An Estimation of Deviation Towards the Mean for Serum Lipid Fractions in Patients Followed for a Varied Duration

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Abstract

We evaluated the deviation towards the mean and attempted to quantify it among the different lipid fractions in patients. The study was done retrospectively on patients who were judged to be metabolically stable and had repeated total cholesterol (TC), high density lipoprotein cholesterol (HDL) and triglyceride (TG) measured in a single laboratory with known coefficient of variation for repeated measurements. The patients and their data were separated into 3 groups. Group A (56 patients) evaluated the difference between the first and its average obtained from an average of 4 samples per patient within a mean of 9 months. Group B, examined pairs of data taken an average of 12 months apart. Group C, evaluated 45 patients with at least 3 data points each a year apart. Linear correlations were applied for the repeats *versus* the first samples. Highly significant correlations were obtained for all the groups. The slopes were less than one (generally between 0.66 and 0.85) and intercepts had positive values. This was seen even for the HDL whose range of values span 25 to 85 mg per cent. These results strongly supported deviation towards the mean such that from our calculation and in this population, a person with an initial TC of 200 mg per cent would have from 37 to 61 per cent chance of obtaining a significantly higher value if the test was repeated. The magnitude of the change would average 30 mg per cent for cholesterol and as much as 30 per cent of the initial values for TG. In this evaluation, the time intervals between repeats did not appear to influence the result. Yearly follow-ups also did not seem to exhibit the effect of aging. However, the latter 2 conclusions rested on a small number of observations. It is suggested that several repeated estimations of these lipid fractions be done before a decision is made towards intervening. In instances of epidemiological studies, it is imperative to obtain representative repeated measurements since this deviation towards the mean will alter the slope of the events *versus* the lipid-variables.

Key word : Total Cholesterol, Triglyceride, High Density Lipoprotein, Repeated Sampling

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Regression towards the mean explains a phenomena whereby a measurement (e.g. blood pressure, blood lipids), when being repeated will fluctuate directionally towards its average and towards the average of the group[1]. The result is that an initially high value will, when remeasured, become lower and vice versa, a low value will become higher. Bland and Altman[2] insisted that this is statistical and not biological. They[2] also showed the earliest description of this phenomena which was reported in 1886. The effects of this in the medical world are quite extensive but can also be seen in non-biological events[3]. In every day practice, some of us hastily start treatment on a single abnormal finding and then become confused as to whether a good response was related to the treatment or to regression towards the mean. Its not only the physician that loses direction but also the patient since he/she would have been exposed, perhaps long term, to a drug which may not be beneficial. Another effect would be seen on drug trials where the improvement such as a reduction of blood pressure or of the total cholesterol would be credited to the interventions especially if the study was designed to evaluate those "high" risks. Deviation towards the mean may explain the observation in the MRC trial[4] on treatment of mild hypertension where 40 per cent of those on placebo whose screened and baseline diastolic blood pressure was 98 mmHg, was found after one year, to have diastolics of less than 90. Kotchen et al[5] showed that this phenomena can be separated from the effect of aging by tracking the systolic blood pressure every two years. In epidemiology, the result of this deviation towards the mean would be in underestimating the slope of the relationship between events and the measured variables[6]. Worse still, if one uses the wrong surrogate such as frequently done when one expresses the relationship of cardiovascular disease with total cholesterol rather than the LDL component. This was termed surrogate dilutional effect by Law et al[7]. The examples cited by them suggested that the dilutions due to regression towards the mean and those due to the surrogate effect can be substantial enough to change the ischemic heart mortality slope from 17 per cent to 27 per cent per a 23 mg per cent change in cholesterol concentration.

In an earlier report by us[8], we summarised the result of repeated lipid estimations (average of 6.2 samples per patient) at varied intervals in 86 patients. The SD of repeated measurements of the lipid fraction per patient was expressed in terms of coefficient of variation (CV=SD/average) and the CV from different patients were further averaged. The result showed that the average CV for total cholesterol (TC) was 8.9 per cent, for HDL-cholesterol (HDL) was 12.6 per cent, and for triglyceride (TG) was 25.8 per cent and these CV were independent of the concentration of these fractions. We were not as rigorous as Smith et al[9] in evaluating the relationship to sampling intervals, number of samples nor duration of follow-up. Neither did we try to account for the effect of "aging", the effects of deviation towards the mean nor for variations due to laboratory methods. This report is our attempt to do so.

Hence the objectives were:

1. Examine the phenomena of deviation towards the mean using the results of repeated lipid evaluation (from a single special laboratory)[10] such that the first sample will be compared to a). the subsequent average obtained within a narrow time interval b). with another sample taken a year and in some, 2 years later.

2. Quantitate the probability that the repeat measurement will have values higher or lower than could be accounted for by the laboratory variation and as well, the relationship of this probability to its initial values.

3. Quantitate the yearly alteration to try and separate the variations due to fluctuations towards the mean and those due to "aging" in the absence of other known perturbation.

