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## GUEST EDITORIAL

### Cholesterol as a Cardiovascular Disease Risk Factor, Why Now?

Donald B. Langille,\* MD, MHSc.

Relationships between and among dietary cholesterol, fat intake, population serum cholesterol and rates of coronary heart disease are complex and controversial, although decades of evidence point to strong associative inferences. It was not until the publication of recent clinical trial results that these associations have come strongly to the forefront of clinical practice. These studies have been interpreted by many to clinch the so-called "lipid hypothesis" and point the way towards a more aggressive approach to this cardiovascular risk factor.

This issue of the *Journal* outlines the extent and distribution of this risk factor in the Nova Scotian population, clinical approaches to it and various aspects of laboratory testing for it. Knowledge about this risk factor has been with us for quite some time and a brief review of the highlights of the epidemiology of diet and serum cholesterol will help us to understand the present approach to these problems as they relate to coronary heart disease, the major cause of death in North America today.

Metabolic ward studies have made it clear that when weight is held constant, dietary fat and cholesterol have a predictable influence upon levels of serum total cholesterol.<sup>1,2,3</sup> Studies in non-clinical free-living societies confirm that when compared with aged matched controls, those eating a low fat "macrobiotic" diet have significantly lower total cholesterol, LDL and VLDL levels.<sup>4</sup> Enholme has demonstrated that placing populations of men and women on a diet typical of Mediterranean countries, low in saturated fat, lowers serum total cholesterol significantly, while return to usual diet reverses this finding.<sup>5</sup> International migration studies have presented data compatible with the hypothesis that changes in lifestyle, which include a "richer" diet, are associated with higher levels of serum cholesterol, for example, Neopolitans in Naples and Boston and Japanese compared with Japanese Americans.<sup>6</sup> Findings of the Ni/Hon/San Study of Japanese migrants to Hawaii and California have led to the conclusion that lower incidence rates of CHD in Japanese as compared with Japanese American men were due to lower mean serum cholesterol levels in Japanese men and that these differences were associated with differences in mean intake of specific nutrients.<sup>7</sup> It is clear that diet plays a major determining effect in levels of population serum cholesterol.

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\*Director, Cobequid Health Unit, Department of Health and Fitness, Province of Nova Scotia.  
Chairman, Community Health Committee, The Medical Society of Nova Scotia.



The role of diet in the pathogenesis of atheroma formation and its subsequent reversal upon cessation of hypercholesteremia inducing diet was demonstrated convincingly in several animal studies, leading to the hypothesis that excess dietary cholesterol might accelerate atherosclerosis.<sup>8,9</sup> These studies showed that when plasma cholesterol is raised by increasing dietary cholesterol, atherogenesis is enhanced. However, in animals resistant to hypercholesteremia, atherosclerosis is less marked. The relationship between habitual dietary fat intake in the development of atherosclerosis is also supported by autopsy studies such as the International Arteriosclerosis Project, in which high degrees of correlation were found between percentage of calories from total dietary fat and advanced arteriosclerotic lesions, and between population mean serum cholesterol and occurrence of such lesions. Strength of association and dose response were demonstrated, implying a causal association.<sup>10</sup>

Relationship of habitual diet to CHD development is best demonstrated by FAO food balance data from 20 countries showing statistically significant correlations between several nutrients including saturated fat, cholesterol and calories and CHD mortality rates.<sup>11</sup> Once again strength of association, temporal sequence and consistency were demonstrated. The Seven Countries Study was a comprehensive look at living populations, which carried out observations on approximately 12,000 men, aged 40-59 at the beginning of the Study.<sup>12</sup> Significant high order correlations were observed between intake of saturated fat (and thus cholesterol, although not measured) and 5-year CHD incidence, as well as between fat intake and population serum cholesterol levels. These findings have been confirmed by a 10-year follow-up of the original cohort.

The Seven Countries Study also demonstrated high order correlation between population serum cholesterol levels and CHD rates. A follow-up of this cohort has been demonstrated by Rose to indicate that differences in blood cholesterol levels accounted for most of the differences in CHD Mortality seen in these countries.<sup>13</sup> A similar strong association was observed between population mean total cholesterol levels and CHD incidence in cohorts of men aged 45-64 in the U.S. mainland (Framingham, Mass.), Hawaii and Puerto Rico.<sup>14</sup>

Migration studies also lead to the conclusion that CHD incidence is independently related to mean values of total cholesterol and increases in parallel with increased total cholesterol levels.<sup>15,16</sup> It is felt that dietary change involving the ingestion of increased amounts of saturated fat and cholesterol as migration takes place, combined with increasing levels of obesity and a more sedentary lifestyle lead to the risk factor gradient observed.<sup>17</sup>

The Pooling Project, combining data from several similar epidemiological studies in the United States,

compared CHD risk with serum cholesterol concentration through five stages of increasing cholesterol level in 8,422 men aged 40-64. In all four age groups analysed by quintile, the mean value of serum cholesterol was significantly elevated for men experiencing non-fatal and fatal myocardial infarction and sudden CHD death, and the average difference in cholesterol level between those with and without first events was inversely related to age.<sup>18</sup> Also of importance was the observation that men with cholesterol levels often referred to as being in the "normal" range, in that their levels were below the 95th percentile, accounted for most of the attributable risk.

