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### HIGH DENSITY LIPOPROTEINS AND EXERCISE

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#### ABSTRACT

High density lipoprotein (HDL) and total cholesterol (TC) levels have been measured and their ratio compared in four groups of subjects — those with vascular disease, controls, middle-aged “keep-fit” enthusiasts and young physical education students. Each group has also been subjected to analysis of risk factors known for atherosclerosis.

The HDL level was significantly raised in the Athletic and Exercise groups even though the latter were more overweight and had the highest total cholesterol level. This would appear to indicate that exercise may exert its protective effect against atherosclerosis, at least in part, by elevating the HDL level above a certain critical level.

The HDL/TC ratio was significantly lower in the Vascular group and we would advocate that any ratio less than 20% is highly suspicious of atherosclerosis.

We suggest that both the HDL level and HDL/TC ratio should be viewed together as reflecting the risk of atherosclerosis.

**KEY WORDS:** High density lipoproteins, Exercise, Atherosclerosis.

#### INTRODUCTION

Increasingly nowadays, the ordinary individual is advised at all levels to take more physical exercise. There has been some response to this as seen by the recent vogue for jogging, which has reached almost epidemic proportions in some Western countries. Apart from the effect of regular exercise on respiratory function, pulse rate, blood pressure, hormones and the creation of a feeling of “being fit” (Lopez-S et al, 1974), it may be the continuous effect on serum lipoproteins over the long term which is of greater importance by limiting or overcoming occlusive atherosclerotic disease of the arteries.

The cholesterol content of the blood is carried as very low (triglyceride), low, and high density lipoprotein molecules. It is the low density lipoproteins (LDL) which are implicated in the pathogenesis of atherosclerosis, whereas the high density lipoproteins (HDL) are believed to be protective against atherosclerosis. Recent reports indicate that there is an inverse relationship between the HDL level and the risk of developing Ischaemic Heart Disease (IHD) (Miller et al, 1977; Castelli et al, 1977). If the atherosclerotic process producing IHD is the same as that producing peripheral vascular disease (PVD), then one would expect the same inverse relationship to hold.

Regular physical exercise has been shown to elevate the HDL level and a variety of mechanisms have been postulated (Wood et al, 1976; Miller et al 1979; Nikkila, 1978). This increased concentration of HDL is believed to decrease the binding, uptake and degradation of LDL, and increase the removal of cholesterol from the tissues (Miller et al, 1977). Therefore elevation of the HDL level would appear to be one of the mechanisms by which exercise may protect against atherosclerosis.

Whether regular exercise has a role in the prevention of peripheral vascular disease has not been established, and we have therefore studied the HDL status of adult subjects with and without PVD, and compared them to two groups of subjects undergoing regular physical exercise. We have also compared the various risk factors for atherosclerosis in each group as defined by Williams et al (1979).

## SUBJECTS AND METHODS

There were four subject groups as follows:—

- (a) *Vascular group* — patients about to undergo major arterial reconstruction for severe vascular disease of the lower limbs. (n=21)
- (b) *Control group* — patients about to undergo minor procedures e.g. hernia repair or were members of this department. They had no history or evidence of IHD or PVD. (n=25)
- (c) *Exercise group* — middle aged "keep-fit" enthusiasts who underwent a minimum of five hours a week of vigorous physical training in hourly sessions at the Leeds Athletic Institute and had been doing this for an average of nine years each. Most were professional people who usually spent their lunch hour in the gymnasium. (n=37)
- (d) *Athletic group* — young students at the Carnegie Physical Education Institute who underwent an average of ten hours a week of physical activity, and had been doing this for an average of eight years each.

The subjects were asked about their past medical, drug and smoking history and whether or not they were on a special diet. The type and duration of physical exercise taken was recorded and then their height, weight, pulse rate and blood pressure were measured prior to venepuncture.

