	293	0.0892	15	182	197	0.0824
30	422	452	0.0711	18	172	190	0.1047
39	418	457	0.0933	15	274	289	0.0547
24	294	318	0.0816	23	192	215	0.1198
18	363	381	0.0496	23	230	253	0.1000
16	353	369	0.0453	27	327	354	0.0826
24	274	298	0.0876	18	338	356	0.0533
12	228	240	0.0526	27	299	326	0.0903
21	290	311	0.0724	24	386	410	0.0622
24	238	262	0.1008	27	255	282	0.1059
27	265	292	0.1019	30	405	435	0.0741
27	387	414	0.0698	18	331	349	0.0544
21	239	260	0.0879	18	302	320	0.0596
39	405	444	0.0963	15	207	222	0.0725
15	263	278	0.0570	15	276	291	0.0543
21	293	314	0.0717	21	241	262	0.0871
30	243	273	0.1235	15	205	220	0.0732
12	163	175	0.0736	18	287	305	0.0627
18	246	264	0.0732	17	397	414	0.0428
30	275	305	0.1091	18	343	361	0.0525
18	244	262	0.0738				
Sum of RATIOS for 45 men--->			3.8357	Sum of RATIOS for 44 men---->			3.4150

Sum of RATIOS for 89 men = 3.8357 + 3.4150 = 7.2507

For Decile 1, Mean RATIO, all 89 men = 7.2507 / 89 = 0.0815

RATIO, defined in text:

$$\frac{\text{Concentration of HDL-1 Lipoproteins}}{\text{Concentration of Std Sf 0-12 Lipoproteins MINUS Concentration of HDL-1 Lipoproteins}}$$

Related text = Part 6b.