The notion of population attributable risk is an important concept for the understanding of approaches to the problem of elevated serum cholesterol.<sup>19</sup> This is the excess risk associated with the factor (cholesterol) in the population, dependent upon the product of the individual attributable risk and the prevalence of the factor in the population. It follows that if the greater proportion of individual attributable risk is scattered throughout the range of cholesterol distribution in the population, then it might be more beneficial to attempt to modify levels in a large proportion of those at moderate risk than to identify and modify risk in relatively few people at high individual risk. This concept is realized to be of even more importance in light of the results of long-term follow-up of the Multiple Risk Factor Intervention Trial's screenees. (MRFIT) This statistically very powerful study of the more than 350,000 primary screenees of MRFIT indicates that the relationship of serum total cholesterol to coronary heart disease is graded, continuous and without threshold level, and indicates a degree of relative risk in the great majority of middle-aged American men.<sup>20</sup>

It should be pointed out that most of total cholesterol is represented by the LDL fraction, and the epidemiology of this risk factor, including in particular data from Framingham, indicates that the high correlation of total cholesterol and CHD risk suggests that it is indeed high concentrations of LDL which are atherogenic.<sup>21,22</sup> It is also agreed that more predictive value may lie in LDL measurement itself, particularly when considered together with other lipoprotein fractions. It is recognized that studies indicate an inverse relationship between CHD rates and HDL levels in populations with high total cholesterol levels, although this may not necessarily hold true for situations where LDL is relatively low.

These relationships are complex, and is for this reason that various National bodies such as the NIH Consensus Group in the United States and the Canadian Consensus Panel have been formed to determine a rational approach to serum cholesterol as a CHD risk factor. The extensive findings indicating strong relationships between and among the variables diet, serum cholesterol and coronary heart disease have led to recommendations



from these groups, sparked by the results of the LRC-CPPT<sup>23</sup> and based upon a literature best summarized as follows: Epidemiological, experimental and clinical evidence of the relationships between blood lipoproteins, atherosclerosis and disease rates in different cultures is strong, consistent and congruent. Populations vary in mean levels and distribution of total cholesterol while associations are strong between population means of serum cholesterol and coronary heart disease. Serum total cholesterol means and distribution of serum cholesterol of migrants approach those of adopted countries (environmental influence), whether these are higher or lower than the country of origin. Individual risk of development of coronary heart disease, as observed in longitudinal studies, shows a rising risk with level of serum total cholesterol (and LDL) until at least late middle age. A strong inverse relationship between HDL cholesterol and CHD incidence is found and is greater at older ages. It is observed that a large proportion of attributable risk arises from the mid range of the population serum total cholesterol distribution.<sup>24</sup>

With the publication of the LRC-CPPT in 1984 and more recently the Helsinki Heart Study a heightened interest in cholesterol as a CHD risk factor has been created.<sup>25</sup> These trials, from the point of view of the supporters of their results, not only lend credence to the whole concept of the "lipid hypothesis", but in the view of many add weight to a pharmacologically oriented approach to this risk factor. It would therefore appear that the "cholesterol era" is now upon us.

This issue of the *Journal* addresses this risk factor both in general and with reference to our own particular population. It is to be hoped that the apparent prolonged hesitancy of both Society and the profession to modify this major cause of death and disability will soon be a thing of the past. □

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## EATING DISORDERS CLINIC

An eating disorders clinic has been established in the Ambulatory Care Centre at the Victoria General Hospital.

The clinic treats patients with anorexia nervosa and bulimia nervosa. At present it is open four days per week.

Patients are accepted by physician referral only. Patients must fill out and return pre-assessment questionnaires before receiving an appointment date.

Telephone 428-2288 for referral requests or address correspondence to Dr. Dianne MacDonald or Dr. Neelma Dhar, Eating Disorders Clinic, Department of Psychiatry, VG Hospital, Halifax, N.S. B3H 2Y9.



# The Prevalence of Hyperlipidemia in Nova Scotia

David MacLean,\* MD, CCFP, MHSc. and Andres Petrasovits,\*\* PhD, MPH,

*Halifax, N.S. and Ottawa, Ont.*

Cardiovascular disease is the main cause of death in Canada being responsible for approximately 43% of all deaths.<sup>1</sup> Internationally, Canada stands somewhere in the middle of industrialized nations, with rates which are less than some countries e.g.: Finland, but twice those found in France and five times those found in Japan. Within Canada CVD death rates vary quite considerably from province to province. In general death rates are lower in the west than the east, with the highest rates in Atlantic Canada.<sup>2</sup> It has been calculated that if Saskatchewan rates for ischemic heart disease were to apply to the other Canadian Provinces there would be approximately 7,500 fewer deaths per year in Canada due to ischemic heart disease.<sup>3</sup>

Elevated blood cholesterol has been established as one of a number of independent risk factors for the development of ischemic heart disease.<sup>4,5</sup> Diets rich in saturated fats, dietary cholesterol, and high in caloric intake — relative to energy expenditure — play a dominant role in determining the blood cholesterol level of the vast majority of individuals with moderate elevations.<sup>6</sup> Population studies indicate that diets low in saturated fat and cholesterol are associated with lower rates of heart disease.<sup>7</sup> Carefully controlled metabolic studies have shown that modification of polyunsaturated and saturated fat, and cholesterol content of the diet, produces predictable changes in blood cholesterol.<sup>8,9,10</sup> The results from the Lipid Primary Prevention Trial<sup>11</sup>, and the recently released Helsinki Heart Study<sup>12</sup>, among others<sup>13,14</sup>, provide evidence that lowering serum cholesterol and/or LDL-cholesterol and increasing HDL-cholesterol reduces the risk of heart attack.

Nova Scotia has higher mortality rates for cardiovascular disease than most other provinces in Canada. It has been suggested that these excessive rates may be due, at least in part, to a higher prevalence of risk factor for CVD in the Nova Scotian population.<sup>15</sup>

The data on lipids presented here were obtained through the Nova Scotia Heart Health Survey. This was undertaken to define the level of population risk for cardiovascular disease and to support the development of a cardiovascular disease prevention program in the province. Its main purpose was to estimate the prevalence and distribution patterns of cardiovascular disease risk factors including: high blood pressure, abnormal serum lipids, smoking and comorbid conditions such as obesity and sedentary lifestyle. The survey

also addressed some aspects of knowledge and awareness on the causes and consequences of cardiovascular disease with special emphasis on dietary factors such as fat and dietary cholesterol. The survey was carried out by the Nova Scotia Department of Health & Fitness in collaboration with the Department of National Health & Welfare. This paper gives an overview of some of the serum lipid findings from the survey.