### Biochemistry

As the triglyceride content was not measured in all

subjects, fasting samples were not taken routinely. The HDL and total cholesterol (TC) levels were estimated using the Heparin/Manganese Chloride Precipitation (McTaggart et al, 1978) and CHOD-PAP Enzymatic Colorimetric (Trinder, 1969) methods respectively, on an ultra-violet spectrophotometer.

### Risk Factor Analysis

We also subjected each subject to risk factor analysis as used by Williams et al (1979) (Table 1). With this method, each of the risk factors —

relative weight (as calculated from American Insurance Tables)  
diastolic blood pressure  
cigarette smoking  
total cholesterol  
exercise

are scored 0-2. Having scored every patient with regard to all five risk factors, the total for each group was added together and divided by the number in each group, to give the average cumulative risk rating for that group.

### Statistical Analysis

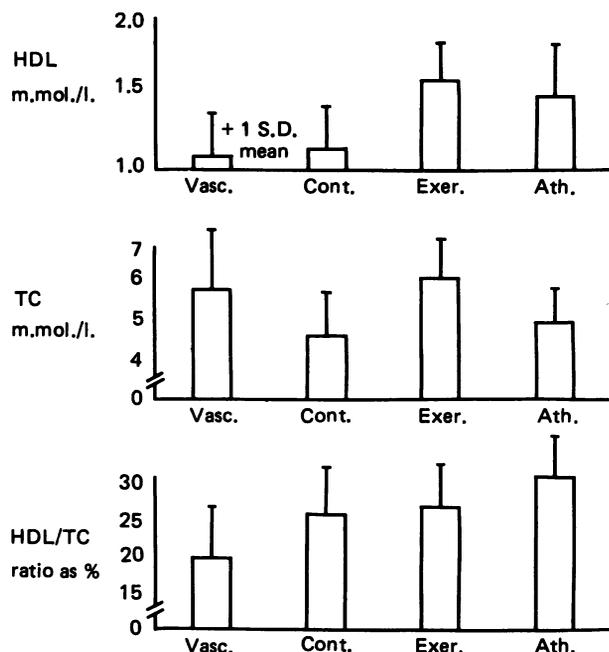
The Student's t test or the z test were used where appropriate.

## RESULTS

(a) *HDL level* — The mean HDL levels in the Exercise group ( $1.58 \text{ mmol/l} \pm 0.23$ ) and Athletic group ( $1.49 \text{ mmol/l} \pm 0.33$ ) are both significantly greater than in either the Control ( $1.15 \text{ mmol/l} \pm 0.27$ ) or Vascular ( $1.09 \text{ mmol/l} \pm 0.28$ ) groups ( $p < 0.0005$  for both groups). There is however no statistically significant difference between either the Exercise and Athletic groups or the Control and Vascular groups (Fig. 1).

(b) *TC level* — The mean TC level in the Control group ( $4.72 \text{ mmol/l} \pm 1.17$ ) is significantly less than in either the Vascular ( $5.89 \text{ mmol/l} \pm 1.54$ ) or Exercise ( $6.17 \text{ mmol/l} \pm 0.92$ ) groups ( $p < 0.01$  and  $0.0005$  respectively). Similarly the mean TC level in the Athletic group ( $5.02 \text{ mmol/l} \pm 0.86$ ) is significantly less than either the Vascular or Exercise groups ( $p < 0.01$  and  $0.005$  respectively). There is no statistically significant difference between either the Control and Athletic groups or the Vascular and Exercise groups (Fig. 1).

(c) *HDL/TC ratio* — The mean HDL/TC ratio in the Vascular group ( $19.51\% \pm 6.65$ ) is significantly lower than in the Control ( $25.12\% \pm 6.06$ ), Exercise ( $26.17\% \pm 5.52$ ) and Athletic ( $29.93\% \pm 5.37$ ) groups ( $p < 0.0005$ ). There is no statistical significance between the ratios in the Control and Exercise groups, but the ratios in these latter two groups are both significantly lower than the ratio in the Athletic group ( $p < 0.0025$  and  $0.005$  respectively) (see Fig. 1).