MATERIAL AND METHOD

The subjects for the present study have been reported[8]. In general, they were candidates followed at the cardiac lipid clinic until 1994 at this University Hospital. The fasting blood lipid fractions were estimated by the division's laboratory using the enzymic calorimetric method (Boehringer Mannheim). The coefficients of variation (CV) for repeated measurements for this laboratory were: 2.7±1.2 per cent for TC (range 0.5 to 5.0%); for HDL this was 1.2±0.6 (range 0 to 3.3%); and for TG, 3.9±1.5 (range 1.0 to 6.6%)[10]. These patients were non-diabetic, had no proven thyroid dysfunction, not on medication for weight reduction nor lipid lowering within 4 months prior to any of the blood tests. They, however, could be on anti-

hypertensives and anti-ischemics including beta-blockade and low dose diuretics. All were walk-in candidates and for this analysis, no selection was made on samples that had TG greater than 400 mg per dL (mg%). We subdivided their data into 3 groups (A, B, C) depending on the choice of intervals between data points. Within each group and for each subject, the inclusion of the data was such that the lowest and highest body weight during the interval of comparison or analysis did not exceed 3 Kg.

Group A consisted of candidates with 3 or more lipid samples such that adjacent data-points were separated by intervals less than or equal to 6 months and the total duration for the evaluation of each patient did not exceed 2 years. The average of all data for each lipid fraction per patient was then calculated. Group B consisted of pairs of samples in which the interval between collections had to be within 6 to 18 months under similar constraints as in group A. In this group, some patients had more than one possible pair of data, hence, initial data analysis also compared the 56 pairs from 56 patients and the 105 pairs from the same 56 subjects. This artificial increase in number of observations did not essentially alter the final conclusions, hence, the presented results only included these 56 pairs. In group C, we examined long term follow-up using the same constraints such that intervals between successive data had to be 6-18 months apart and there had to be more than 2 data points per subject. This resulted in approximately yearly data for at least 2 years. We then evaluated the pattern of differences in lipid values between year 1 or year 2 *versus* year zero which would be the first sample.

Data Analysis

1. Descriptive data utilised the mean and standard deviation (SD).

2. The relationship between the first and subsequent samples was examined with linear correlations using the first sample as the independent variable. Similar assessment was made using the difference between the subsequent sample and the first as a function of the first. The assumption was that if this latter showed a negative relationship then deviation towards the mean would have been substantiated.

3. In the evaluation of the per cent probability of a repeat measurement having a "significantly" higher or lower value than the initial, we defined significance as to mean different by more than the laboratory variation. This is the average plus 2 SD of the CV for repeated measurements from this laboratory (given in the methods section) and came to 5.1 per cent, 2.4 per cent and 6.9 per cent for TC, HDL and TG respectively. The probability was then calculated along this manner. A subclass with closely related values were arbitrarily chosen (e.g. TC between 200 to 210) such that there will be at least 3 samples per class and the limits are well separated from the next subclass. We did not partition these according to the percentile distribution. For each subject within this class, the difference between the subsequent and initial samples was expressed as a per cent of the first sample and then noted as either + (where the % difference was greater than the laboratory variation), negative or not significantly different (where the difference was within the laboratory variation). Then the number of subjects with + or - were added up and expressed as percentage of the total possible for that class. This was done separately for each lipid fraction since the number of subjects per subclass were different. These probabilities were then plotted as a function of the average value of each subclass and the relationship approximated linearly.

4. In order to evaluate the magnitude of the deviation, the values of the percentage difference which were considered significant in group C subjects were expressed in absolute terms (i.e. disregarding the direction of the differences). These were then grouped and averaged according to certain ranges of values of the initial samples.

Simple statistical methods were used such as F statistics for the significance of the linear regression and *t* statistics for the paired differences.

RESULT

Group A. There were 56 data sets from 56 subjects. The mean age was 51.5 $\pm$ 9.5 and 53.6 per cent were females. The average duration of data collection per subject was 9.1 $\pm$ 5.1 months, and the average number of data-points per subject was 4.0 $\pm$ 1.1 The mean values of the average TC, HDL and TG were 256.2 $\pm$ 32.8, 48.0 $\pm$ 12.0 and 148.6 $\pm$ 63.3 all in mg per cent respectively. The high TC suggested that these subjects were biased towards being hypercholesterolemic and hence the need for repeated tests at close intervals. Table 1 shows the results of the linear regressions. The averages *versus* the initial samples were, as expected, highly correlated showing coefficients exceeding 0.80 for all

Table 1. Linear regression of group "A" subjects comparing the average with the first sample (N=56).