## METHODS

A detailed account of the methodology employed in the Nova Scotia Heart Health Survey has been published elsewhere.<sup>16</sup> The target population of the survey was the non-institutionalized adult population of Nova Scotia — ages 18 to 74, nursing home residents being included.

The survey field operations were carried out in the first quarter of 1986 by specially trained community health nurses employed by the Community Health Division of the Nova Scotia Department of Health & Fitness. Epidemiological research support was provided by the Department of Community Health and Epidemiology, Faculty of Medicine, Dalhousie University. The statistical sample design was prepared by the Special Survey Division of Statistic Canada.

Fasting venous blood samples were obtained using vacuumtainer tubes and tourniquet. Ten ml. Lavender-Stopper Vacuumtainer tubes, containing sodium EDTA, were filled as completely as possible. The filled tubes were promptly mixed by inverting the tubes eight times. They were labeled and placed in wet ice pending centrifugation, which was carried out at special survey clinics. The serum was transferred to Byau bottles by disposable pipettes and shipped, on ice, for lipid analysis to the Lipid Research Clinic Laboratory at the University of Toronto.

The lipid fractions determined were total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol, and triglyceride. The lipid determinations were made according to procedures specified in the Lipid Research Clinic laboratory methods manual, and met strict requirements for standardization and quality control, which have been described elsewhere.<sup>17</sup>

The data were collected at a home interview and at a subsequent visit to a survey clinic by each participant in the survey. Two thousand seven hundred thirty-five people were invited to participate in the survey; of these, 1798 (66%) came to the clinic where blood was taken. Among these 1590 fasted eight hours or more and make up the results which are reported here (Table I).

\*Director, Atlantic and Lunenburg/Queens Health Units, Nova Scotia Department of Health and Fitness, Halifax, N.S.

\*\*Senior Policy Advisor, Health Promotion Directory, Department of National Health and Welfare, Ottawa, Ontario.



TABLE I

NUMBER OF INDIVIDUALS FOR WHICH FASTING  
(8 HOURS OR MORE) LIPID DETERMINATIONS WERE MADE  
BY AGE AND SEX

Male			Female			Total
18-34	35-64	65-74	18-34	35-64	65-74	
409	268	87	445	302	79	1590

## RESULTS

The lipid results are given in Tables II to V. Mean serum cholesterol increases with age. In older men it tends to level off, whereas in older women it continues to rise. Young and middle aged men have higher mean values than the corresponding ages of women.

Forty-seven percent of population have a serum cholesterol value over 200 mg/dL (5.2 mM/L), with 16% over 240 mg/dL (6.2 mM/L). The prevalence of elevated serum cholesterol is somewhat higher for middle aged men and older women.

TABLE II

MEAN AND FREQUENCY DISTRIBUTION OF TOTAL  
SERUM CHOLESTEROL BY AGE AND SEX\*

	Male			Female			Total
	18-34	35-64	65-74	18-34	35-64	65-74	
Mean mg/dL (mM/L)	183 (4.7)	213 (5.5)	211 (5.4)	178 (4.6)	207 (5.3)	225 (5.8)	—
% less than 200 mg/dL (5.2 mM/L)	73	37	47	78	49	27	53
% from 200-239mg/dL (5.2-6.2 mM/L)	22	42	28	16	34	37	30
% over 240 mg/dL (6.2 mM/L)	5	21	25	6	17	36	16

\*All individuals were fasting 8 hours or more

The mean LDL-cholesterol values have a similar pattern as described for total cholesterol. They generally rise with age but level off in older men (Table III). Likewise, the mean values for young and middle aged men tend to be higher than the similar age groups of women. Sixteen percent of the sample have values greater than 160 mg/dL (4.1 mM/L). The pattern of prevalence of elevated LDL-cholesterol is similar for both sexes.

The results for HDL cholesterol are given in Table IV. Mean values tend to decline with age, with the exception of older men where the values again level. Women have higher mean values than men.

Eight percent of the sample have values less than 35 mg/dL (0.9 mM/L), with 36% above 50 mg/dL (1.79 mM/L). The distribution pattern between the sexes seems to differ quite markedly, with a higher percentage in men than in women, in all age groups with values at the lower levels of HDL cholesterol. However, at the higher levels of HDL cholesterol the reverse appears to apply.

The triglyceride results are given in Table V. The mean values display a similar pattern as some of the other lipid fractions i.e. rising with age, except for older men where they level. Young and middle aged men have higher mean values than women in the same age groups. Eighty-eight percent of the population have values less than 240 mg/dL (2.7 mM/L).

TABLE III

MEAN AND FREQUENCY DISTRIBUTION OF LDL  
CHOLESTEROL BY AGE AND SEX\*

	Male			Female			Total
	18-34	35-64	65-74	18-34	35-64	65-74	
Mean mg/dL (mM/L)	109 (2.8)	132 (3.4)	— (3.4)	105 (2.7)	128 (3.3)	139 (3.6)	—
% less than 130 mg/dL (3.4 mM/L)	74	48	49	80	59	45	61
% from 130-159 (3.4-4.1)	19	31	26	15	21	26	23
% 160 and over (4.1)	7	21	25	5	20	29	16

\*All individuals were fasting 8 hours or more

TABLE IV

MEAN AND FREQUENCY DISTRIBUTION OF HDL  
CHOLESTEROL BY AGE AND SEX\*

	Male			Female			Total
	18-34	35-64	65-74	18-34	35-64	65-74	
Mean mg/dL (mM/L)	46 (1.19)	43 (1.11)	44 (1.14)	52 (1.35)	53 (1.37)	49 (1.27)	—
Less than 35 mg/dL (0.9 mM/L)	8	13	13	4	2	12	8
35-50 mg/dL (0.9-1.3 mM/L)	63	67	65	47	45	56	56
50 mg/dL and over (1.3 mM/L)	29	20	22	49	53	32	36