Vasc. = Vascular group (n = 21) Cont. = Control group (n = 25)  
Exer. = Exercise group (n = 37) Ath. = Athletic group (n = 27)

Figure 1

TABLE I

FACTOR	SCORE
<b>Relative weight as %</b>	
< 100	0
100 – 120	1
120 +	2
<b>Diastolic blood pressure (mm Hg)</b>	
< 90	0
90 – 100	1
110 +	2
<b>Cigarette smoking (no/day)</b>	
Non or Ex smoker	0
0 – 20	1
20 +	2
<b>Total cholesterol (mmol/l)</b>	
< 6.7	0
6.7 – 7.7	1
7.7 +	2
<b>Exercise</b>	
Very active	0
Active or slightly active	1
Inactive	2

(d) *Risk Factor Analysis* (Tables I and II) – The Vascular group had a high score for cigarette smoking (scoring a total of 25 out of a possible maximum score

for the group of 42) and took little exercise (scoring 38 out of a maximum of 42). More than half of this group had a diastolic blood pressure above 90 mm Hg and scored 12/42.

TABLE II

RISK FACTOR SCORING

Risk Factor	Vascular Group n = 21	Control Group n = 25	Exercise Group n = 37	Athletic Group n = 27
Relative weight	9	8	16	7
Diastolic blood pressure	12	4	6	0
Cigarette smoking	25	16	6	4
Total cholesterol	11	3	13	3
Exercise	38	20	0	2
Total	95	51	41	16
Average cumulative risk rating	$95 = 4.52$ 21	$51 = 2.04$ 25	$41 = 1.10$ 37	$16 = 0.59$ 27

The Control group had low scores for relative weight, diastolic blood pressure and total cholesterol, but relatively high scores for smoking (16/50) and exercise (20/50).

Almost half the Exercise group were overweight and nearly a third had a raised TC. However, they were extremely active and scored 0/74 for exercise.

The Athletic group had low scores for all risk factors except for relative weight, analysis of which revealed more than a quarter of this group were over their ideal weight (scored 7/54), though this was due to mesomorphy rather than endomorphy.

(e) *Average Cumulative Risk Rating* (Table II) – The Vascular group's rating was 4.52; Control group = 2.04; Exercise group = 1.1 and Athletic group = 0.59. Using the table comparing mean HDL/TC ratio with cumulative risk rating, as compiled by Williams et al, (1979), the Vascular group would be expected to have a mean HDL/TC ratio of 19.4% (actual 19.51%) the Control group – expected 23.4% (actual 25.12%) the Exercise group – expected 25.6% (actual 26.27%) and the Athletic group – expected 27.9% (actual 29.9%). There was no statistical difference between the expected and actual values in any of the four groups.

## DISCUSSION

Atherosclerosis is the major cause of death in the Western Hemisphere, usually by its involvement of the coronary arteries as Ischaemic Heart Disease which is manifest in the acute sense (myocardial infarction) or as a chronic condition (angina pectoris). It also affects the peripheral

arteries causing intermittent claudication or gangrene of the tissues of the leg, and cerebro-vascular accidents. Any factor that decreases the incidence of atherosclerosis is therefore of major benefit. Stopping smoking, eating a normal balanced diet and controlling adequately diseases such as diabetes mellitus and hypertension are established measures. Taking regular physical exercise is rapidly becoming established as an equally important form of prophylaxis against the development of atherosclerosis.

The HDL level has been shown to be uninfluenced by age (Williams et al, 1979) and therefore the significantly greater mean HDL levels in the Exercise (1.58 mmol/l) and Athletic (1.49 mmol/l) groups compared to the Control (1.15 mmol/l) and Vascular (1.09 mmol/l) groups, must be due to some other factor or factors. Admittedly the Athletic group had low scores on risk factor analysis (apart from relative weight) but the Exercise group were, surprisingly, more overweight and had the highest mean TC level. Although they smoked less, the way in which these two groups differed most from the other two groups, was in the amount of physical exercise taken. One must conclude that this was a major factor in elevating their mean HDL levels.