	Y	r	intercept	slope	F
TC	Mean	0.84	72.8	0.690	133.7
	Mean-TC1	-0.57	72.8	-0.305	25.7
HDL	Mean	0.90	6.0	0.856	232.2
	Mean-HDL1	-0.33	6.0	-0.144	6.6
TG	Mean	0.80	37.9	0.780	94.8
	Mean-TG1	-0.34	37.9	-0.213	7.1

TC1, HDL1, TG1 represent the first serum estimations.
Mean = the average as defined in the text.
Mean-TC1= the absolute difference between the mean and the first total cholesterol.
F = F statistic. r = regression coefficient

the three lipid fractions. However, when examining their differences as a function of the initial values, the 'r' lessened but were still significant and all showed negative slopes. From these one can calculate the values at which the difference changes direction (i.e. change from negative to positive): 239 from a group mean of 256 mg per cent, 42 from a group mean of 48 and 176 from a group mean of 149 (all in mg%) for TC, HDL and TG respectively. (These values were subsequently regrouped in Fig. 5). Fig. 1 shows the distribution of the probabilities as a function of the varied classes of initial concentration and varied lipid fractions (TC1, HDL1 and TG1, where 1 implies the first blood sample). Except for HDL, these relationships could be expressed linearly (shown as * on the regression equation). A negative slope for the subgroups with positive possibility implying that the probability of the average having higher value than the initial sample lessened as the initial values become larger, and vice versa, a higher percentage of obtaining negative difference as the initial value lessened. Hence, for TC and TG, and given this bias of patients with high TC, deviation towards the mean occurred and could be quantified. Using TG as an example, one can estimate from the equation for the regression line, that if the first value for TG was 80 mg per cent, then there would be a 65 per cent chance of the mean being more than 6.9 per cent (this is the mean +2SD of the laboratory variation) and 18 per cent chance of the mean being lower. If the first TG was 200 mg per cent, then there would be a 1 in 5 chance of the mean being

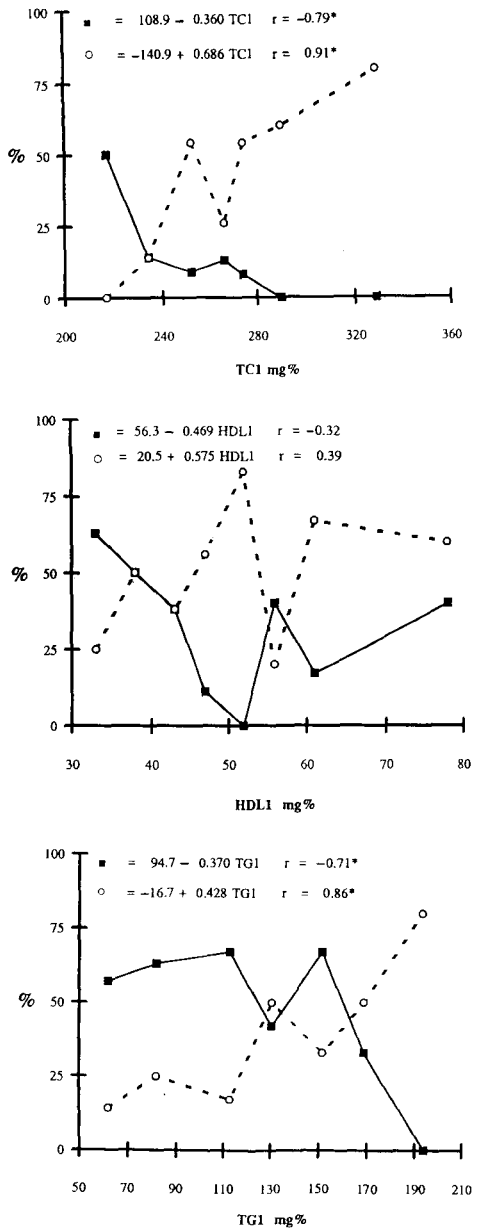

Fig. 1. This consists of 3 panels (for TC, HDL and TG) from group A subjects. It shows per cent probability of a mean (of the lipid fraction) of a patient being significantly higher (+) or lower (-) than the initial measurement designated as TC1, HDL1 and TG1. These probabilities were plotted as a function of the initial values and were then fitted to a linear regression line whose equation are shown on the top of each panel.
■ = positive probability, o = negative probability and * implies statistically significant linear regression using the F distribution.

higher but a 69 per cent chance of it being lower than 6.9 per cent of 200 mg per cent (these values are also summarised in Table 6). It has to be noted that samples were discarded if the TG was greater than 400 mg per cent, and the choice of the subclasses was really arbitrary.