\*All individuals were fasting 8 hours or more

TABLE V

MEAN AND FREQUENCY DISTRIBUTION OF  
TRIGLYCERIDES BY AGE AND SEX\*

	Male			Female			Total
	18-34	35-64	65-74	18-34	35-64	65-74	
Mean mg/dL (mM/L)	128 (1.45)	178 (2.00)	160 (1.81)	103 (1.16)	121 (1.37)	187 (2.11)	—
% less than 240 mg/dL (2.7 mM/L)	91	84	81	96	94	73	88
% greater than 240 mg/dL (2.7 mM/L)	9	16	19	4	6	27	12

\*All individuals were fasting 8 hours or more



## DISCUSSION

Lipid analyses for this survey were carried out according to the Lipid Research Clinic standards. Direct comparisons of these results with those from other studies, using different methodology, are not warranted unless allowance is made for the considerable inter-method and inter-laboratory variability, which is known to exist for lipid determination.<sup>18</sup>

The population mean values for total serum cholesterol for different age and sex group follows the pattern reported by the Lipid Research Clinics Prevalence Study.<sup>19</sup>

For individuals 35 years of age and over the mean values for total serum cholesterol are about 20 mg/dL (0.5 mM/L) over the level of 190 mg/dL (4.9 mM/L) which has been recommended for populations<sup>5,20</sup>. Desirable values for population means for the other lipids measured in the survey have yet to be established.

According to recent scientific consensus criteria on risk levels for serum cholesterol<sup>4,5</sup> and results from major follow-up studies of cardiovascular disease<sup>21,22</sup>, there are a significant number of Nova Scotians at increased risk of heart disease due to elevated serum cholesterol — above 200 mg/dL (5.2 mM/L) — and would in all likelihood benefit from having it reduced. Many are at particular high risk — greater than 240 mg/dL (6.2 mM/L) — and require medical attention. Key groups for intervention are middle aged men and older women. The age-lag in women's lipid values behind those of men seems consistent with the similar lag observed in ischemic heart disease mortality rates.<sup>2</sup>

When compared with the Lipid Research Clinic prevalence data<sup>19</sup> (Figure 1) young and middle aged Nova Scotian men and older Nova Scotian women appear to have higher levels of cholesterol than their American counterparts. Although comparison of the Nova Scotia Heart Health Survey data with other national data is not possible, data from the 1978 Canada Health Survey suggest that mean levels of serum cholesterol in Nova Scotians are higher than the Canadian average.<sup>15</sup> These facts suggest that the excess mortality from CVD found in Nova Scotia, as compared to the rest of Canada, may be attributable, at least in part, to elevated levels of serum cholesterol, particularly in middle aged men and older women.

LDL cholesterol is generally recognized as the main lipid fraction responsible for atherogenesis.<sup>23</sup> Recently published guidelines recommend intervention in adults with LDL cholesterol in excess of 160 mg/dL (4.1 mM/L).<sup>24</sup> A significant number of Nova Scotian adults (16%) fall into this category (Table III). Many among those would be eligible for dietary counselling and/or drug treatment. For those with two or more risk factors for CVD, intervention is suggested at an LDL cholesterol level of 130 mg/dL (3.4 mM/L). As Table III clearly illustrates, at this level, about 40% of the adult population of Nova Scotia could quite conceivably

MEDIAN, 25TH AND 75TH PERCENTILES OF SERUM CHOLESTEROL DISTRIBUTION  
FOR THE NSHHS AND THE LIPIDS RESEARCH CLINICS  
NORTH-AMERICAN POPULATION  
(plotted values for the LRC age group 65-74,  
including age 75 and over)

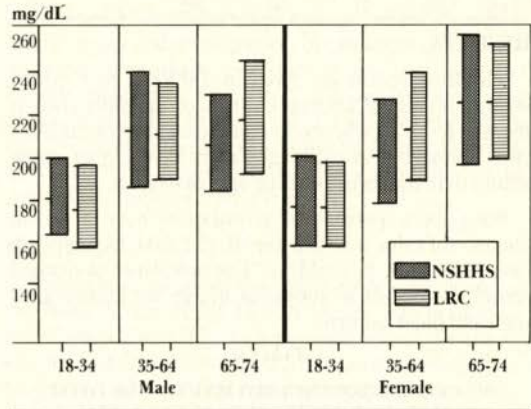


Figure 1

require attention to their serum lipids.

Metabolic studies indicate that HDL-cholesterol is antiatherogenic.<sup>25</sup> Epidemiological evidence from Framingham suggests that a HDL-cholesterol below 35 mg/dL (0.9 mM/L) places an individual at increased risk for coronary heart disease.<sup>26</sup> By this criterion many Nova Scotians, particularly males, are at risk (Table IV). The HDL cholesterol results presented here demonstrate distinct differences between men and women, being most apparent in young and middle aged groups. The weighing of men to the lower levels of HDL and women to the higher levels of HDL, as illustrated in Table IV, may explain, at least in part, the differences in cardiovascular disease mortality between the sexes.

There is firm evidence linking severe hypertriglyceridemia — over 500 mg/dL (5.7 mM/L) to pancreatitis.<sup>27</sup> While the relation of elevated triglyceride levels for the development of cardiovascular disease is more controversial, there is increasing evidence of an association between moderate hypertriglyceridemia — above 250 mg/dL (2.8 mM/L) — and coronary artery disease. Framingham data suggest that above this level, triglycerides are an independent risk factor for coronary heart disease in women, and as well for men with HDL cholesterol below 40 mg/dL (1 mM/L).<sup>28</sup>

From the data presented here, between 5-20% of women, depending on age, are at risk for cardiovascular disease due to elevated triglycerides (Table V).