Most workers have found the HDL level to be low in patients with IHD and PVD (Castelli et al, 1977; Williams et al, 1979; Miller et al, 1977; Zilcher et al, 1979), although conflicting reports exist (Bradby et al, 1978). The disparity in results has been attributed to the various methods used for estimation of the HDL level, the Phospho-tungstic Acid/Magnesium Chloride Method giving different values from the well-proven Heparin/Manganese Chloride Method (Thompson and Trayner, 1979; Warnick and Albers, 1978) which we have used in our study. The HDL level in our patients with PVD would be regarded as being low when compared to the results (using the Heparin/Manganese Method) of some workers (Zilcher et al, 1979; Moore et al, 1979) but normal compared to those of other workers (Miller et al, 1977; Wood et al, 1979). There was no significant difference between the HDL levels of the Vascular and Control groups. This may indicate that the Control group are at risk from atherosclerosis which was not obvious clinically at the time of this study. However, when the HDL is taken as a ratio of the TC, and the risk factors are analysed, the difference between the two groups becomes clear.

The Framingham study has shown (Gordon et al, 1977) the HDL/TC ratio as one of the most predictive measurements in identifying the risk of a person developing IHD due to atherosclerosis. Zilcher et al (1979) have stated that the cut off between normal and patients with atherosclerosis is in the range 20-25%. Our patients with PVD have a significantly lower ratio than the mean ratios of the other three groups and the ratio is less than

20%. This would seem to indicate that it is the same process or processes causing atherosclerosis in PVD as in IHD and is independent of the anatomical location of the arterial disease. Also there is good correlation between the actual HDL/TC ratios of our subjects and their expected ratios calculated from their cumulative risk factor ratings, suggesting the ratio is a true reflection of the subject's actual risk of developing atherosclerosis. This is confirmed, for example, in the Athletic group who have as one would expect a low cumulative risk rating (0.59) on risk factor analysis. The significantly greater HDL/TC ratio of the Athletic group (29.9%) compared to the Control (25.12%) and Vascular (26.17%) groups, reflects this low risk rating and confirms the predictive power of the HDL/TC ratio.

The TC value represents the cholesterol of all the different lipoprotein fractions and therefore the effect of exercise on the TC will reflect the changes in these different lipoproteins. Wood and his co-workers found a lower TC level in male runners compared with controls (Wood et al, 1976) and his findings have substantiated work done by other workers (Lopez-S et al, 1974; Mann et al, 1969; Campbell, 1965). In addition, the TC is frequently elevated in patients with IHD or PVD compared with controls (Castelli et al, 1977; Zilcher et al, 1979). Our TC results show a high level in the Vascular group (5.89 mmol/l) and normal levels in the Control (4.72 mmol/l) and Athletic (5.02 mmol/l) groups. Surprisingly the Exercise group had the highest level of TC (6.17 mmol/l) and we are unable to explain this finding fully. However, other reports have shown that exercise not only affects the HDL fraction, but also has the effect of reducing the serum very low density lipoprotein (VLDL) level and possibly the LDL level (Lopez-S et al, 1974; Gustafson, 1971). It may be that the rise in the HDL level in the Exercise group in our study was more than any fall in the VLDL and LDL levels, resulting in a raised TC level. We have not measured VLDL and LDL levels in all our subjects, but Jenkins has stated that the biological variability in any person is less for HDL cholesterol than for VLDL triglyceride, and that a single measurement of the HDL concentration may therefore be more representative of a person's usual lipid status than an isolated measurement of the VLDL triglyceride concentration (Jenkins et al, 1978).

In conclusion, we would agree with Williams et al, (1979), that the HDL/TC ratio should be included in any profile for atherosclerosis and our findings would suggest that a level of less than 20% be regarded as suspicious, especially in peripheral vascular disease. We would add that the actual level of HDL in the plasma should also be seen as reflecting the risk of atherosclerosis, but must be viewed in conjunction with the high density lipoprotein: total cholesterol ratio. It may be that the HDL has to be above a certain absolute

level to be protective. Our Exercise group, by taking regular physical activity, have increased their HDL level to a level comparable to young athletes twenty years their junior. This is despite a relatively high incidence of deleterious risk factors, and would indicate that exercise on its own, would seem to exert a protective effect against atherosclerosis.