Group B. There were 56 patients and 35 of them were the same as the previous group A and with 8 of the 35 having the same starting initial blood samples. The average age was 52.8 ± 11.7, and the average time interval between the 2 samples was 12.4 ± 2.3 months. The average lipid values for the first samples and the difference between the second and the first samples were: 241.1 ± 34.7 and 1.2 ± 31.5 mg per cent for TC; 49.4 ± 12.9 and -1.5 ± 9.9 mg per cent for HDL; 125.3 ± 55.3 and 7.7 ± 49.7 mg per cent for TG. Again this group comprised subjects with relatively high TC. It should also be noted that these selected pairs per patient needed to be separated by intervals of 9 to 18 months while in between samples were discarded. Table 2 shows the result of the linear regressions presented in a similar manner to Table 1. The two sets of data (groups A and B) were quite similar except the slope of TG *vs* TG1 was less steep in group B. With regards to the assessment of probabilities in group B, (Fig. 2) only the TG showed a grossly linear relationship. The poor relationships for TC and HDL could be due to the small number of patients per subgroups (varying from 3 to 13), although the distribution of these numbers of patients per subclass were not markedly different among the 3 lipid fractions.

Group C consisted of 45 patients with ages averaging 51.8 ± 11.7. Sixteen were patients who

Table 2. Linear regression of group "B" subjects comparing the second to the first measurements (N=56).

	Y	r	intercept	slope	F
TC	TC2	0.65	64.2	0.739	39.0
	TC2-TC1	-0.29	64.2	-0.261	4.9
HDL	HD2	0.74	6.6	0.835	67.2
	HDL2-HDL1	-0.21	6.6	-0.164	2.6
TG	TG2	0.60	55.8	0.465	30.8
	TH2-TG1	-0.43	55.8	-0.383	12.0

TC2, HDL2, TG2 represent the second serum values.
TC2-TC1 = absolute difference between TC2 and TC1
The other abbreviations are similar to those of Table 1.

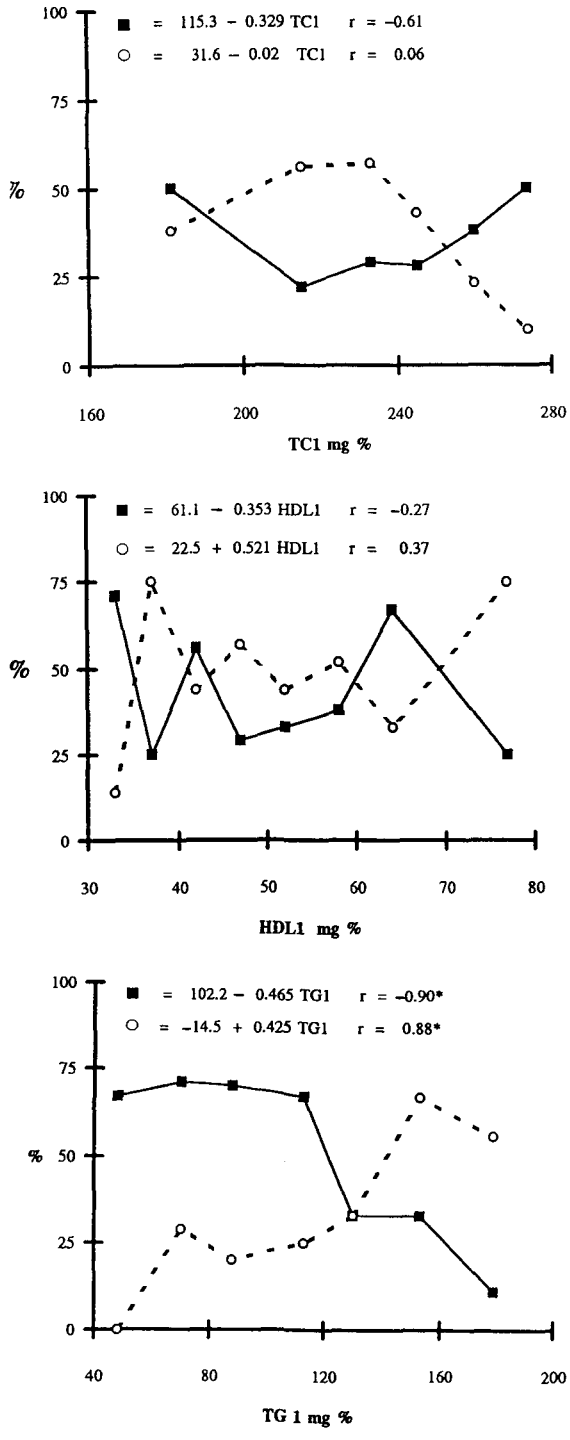

Fig. 2. Similar plot as in Fig. 1 but represents group B and comparing the second measurement a year later to the first. Note that only TG showed a linear-like pattern between these probabilities and their initial values.

Table 3. Average (± 1 SD) values (in mg%) for lipid fractions in successive years in group "C" subjects. (N = 45).

	Sample 1 (year 0)	Sample 2 (year 1)	Sample 3 (year 2)
TC	213.4 ± 43.4	219.3 ± 43.6	218.3 ± 43.1
HDL	50.8 ± 14.2	51.5 ± 14.2	50.3 ± 15.0
TG	112.3 ± 56.8	105.5 ± 53.3	112.5 ± 65.0

were also included in group A and B. Two thirds were females. There was an average of 4.1 ± 1.2 samples per patient. The method of selection allowed 45 patients with at least 3 data points averaging 12-13 months between these samples. There were 26 patients who had 4 data points and 15 with 5 data points, the latter covered 4 years with year zero being the first sample.