## CONCLUSIONS

The results of the Nova Scotia Heart Health Survey demonstrate that many Nova Scotians are at risk to



develop cardiovascular disease due to elevated blood lipids. The risks appear to be so widespread as to suggest that public health measures directed to the population at large, as well as those at high risk, are warranted.

To address the needs of the population at large a nutrition strategy is required to deal effectively with the main determinants of elevated population levels of blood lipids, namely diets rich in saturated fats, cholesterol and excess calories. To develop such a strategy there is a need to acquire reliable, up-to-date data on macronutrients intake for the population at large. These data do not exist at present.

The results reported here indicate that many Nova Scotians are at high risk to develop CVD due to their blood lipids. The number is sufficiently large, particularly among middle aged men, to justify measures for case finding. The recently released preliminary report of the Canadian Cholesterol Consensus Conference gives guidance in this regard.<sup>5</sup> If studies in the United States are a guide to the Canadian situation, bringing about control of individuals at high risk from elevated serum cholesterol will require addressing the lack of awareness on the part of the general public and also physicians on the importance of serum cholesterol as a cardiovascular disease risk factor.<sup>29,30</sup>

It would appear that the "lipid problem" in Nova Scotia requires a coordinated cholesterol strategy, one which deals with the areas of public and professional education, but as well with issues of laboratory measurement and standardization. Such a strategy, of necessity, will have to be intersectoral, in that it involves not only the public and health professionals but the food and agricultural sectors as well. It is important that those who provide what we eat are intimately involved, so that individuals will be provided a range of foods that will enable them to make healthy choices.

The Nova Scotia Heart Health Survey measured the levels of other risk factors to CVD. It found that 71% of Nova Scotians had one or more of the major risk factors to cardiovascular disease (elevated blood pressure, elevated serum cholesterol, regular cigarette smoking). It is well recognized that significant elevation of any one of the major CVD risk factors can pose a significant risk to health. However, it is less well appreciated that combined moderate elevations of several risk factors may also confer a significant increase of cardiovascular disease risk. For example, cigarette smoking about doubles the risk for heart disease at all levels of serum cholesterol.<sup>22</sup> Therefore, efforts directed at the control of elevated blood lipids would best be considered within the context of a multifactorial approach which addresses simultaneously the other risk factors for CVD. This comprehensive strategy reflects the multifactorial nature of the risk to CVD and is needed if a major impact on the morbidity and mortality of this disease is to be realized. □

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# Guidelines for the Diagnosis and Management of Hypercholesterolemia

M. H. Tan, MD, FRCP(C), FACP, and K. Travers, Pdt, BSc, MA,

Halifax, N.S.

It is now generally accepted that hypercholesterolemia due to increased low density lipoproteins (LDL) is a cardiovascular risk factor. Evidence for this comes from epidemiological, genetic, metabolic, pathologic, animal, and human studies. Recently, the beneficial effects of correcting hypercholesterolemia by lowering LDL in humans with diet and drugs were established. Guidelines for the diagnosis and management of hypercholesterolemia have now been developed in both the United States (National Cholesterol Education Program — NCEP) and Canada (Canadian Consensus Conference on Cholesterol — CCCC). It is now suggested that persons with a serum cholesterol at the 75th percentile for serum cholesterol in the population are at moderate risk of developing atherosclerosis. This implies that one in four Canadians is at moderate risk of developing atherosclerosis. This review will summarize the recommendations of the NCEP and the CCCC so as to guide the physician in the diagnosis and management of this common metabolic problem.

## WHAT IS HYPERCHOLESTEROLEMIA?

Hypercholesterolemia implies an increase in serum total cholesterol. According to the NCEP, hypercholesterolemia is a serum total cholesterol of  $>6.2$  mmol/L or 240 mg/dL. This applies to all adults (over 20 years) irrespective of age and sex. According to the panel of the CCCC, for adults over 30 years, intervention to lower serum total cholesterol should be considered if serum total cholesterol exceeds 6.2 mmol/L. For adults between the ages of 18 and 29 years, intervention should be considered when the level of serum total cholesterol is  $>5.7$  mmol/L or 220 mg/dL.

## LDL AND HDL CHOLESTEROL

Lipids (cholesterol and triglycerides) are insoluble in water. When they are complexed with proteins (apoproteins) and phospholipids to form lipoproteins, they become soluble and can be transported from one part of the body to another. Lipoproteins can be separated into five classes — chylomicrons, very low density lipoproteins (VLDL), intermediate density lipoproteins (IDL), LDL, and high density lipoproteins (HDL). Each

lipoprotein fraction carries different proportions of cholesterol, triglycerides, phospholipids, and apoproteins. In the fasted state, most serum cholesterol is carried in the LDL and most serum triglycerides in the VLDL.

"Serum cholesterol" refers to the total amount of cholesterol in all five lipoprotein fractions. Thus an increase in serum cholesterol can be due to an increase in LDL, VLDL, IDL, and/or HDL.

Not all lipoproteins are atherogenic. Whereas LDL and IDL are atherogenic, HDL is not. Hence, in a patient with hypercholesterolemia, it will be important to establish which fraction of lipoprotein is elevated as the management and prognosis are different.

According to the NCEP, the desirable LDL-cholesterol level in adults is  $<3.4$  mmol/L or 130 mg/dL and a high risk LDL-cholesterol is  $>4.1$  mmol/L or 160 mg/dL. A HDL-cholesterol  $<0.9$  mmol/L or 35 mg/dL is considered a risk factor (see below).