## CONCLUSIONS

Our study supports the contention that

- (1) An HDL/TC ratio of less than 20% is highly suspicious of atherosclerosis.

- (2) Exercise appears to protect against atherosclerosis at least in part by elevating the HDL level.
- (3) Both the HDL/TC ratio and HDL level should be viewed together as reflecting the risk of atherosclerosis, and should be used as a screening procedure. They are easy to perform and form an objective basis upon which to base future therapy.

## ACKNOWLEDGEMENT

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## REFERENCES

- Bradby, G. V. H., Valente, A. J. and Walton, K. W., 1978 "Serum high density lipoprotein in peripheral vascular disease". *Lancet* ii: 1271-1274.
- Campbell, D. E., 1965 "Influence of several physical activities on serum cholesterol concentration in young men". *J.Lipid Res.* 6: 478-480.
- Castelli, W. P., Doyle, T. J., Gordon, T., Hames, C. G., Hjortland, M. C., Hulley, S. B., Kagan, A. and Zukel, W. J., 1977 "HDL cholesterol and other lipids in Coronary Heart Disease". *Circulation* 55: 767-772.
- Gordon, T., Castelli, W. P., Hjortland, M. C., Kannel, W. B., Dawber, T. R., 1977 "High density lipoprotein as a protective factor against coronary artery disease. *Am.J.Med.* 62: 707-714.
- Gustafson, A., 1971 "Effect of training on blood lipids". In: *Coronary Heart Disease and Physical Fitness*, (Larsen, O. A. and Malborg, R. O. (Eds.) University Park Press, Baltimore.
- Jenkins, P. J., Harper, R. W. and Nestel, P. J., 1978 "Severity of coronary atherosclerosis related to lipoprotein concentration". *Br.Med.J.* 2: 388-391.
- Lopez-S, A., Vial, R., Balart, L. and Arroyave, G., 1974 "Effect of exercise and physical fitness on serum lipids and lipoproteins". *Atherosclerosis* 20: 1-9.
- Mann, G. V., Garrett, H. L., Farhi, A., Murray, H. and Billings, F. T., 1969 "Exercise to prevent coronary heart disease". *Am.J.Med.* 46: 12-27.
- McTaggart, F., Sennitt, C. M., Dixon, R. M., Williams, T. M. and Stone, M. C., 1978 "A study of two precipitation techniques of HDL-Cholesterol. Symposium on precipitation techniques as an aid to the study of biochemical abnormalities related to atherosclerosis," ICI Pharmaceuticals Division, Alderley Edge.
- Miller, N. E., Førde, O. H., Thelle, D. S. and Mjøs, O. D., 1977 "The Tromsø heart study. High density lipoprotein and coronary heart disease: a prospective case control study". *Lancet* i: 965-968.
- Miller, N. E., Rao, S., Lewis, B., Bjørsvik, G., Myhre, K. and Mjøs, O. D., 1979 "High density lipoprotein and physical activity". *Lancet* i: 111.
- Miller, N. E., Weinstein, D. B., Carew, T. E., Koschinsky, T. and Steinberg, D., 1977 "Interaction between high density and low density lipoprotein uptake and degradation by cultured human fibroblasts". *J.Clin.Invest.* 60: 78-88.
- Moore, R. A., Penfold, W. A. F., Simpson, R. D., Simpson, R. W., Mann, J. I. and Turner, R. C., 1979 "High density lipoprotein, lipid and carbohydrate metabolism during increasing fitness". *Ann.Clin.Biochem.* 16: 76-80.