Table 3 shows the average values for the different lipid fractions for the 3 sets of data separated almost yearly. Compared to the first 2 groups, group C showed a population with lower TC and TG and perhaps reflecting a more generalised set rather than the hyperlipemics. The mean values showed no variation with time and paired differences also showing no significant differences. A similar pattern was seen (data not given) if one examined the group of 26 followed for 3 years (i.e. each subject had 4 sample points) or the group of 15 followed for 4 years. Hence, there is no support for the rising group mean if followed for up to 4 years. Fig. 3 shows subclasses of patients with closely related initial values and their subsequent yearly average for TC, HDL and TG. There are trends that the group which started off with lower values at year zero will show higher yearly repeats and vice versa those with higher initial values will show a fall, but because of the small number per subclass and the wide scatter, very few of these averages reached statistical significance. Also as a function of time, there appeared to be no consistent rising values after the second sample, i.e. after year 2 again showing lack of rise with age. (NB. similar patterns were seen if we were to examine only those who had 4 or 5 years follow-up). Recalculation after slight alteration of the criteria for choosing the subgroups, did not change this pattern.

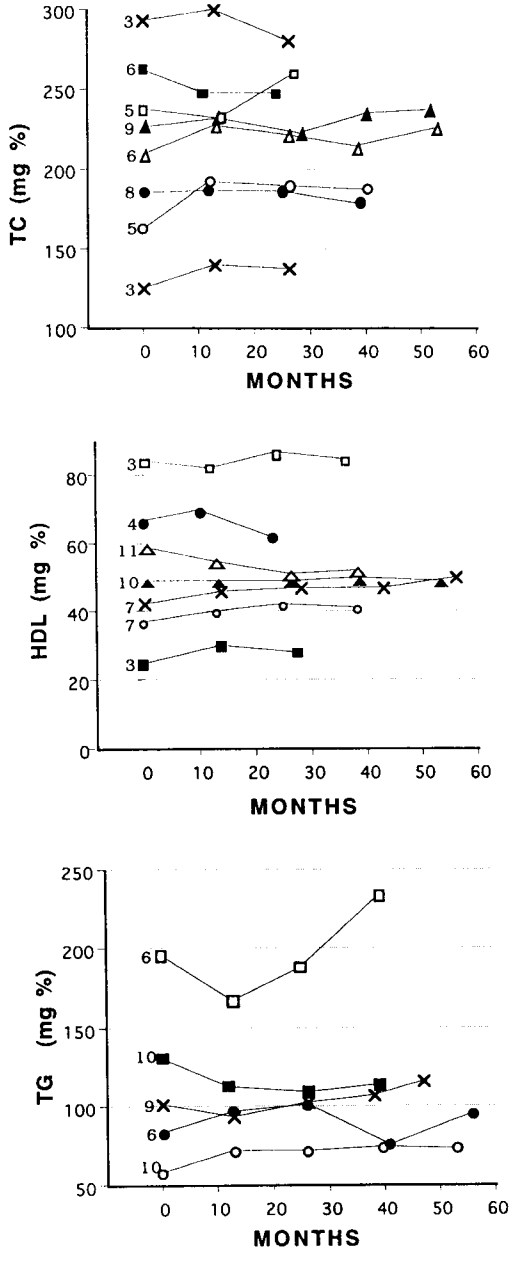

Fig. 3. The 3 panels show yearly averages per subclass of initial values for TC, HDL and TG (from top to bottom). The number besides the symbols are the N's per each subclass being followed longitudinally. For TG these did not add up to 45 because of 4 outliers. After the third data point (i.e. the second year), these N's per class lessen but would still be > 2.

Table 4. Linear regression for group "C" subjects between the second and third samples *vs* the first (N = 45).

	Y	r	intercept	slope	F
TC	TC2	0.81	45.9	0.812	81.3
	TC2-TC1	-0.30	45.9	-0.188	4.4
	TC3	0.79	51.2	0.783	70.3
	TC3-TC1	-0.33	51.2	-0.217	5.4
HDL	HDL2	0.89	6.6	0.884	57.4
	HDL2-HDL1	-0.25	6.6	-0.116	3.8
	HDL3	0.76	9.9	0.794	35.2
	HDL3-HDL1	-0.35	9.9	-0.206	6.0
TG	TG2	0.71	31.1	0.662	42.8
	TG2-TG1	-0.45	31.1	-0.338	11.1
	TG3	0.77	14.0	0.877	61.1
	TG3-TG1	-0.16	14.0	-0.122	1.2

TC3, HDL3 and TG3 represent the third serum values collected at the end of the second year.
TC3 - TC1 = absolute difference between 3rd TC and first.
Other nomenclatures are similar to that of Table 1 and 2.