## IDENTIFYING AND INITIAL MANAGEMENT OF THE PATIENT WITH HYPERCHOLESTEROLEMIA

### National Cholesterol Education Program (NCEP)

1. All adults over the age of 20 years should have their serum total cholesterol measured once every five years and this can be done in the non-fasted state.
2. If the patient has a desirable serum cholesterol ( $<5.2$  mmol/L), he/she is advised to have it repeated in 5 years.
3. If his/her serum cholesterol is borderline high (5.2 to 6.2 mmol/L) and he/she has no definite coronary heart disease (CHD) or two CHD risk factors (see below), the patient is given dietary information and asked to repeat the serum total cholesterol in a year.
4. If the patient has definite CHD or two CHD risk factors, he/she is treated as the patient with high serum cholesterol ( $>6.2$  mmol/L), namely do a lipoprotein analysis and further action depends on the LDL-cholesterol level.
5. The lipoprotein analysis is done on a fasted (12 hours) sample and consist of the measurement of serum total cholesterol, HDL-cholesterol, and triglycerides. Determine which fraction of lipoprotein cholesterol is elevated. The HDL-cholesterol is quantitatively determined. The LDL-cholesterol can be estimated using the Friedwald equation if the serum triglycerides is  $<5.6$

From the Cardiovascular Risk Factor Clinic, Department of Medicine, Halifax Infirmary Hospital, and Division of Endocrinology and Metabolism, Department of Medicine, Dalhousie University, Halifax, N.S.

Correspondence: Dr. M. H. Tan, Department of Medicine, Halifax Infirmary Hospital, 5303 Morris Street, Halifax, N.S. B3J 1B6.



mmol/L or 500 mg/dL as follows: LDL-cholesterol (mmol/L) = Total cholesterol - (0.46 Triglycerides + HDL-cholesterol) or LDL-cholesterol (mg/dl) = Total cholesterol - (Triglycerides/5 + HDL-cholesterol).

It is important to establish the patient's serum cholesterol level accurately as the management plan is affected by the level. This requires two to three consecutive determinations of fasting (12-14 hour) serum cholesterol, triglycerides and HDL-cholesterol over an 1-8 week period as serum cholesterol levels can fluctuate considerably from day to day in an individual.

6. If the LDL-cholesterol is  $<3.4$  mmol/L, the patient is provided with dietary information and asked to have the serum total cholesterol repeated in 5 years.

7. If the serum LDL-cholesterol is borderline high (3.4 to 4.1 mmol/L), the course of action depends on the presence of definite CHD or two CHD risk factors. If both are absent, the patient is instructed to go on the Step one diet of the NCEP (a low cholesterol (300 mg/day), relatively low fat (30% of total calories) diet with a P/S ratio of 1) and have his/her serum total cholesterol remeasured annually and dietary education reinforced. If either is present, the patient is treated as for the case for high risk serum LDL-cholesterol, namely,  $>4.1$  mmol/L.

8. For the patient with high risk LDL-cholesterol, a clinical evaluation (history, physical examination and laboratory tests) is indicated and consists of answering the following questions:

i) What are the clinical manifestations of the hypercholesterolemia?

Assess the patient for evidence of vascular disease (coronary heart disease, cerebral vascular disease, and peripheral vascular disease) and xanthoma. (Pancreatitis is usually associated with hypertriglyceridemia rather than hypercholesterolemia.)

ii) Are there any secondary causes of hypercholesterolemia?

Rule out secondary causes of hypercholesterolemia which include: dietary excess of saturated fats and/or cholesterol, hypothyroidism, nephrotic syndrome, renal dysfunction, diabetes mellitus, obstructive liver disease, and drugs (anabolic steroids, progestins). Appropriate laboratory tests (serum TSH and free thyroxine, urinalysis, serum albumin, creatinine, glucose, alkaline phosphatase and bilirubin) can be ordered as part of the investigation.

iii) Is this a familial disorder?

This can be done in two ways: (a) by obtaining a good family history of hyperlipoproteinemia and (b) screening members of the family for hyperlipoproteinemia. Patients with familial hypercholesterolemia, familial combined hyperlipoproteinemia and familial dysbetalipoproteinemia are at risk of atherosclerosis.

iv) Does the patient have other cardiovascular risk factors?

According to the NCEP, the following are considered to be CHD risk factors: male sex, family history of premature CHD (definite myocardial infarction or sudden death before age 55 years in a parent or sibling), cigarette smoking, hypertension, low HDL-cholesterol (below 0.9 mmol/L or 35 mg/dL confirmed by repeated measure), diabetes mellitus, history of definite cerebrovascular or occlusive peripheral vascular disease, and severe obesity ( $>30\%$  overweight). The presence of two or more of these CHD risk factors affect the choice of the next step of treatment in the management plan.

9. Having done the above, the next step is to set goals of treatment which consist of dietary therapy alone or dietary and drug therapy. In some cases of secondary hypercholesterolemia (e.g. hypothyroidism) treatment of the secondary disorder can correct the hypercholesterolemia. Treatment will be discussed later.

### Canadian Consensus Conference on Cholesterol (CCCC)

1. The panel recommends that serum lipid profile be considered a priority for (a) individuals with CHD, (b) individuals with a family history of hyperlipidemia or premature vascular disease, and individuals with hypertension, diabetes, renal failure and abdominal obesity.

2. A lipid profile can be a part of the periodic health examination for all adult Canadians if resources permit. For individuals with other CHD risk factors this may be given priority.

3. For adults age 30 years and over, a serum cholesterol of  $>5.2$  mmol/L is an indication for consideration for intervention. If it exceeds 6.2 mmol/L intervention is indicated. If it is between 5.2 and 6.2 mmol/L, intervention should be considered if the LDL cholesterol is  $>3.4$  mmol/L, or the HDL cholesterol  $<0.9$  mmol/L, or the serum triglycerides  $>2.3$  mmol/L or 200 mg/dL.