- Nikkila, E. A., 1978 "Metabolic and endocrine control of plasma high density lipoprotein concentration". In: High Density Lipoproteins and Atherosclerosis. (Gotto, A. M. Jr., Miller, N. E. and Oliver, M. R. (Eds.) Elsevier, Amsterdam.
- Thompson, G. and Trayner, I., 1979 "High density lipoprotein and peripheral vascular disease". *Lancet* i: 49.
- Trinder, P., 1969 "Simple turbidimetric method for the determination of serum cholesterol". *Ann.Clin.Biochem.* 6: 24.
- Warnick, G. R. and Albers, J. J., 1978 "A comprehensive evaluation of the heparin-manganese precipitation procedure for estimating high density lipoprotein cholesterol". *J.Lipid Res.* 19 (1): 65.
- Williams, P., Robinson, D. and Bailey, A., 1979 "High density lipoproteins and coronary risk factors in normal men". *Lancet* i: 72-75.
- Wood, P. D., Haskell, W., Klein, H., Lewis, S., Stern, M. P. and Farquhar, J. W., 1976 "The distribution of plasma lipoproteins in middle aged male runners". *Metabolism* 25: 1249-1257.
- Zilcher, H., Kaliman, J. and Muller, M., 1979 "HDL-cholesterol in peripheral vascular disease". *Lancet* i: 558-559.

### BOOK REVIEW

**Title:** IMPACT THERAPY, 3rd Ed., 1979  
**Author:** John B. Tracey  
**Publisher:** Author, Gipsy Lane Gardens, Pinhoe, Exeter  
**Price:** 115 pages Index Approx. 65 figs. Soft Cover

Like the book by Dr. James Cyriax, this is also on the subject of Orthopaedic Medicine. When an object is struck it is compressed in the line of force acting upon it, but expands in the plane at right angles, and this is used by Dr. Tracey for the treatment of a wide variety of joint and soft tissue disorders. The limb is supported on bags filled with sand or seed, another bag is placed above the limb and repeated blows are transmitted through this bag with a sand bag held in the hand. This impact helps to overcome muscle spasm and allows minor degrees of subluxation of the joint to be reduced. In Dr. Tracey's own hands, and in those people he has trained, this appears to be a very successful procedure in many cases. In several demonstrations that I have seen, the technique appears simple, and physiotherapists and others in the audience who have volunteered as subjects have felt relief from the minor orthopaedic disorders from which most of us suffer.

As well as the use of impact by sand bags, certain forms of manipulation are also described, including exercises and even manual impact that the patient can carry out upon himself; for example, for lesions of the tempero-mandibular joint. There is an assumption in the book that most joint lesions are mild degrees of subluxation whose reduction is helped by joint distraction. This distraction also straightens out any tendency to wrinkling of the articular cartilage. I know of no evidence that such wrinkling actually occurs, but those experienced with arthroscopy may have observed this phenomenon during passive movements of joints.

The book itself is not nearly as impressive as Dr. Tracey's lecture demonstrations. There is reduplication of diagrams and of the introductory statements preceding the description of his various procedures. This is because the second half of the book consists to a large extent of the instruction leaflets written for the use of patients, and others compiled for therapists, which have been collected together. The exact technique is not always easy to understand when reading through instructions quickly, but needs to be studied very carefully, together with the illustrations. The free flow of text is interrupted by the overuse of capital letters and bold and italic type, and also by numerous cross references. There is an adequate index. Precise instructions are given not only for carrying out the impact and manipulation procedures, but also for constructing the necessary apparatus or giving lists of suppliers who can provide it.

For those treating soft tissue injuries, both from sport, from occupation or daily living, the theories and practice contained in this book are well worth considering. The indications for treatment are stated clearly and even more clearly the contra-indications and other warnings. I can, therefore, recommend the book to both doctors and physiotherapists, but would like to see more published critical reports of this treatment written by others than the author himself. I know Dr. Tracey has been trying to promote this form of treatment, which brings little or no profit to himself, over a period of many years the first edition of "Impact Therapy" was published in 1967, but based upon methods used for many years before that. His techniques deserve wider trial and acceptance.

H. E. Robson