Table 4 shows the result of the linear correlation between the 2nd or third samples *versus* the first for each of the lipid fraction and the linear correlation between the paired difference *versus* the initial. There were as expected, highly significant linear correlations between the second and first, and the third and first samples for all the lipid fractions, with correlation coefficients (r) all greater than 0.7 and slopes greater than 0.66. No differences were observed (with regards to slopes and 'r') between correlations obtained among those data separated one year apart *versus* those separated at least 2 years apart (e.g. comparing the linear regression equation between tests 2 *vs* 1 with test 3 *vs* 1) perhaps suggesting that the time between samples is not the deciding factor for this deviation to the mean to be apparent. When the relationship of the difference *versus* the initial values were examined, the slopes were all negative similar to the analysis on groups A and B. These negative relationships were all significant except for a portion of the TG (the last row of this table which represented the third minus the first TG samples). Values where positive differences change to negative, calculated from these regression lines showed that for TC (2nd *versus* 1st and 3rd *versus* 1st) these were at 244 and 236 mg per cent respectively; and 57 and 48 mg per cent for HDL and 92 mg per cent for the 2nd *versus* the first TG.

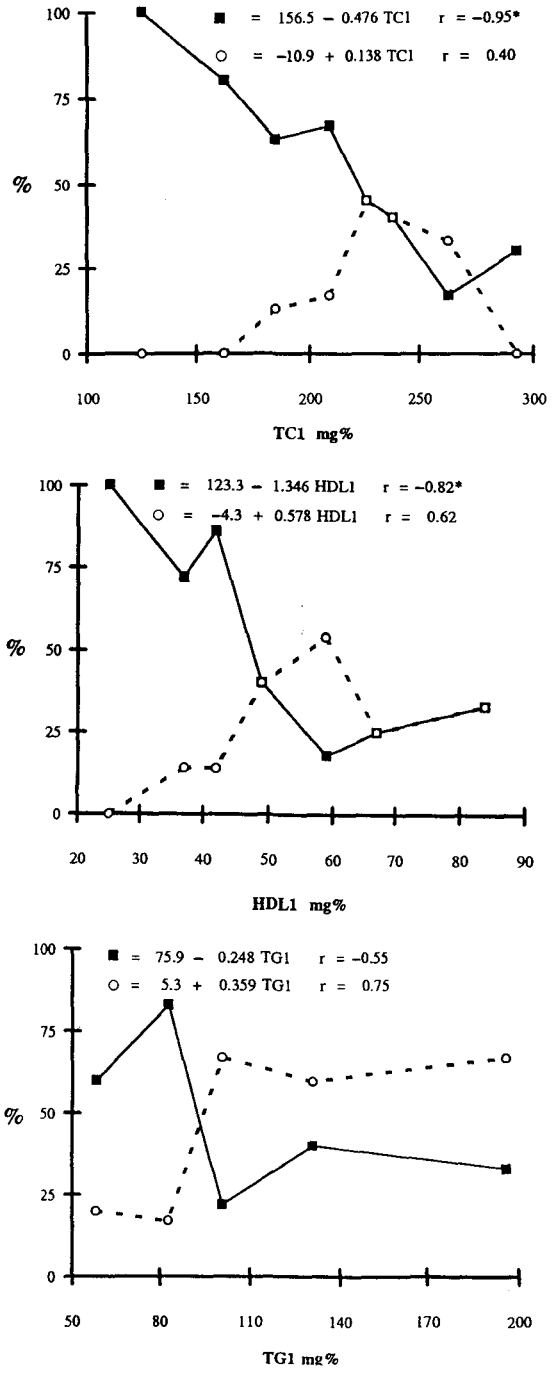

Fig. 4. Similar plot as in Fig. 1 and 2 for group C patients, and shows the relationship of the probabilities of the second sample a year later to be significantly different from the first value. The N's per group are similar to those in Fig. 3. Notice that the ranges of values for the abscissa for TC1 are wider than those of groups A and B.

Fig. 4 shows plots of the probability of the sample a year later to have higher or lower values given a certain range of the initial value and accounting for the laboratory variation. The subgrouping here is the same as those shown for the yearly follow-up in Fig 3. As can be seen, the trend is for those with initially low values to have a greater probability of the yearly repeat to be higher rather than lower, and vice versa for the initially high values. However, the linear regression lines for these relationships generally showed lack of significance. Altering the subgrouping (only done for TG) can affect the statistical significance of the linear relationship although maintaining semblance of the pattern. This was seen with the TG. From these relationships, one can calculate, as in previous sections, that if the first TC sample was 200, or 240 or 300 mg per cent, there should be a 61 per cent, 42 per cent and 14 per cent chance of the next sample being greater by 5.1 per cent of the average of the initial and second sample. For HDL, and choosing values of 30 and 60 mg per cent, the probabilty will be 83 and 43 per cent that the second samples will have a value greater by more than 2.4 per cent.