4. For adults between the ages of 18 and 29 years, a serum cholesterol of  $>4.6$  mmol/L or 180 mg/dL, is indication for consideration for intervention. If it exceeds 5.7 mmol/L or 220 mg/dL intervention is indicated. In the range of 4.6 to 5.7 mmol/L, intervention should be considered if the LDL cholesterol is  $>3.0$  mmol/L or 115 mg/dL, or the HDL cholesterol is  $<0.9$  mmol/L, or the triglycerides  $>2.3$  mmol/L.

5. The presence of other CHD risk factors should alert the physician to intervene at lower levels of total and LDL cholesterol.

### GUIDELINES FOR TREATMENT OF HYPERCHOLESTEROLEMIA

There are three components to therapy. The first component is to treat a secondary disorder (e.g. hypothyroidism) which may be responsible for the



hypercholesterolemia as treatment may correct the hypercholesterolemia. The second component is dietary therapy and the third component is drug therapy.

### **NCEP Guidelines For Dietary Therapy**

1. The first step is to set the goals of therapy. If the patient does not have definite CHD and less than 2 CHD risk factors, the goal is for a serum total cholesterol of <6.2 mmol/L or a LDL-cholesterol of 4.1 mmol/L. If the patient has CHD or two or more CHD risk factors, the goal is for a serum total cholesterol of <5.2 mmol/L or a LDL-cholesterol of <3.4 mmol/L.
2. The patient is then started on a Step 1 diet and his/her serum total cholesterol and LDL-cholesterol are measured in about 6 weeks and again at 12 weeks. If the goal is attained, the lipid profile is repeated four times during the first year and twice yearly thereafter.
3. If the goal is not attained, the patient should be instructed by the dietitian regarding the step 1 (Phase I of the AHA diet) or step 2 (Phase II and III of the AHA diet) diet. The serum cholesterol and LDL-cholesterol are measured in about 6 and 12 weeks. If the goal is attained, the follow-up plan is as above. If not, drug therapy is considered.

### **CCCC Guidelines For Dietary Therapy**

The panel recommended that dietary modification should be the main intervention and the following principles should be observed:

1. The total calories from fat should not exceed 30%. Saturated and polyunsaturated fats should not exceed 10% of calories each. Essential fatty acids should be included in the diet.
2. Intake of high cholesterol foods should also be decreased.
3. Protein intake should be in the range of 10-15% of total calories.
4. The remainder of the calories are to come from carbohydrate, especially complex carbohydrates.
5. Physical activity to attain and maintain cardiovascular fitness is encouraged.
6. The total number of calories prescribed is directed towards attaining desirable body weight.

Details of dietary therapy are presented by us in an accompanying article in this issue of the *Journal*.

### **NCEP Guidelines For Drug Therapy**

If dietary therapy for 6 months do not result in the desired goal, then hypolipemic drug therapy is considered. Again the management plan is influenced by whether there is CHD and two or more CHD risk factors in the patient.

1. If the patient does not have definite CHD and less than two CHD risk factors and the LDL-cholesterol is between 4.1 and 4.9 mmol/L (189 mg/dL), efforts to

enhance compliance with regards to dietary therapy and exercise should be made. Follow-up plans include annual determination serum total and LDL cholesterol, monitoring the presence of other CHD risk factors, and considering the use of low dose of bile acid sequestrants.

2. If the patient's LDL cholesterol is >4.9 mmol/L, drug therapy is indicated. Alternatively, if the patient has definite CHD or more than 2 CHD risk factors and has a LDL-cholesterol >4.1 mmol/L, drug therapy is indicated.
3. If after 6 to 12 weeks of drug therapy, the LDL-cholesterol goal is attained, the serum total cholesterol is determined every 4 months and the LDL-cholesterol annually. If later on the LDL-cholesterol goal is not attained, another drug or combination therapy can be considered.
4. If after 6 to 12 weeks of drug therapy, the LDL-cholesterol goal is not attained, another drug may be substituted or combination therapy initiated. The latter has the advantage of additive efficacy with potentially less side effects. If the LDL-cholesterol goal is attained, the follow-up plan is as outlined in (3) above.

### **CCCC Guidelines For Drug Therapy**

The panel recommends that drug therapy should be used only after dietary therapy alone has failed to attain the desired goal. When on drug therapy, dietary treatment should continue.

### **HYPOLIPEMIC DRUGS**

Drugs currently used for lowering serum cholesterol include the following:

- a. Bile acid sequestrants (cholestyramine, colestipol)
- b. Nicotinic acid
- c. Fibric acid derivatives (Gemfibrozil, Clofibrate)
- d. Probucol
- e. HMG CoA reductase inhibitors (Lovastatin)

For patients with just hypercholesterolemia, the drugs of first choice are the bile acid sequestrants and nicotinic acid. They can lower LDL-cholesterol by 15-30%. When the patient has both hypercholesterolemia and hypertriglyceridemia, nicotinic acid is the preferred drug as it can also lower serum triglycerides. Cholestyramine can potentially increase serum triglycerides. Lovastatin can be used for lowering hypercholesterolemia alone or in combination with hypertriglyceridemia. It is very potent and can lower LDL-cholesterol by 25-45%.

The fibric acid derivatives and probucol are usually not the drugs of first choice as they lower LDL-cholesterol by 5-15%. However, compliance to taking these drugs can be higher than those for bile acid sequestrants and nicotinic acid.

In selecting the hypolipemic drug, the physician should consider the following:

1. Have the drugs been shown to reduce CHD risk? The



bile acid sequestrants, nicotinic acid and gemfibrozil have been shown to reduce CHD.

2. Is there any evidence of long term safety? This has been shown for the bile acid sequestrants and nicotinic acid. Preliminary evidence suggest it is so for Gemfibrozil.

3. What is the effect of the drug on the various lipoprotein fractions? Nicotinic acid, lovastatin and gemfibrozil lower LDL and VLDL whilst they increase HDL, meeting the objectives of treatment. Both cholestyramine and probucol can increase serum triglycerides and should not be used in patients with hypertiglyceridemia. Although it lowers both LDL and HDL, probucol has anti-oxidant effects of LDL and this can affect the uptake of LDL by macrophages.