Table 5 presents projected values from the linear regression lines in Table 1, 2 and 4 where the difference between the first and subsequent values changes signs. These projected values were shown with the mean values for each group. The TC were surprisingly constant for groups A, B and C despite differing population means. The HDL showed a wider range between 42 and 57 mg per cent despite a similar population means among the 3 groups. Only the TG showed, as expected that the cut off points were related to the group mean.

Table 6 gives per cent probabilities from the linear regression lines in Fig. 1, 2 and 4 for selected initial sample values. There is practically no data for HDL since the regression lines were generally not significant.

Table 7 shows the magnitude of the significant deviations independent of the direction of the differences i.e. independent of whether it would be greater or smaller. For the TC, the difference between the second and the first samples varied from 25 to 38 mg per cent or 11 to 14 per cent. For the HDL, these came to 5-6 mg per cent or 10-13 per cent. For the TG, these turned out more expectedly in that they showed concentration dependency ranging from 21 to 67 mg per cent or 29 to 34 per cent for initial TGs of 50 to 230.

Table 5. Projected values *vs* their averages from the slopes of the regression lines in Tables 1, 2 and 4.

	Group A		Group B		Group C	
	Project	Mean	Project	Mean	Project	Mean
TC (mg%)	239	256	246	241	244	213
HDL (mg%)	42	48	40	49	57	51
TG (mg%)	176	149	146	125	92	112

Table 6. Per cent probability that a second measurement will be significantly different for specific values of the first.

First values		Group A		Group B		Group C	
		+	-	+	-	+	-
TC at	200 mg%	37	-4	NS	NS	61	NS
	240 mg%	23	24	NS	NS	42	NS
	300 mg%	1	65	NS	NS	14	NS
HDL at	30 mg%	NS	NS	NS	NS	83	NS
	60 mg%	NS	NS	NS	NS	43	NS
TG at	80 mg%	65	18	65	20	NS	NS
	200 mg%	21	69	9	71	NS	NS

The projections from this table come off Fig. 1, 2 and 4.
The values are in %. NS implies non-significant linear relationship hence not calculated.
NB. The positive and negative percentages will not add up to 100 because some proportion have differences within the laboratory variations.

DISCUSSION

The present data showed that even with the small number of observations, deviation towards the mean can be demonstrated for the 3 independently measured lipid fractions, TC, HDL and TG. This was shown by using linear correlations between subsequent and first samples and looking at various manipulations of the differences such as percentage or absolute differences and excluding those due to variations which may have arisen from the method of measurements. Perhaps one can expand on the finding that for all lipid fractions, linear correlations between subsequent and initial samples showed significant slopes of less than one and positive intercepts implying that an initially lower value will tend to increase if the

Table 7. Magnitude of the deviation excluding laboratory variations. (Group C patients comparing second and first samples).

	Range	N	MEAN	SD	N'	%MN	%SD	MN'	SD'
TC	150-200	12	178.6	11.6	9	16.0	8.2	28.1	13.1
TC	200-240	19	222.8	10.6	16	11.2	4.6	24.8	10.0
TC	>240	10	270.7	17.7	5	14.3	11.0	38.1	31.0
HDL	35-45	14	39.8	2.9	13	12.7	7.4	5.1	3.1
HDL	50-65	13	57.6	3.5	11	9.9	8.5	5.8	5.2
TG	50-100	18	76.3	16.5	16	29.3	25.5	20.8	14.5
TG	100-130	10	116.7	11.3	9	33.0	22.6	40.0	27.1
TG	180-230	7	199.3	13.7	7	34.0	21.6	67.0	40.9

Range = range of values for the initial samples selected for this analysis.
N, MEAN, SD = number of observation, the average and standard deviation of the data (all in mg%) within these ranges.
N', MN' and SD' represent those whose absolute differences in mg% exceeded the laboratory variations.
%MN and %SD are the absolute differences expressed as percentages of the initial samples.

test is repeated and vice versa with an initially high value. As an aside, the correlation coefficient previously reported was 0.65 for TC taken one year apart[11] on 1,556 subjects. In the Framingham study[12], the samples were taken 8 years apart and the correlations were examined separately for the 620 males and 985 females. The correlations between repeated measurements were 0.692 and 0.675 for TC and HDL in males; and 0.613 and 0.604 for TC and HDL in females. The report[12] also showed that the averages for the HDL decreased with time (46.0 to 44.5 mg per cent in males and 58.0 to 54.2 in females) in a similar direction to the TC suggesting perhaps that these changes were unlikely to be biological where one would expect that TC and HDL would alter in the opposite directions.

The present report showed as well that these deviations had appreciable magnitude, of the order of 30 mg per cent for TC, 5-6 mg per cent for HDL and 30 per cent for TG. These are not far off from the range of acceptable therapeutic response.

The weakness of the present analysis are many but probably does not affect the conclusion but the quantification. One of the main weaknesses is in the small number of observations resulting in using data from the same patients for the different groups although not all of them from the same initial values. There was a pool of 86 patients, and of these, 15 were shared by all the 3 groups, 34 were shared by at least 2 of the 3 groups. One cannot be certain whether the analysis would yield a different conclusion if one chose all the possible combinations of pairs of repeats from all patients independent of the time intervals. In the same vein with regards to the quantification of the per cent probabilities of obtaining significantly different values on repeating a test, we did not try varied combinations of separating the classes. In group C and for TG, we found that there were differences in the statistical significance with a different selection of subclasses but the pattern did not alter.

The present study cannot give an answer as to the appropriate interval to repeat the blood sampling. However, extrapolating from the intervals (varying from 4 months to 2 years) between samples in the 3 groups, and also assuming that these deviations were purely statistical, then the repeats could be performed at any time. Perhaps the reason for not repeating at too short an interval may be to circumvent potential factors operating at longer periodicity. Bookstein et al[13] found that a repeat 2 days later for cholesterol in 51 volunteers gave a slope of 0.96 for the linear relationship.

How should this deviation towards the mean be used to guide our daily practice?. Unless urgent, such as excessively high TC values in proven severe coronary artery disease, perhaps it is more prudent to try and obtain an average with an emphasis on calculating out the LDL-C. If an intervention (a diet or drug) is deemed necessary on an individual basis, then another mean should be obtained months afterwards to help in the decision making as to alter the dose or to alter therapy. However, for a longitudinal study such as to obtain

incidences of stroke or coronary artery disease as a function of these lipid fractions, then a repeat is imperative, in order to correctly delineate the slope of the relationship. The repeat, however, may need to be only a proportional representation rather than on all subjects.

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การศึกษาในด้าน deviation towards the mean ของระดับไขมันต่างชนิดในผู้ป่วยติดตามต่างระยะเวลา

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ศึกษาผู้ป่วยโดยที่คาดว่าขณะติดตามเขาเหล่านี้ ไม่มีการเปลี่ยนแปลงทางเมตาบอลิซม (เช่น น้ำหนักคงที่ ไม่เกิดโรคแทรก ไม่ทานยาลดน้ำหนัก ฯลฯ) เจาะเลือดซ้ำในระยะเวลาต่างกันเพื่อวัดระดับโคเลสเตอรอล (TC), HDL-โคเลสเตอรอล (HDL) และไตรกลีเซอไรด์ (TG) และวิเคราะห์เลือดในห้องตรวจของหน่วย โดยที่มีข้อมูลในด้านค่าผันแปรของการวัดสารเหล่านี้

แบ่งข้อมูลเป็น 3 จำพวก แต่ละกลุ่มมีข้อมูลของ 45–56 คน ขึ้นกับระยะเวลาและวิธีเปรียบเทียบผลเลือด ศึกษาข้อมูลเหล่านี้โดยใช้ linear regression เพื่อหาความสัมพันธ์ระหว่างค่าของไขมันต่างชนิดที่เจาะซ้ำและที่เจาะครั้งแรก พบว่าไม่ว่าเลือกกลุ่มเปรียบเทียบชนิดใด ค่าที่ได้จากการเจาะซ้ำสัมพันธ์อย่างใกล้ชิดกับค่าแรก โดยที่ slope จะน้อยกว่าหนึ่งเสมอไป (ส่วนมากจะเกิน 0.7) และ intercept มีค่าเกิน 0 สิ่งนี้สนับสนุน deviation towards the mean ซึ่งแปลว่าถ้าได้ค่าสูงจากการตรวจเลือดครั้งแรก โอกาสจะสูงที่จะได้ค่าต่ำกว่าเมื่อเจาะซ้ำ. ค่าแตกต่างนี้จะประมาณ 30 มก% สำหรับ TC และร้อยละ 30 สำหรับ TG การศึกษาไม่พบว่าผลที่ได้นี้ขึ้นกับช่วงเวลาของการเจาะเลือดซ้ำ หรือการติดตาม 2–3 ปี เมื่อเป็นเช่นนั้นจึงแนะนำว่า ในการดูแลผู้ป่วยควรวัดระดับไขมันให้ได้ค่าเฉลี่ยและค่าเบี่ยงเบนก่อนตัดสินใจรักษา หรือก่อนปรับเปลี่ยนการรักษาในด้านการศึกษาเชิงระบาดวิทยาเพื่อหาอุบัติการณ์ของโรคและระดับไขมันเหล่านี้ การตรวจซ้ำจะช่วยเพิ่มความเที่ยงตรงในการคำนวณความสัมพันธ์นี้.

คำสำคัญ : โคเลสเตอรอลรวม, ไตรกลีเซอไรด์, เอ็ชดีแอล, การเก็บตัวอย่างซ้ำ

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