4. What is the cost of therapy? Patients have to take hypolipemic drugs for a long time and cost can be a major factor for compliance to drug therapy. According to Eastern Drug Services Pharmacist's Catalogue wholesale list price, the approximate monthly (30 days) costs for the various drugs are as follows:

Cholestyramine	16 g daily	\$119 (package) \$ 89 (can)
Colestipol	20 g daily	\$ 83 (package)
Nicotinic acid	3 g daily	\$ 18
Gemfibrozil	1.2 g daily	\$ 49
Clofibrate	2 g daily	\$ 20
Probucol	1 g daily	\$ 26
Lovastatin	40 mg daily	\$ 98

The mark-up will be different at various retail pharmacies. Add to it the dispensing fee of \$7 per prescription, the total cost to the patient can be quite substantial.

5. What are the side effects of the drug? Each drug has many side effects. The physician should be aware of them and explain them to the patient. In addition, during follow-up, tests should be done to monitor these potential side-effects.

## COMPLIANCE

As treatment is life-long, compliance to the therapeutic regimen is often a problem. The physician and members of the health care team at lipid clinics can promote patient compliance in several ways:

- make the treatment programme simple;
- provide simple instructions;
- be prepared to modify treatment plan to increase compliance;
- praise patients when they are compliant;
- review with the patient the progress or lack of it made;
- educate the patient regarding the whys and hows of the management programme;
- involve other members of the family in the management programme.

Patient compliance is a key to the success of the treatment programme.

## IN CLOSING

There are many other aspects of care of the hypercholesterolemic patient that have not been discussed. We feel the physician should try to modify all risk factors that can be changed (hypertension, cigarette smoking, obesity, diabetes mellitus) to reduce cardiovascular risk. In following the patient, the physician should be aware of the effect of posture on serum cholesterol and triglyceride levels — changing from an upright to sitting position for 20 minutes can decrease the serum lipid levels by 5-7%. The physician should be aware of the normal reference ranges for serum cholesterol, triglyceride and HDL-cholesterol in his/her hospital's laboratory and whether the laboratory participate in a quality control programme. Today precision of cholesterol determination is not difficult to attain. But accuracy of cholesterol measurement can be difficult to attain. We have also not discussed other lipid risk factors. We refer the reader to the third reference for this.

In closing we hope the guidelines provided by the NCEP and the CCCC can be adapted by the primary care physician in the management of the patient with hypercholesterolemia. □

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# The Benefits Vs. Risks of Pharmacotherapy of Hypercholesterolemia

## A REVIEW OF THREE TRIALS

D. B. Langille,\* MD, MHSc, and P. M. Lavigne,\*\* MD,

Halifax, N.S.

While mortality rates due to cardiovascular disease (CVD) have been declining steadily since the early 1970s, this disease is still the leading cause of death in Canada and is killing almost 80,000 Canadians per year. Of these deaths, 60% are due to ischemic (coronary) heart disease (IHD). In 1986, in Nova Scotia, there were 7,260 hospital separations for IHD (ICD-9, 410-414), accounting for 75,819 hospital days. Efforts aimed at the control of two of the major risk factors for IHD, smoking and hypertension, are believed to have contributed to much of the decline in mortality rate over the past 15 years. The role played by dietary factors, however, remains somewhat controversial. Nevertheless, there is a large body of evidence in the literature that consistently indicates strong positive associations between diet, serum cholesterol and IHD.<sup>1</sup>

Various expert groups have attempted to define optimal levels for total serum cholesterol. A Canadian Consensus Conference on cholesterol was held in Ottawa in March 1988. Its preliminary report has set levels for intervention at 240 mg/dL (6.2 mmol/L) for those above age 29 and 220 mg/dL (5.7 mmol/L) for those 18-29 years-of-age.<sup>2</sup> Based on the results of the Nova Scotia Heart Health Study, *one out of six individuals in Nova Scotia requires medical intervention as this proportion has a total cholesterol of more than 240 mg/dL (6.21 mmol/L).*<sup>3</sup> The Canadian Consensus Conference recommended, however, that drugs be used only after an "adequate trial of rigorous diet modification", or when dietary therapy is obviously insufficient. Drugs mentioned in this report were cholestyramine, clofibrate, gemfibrozil, nicotinic acid, probucol and HMG-CoA reductase inhibitors.

The clinician will face increasing pressure to prescribe drug therapy for hypercholesterolemia in the future as more potent agents with fewer side effects, such as Lovastatin (Mevinolin), are made available on the Canadian market. In fact, Lovastatin may soon become the drug of choice, especially for treating non-familial and heterozygous familial hypercholesterolemia.<sup>4</sup> Accordingly, physicians will need to be familiar with the quality of the scientific evidence in order to make

informed decisions as to the benefits vs. the risks of a particular therapeutic regimen. While there are many published studies on these drugs which document their efficacy as cholesterol-lowering agents and their short-term side effects, many have not been evaluated for their effectiveness in actually reducing morbidity and mortality, and their long-term safety. Reliable evidence upon which to base this latter assessment is best if available from large scale randomized clinical trials. Clofibrate, cholestyramine, and gemfibrozil, are cholesterol-lowering drugs that have received this kind of investigation and thus warrant critical evaluation.

In a review of such trials, what do we want to assess? The basic questions are: Why? — are the purpose and hypothesis clearly stated? How? — what is the design? Who? — how was the study population selected? Are groups comparable after randomization? What? — is the intervention clearly described? Were outcome measures clearly defined? How many? — was the study large enough to detect important differences? So what? — were detected differences clinically significant? Can results be generalized to other populations? In a review of this nature it is not possible to exhaustively critique each of these trials; however, major methodologic features will be described from the perspective of clinical epidemiology in order to assist the clinician to arrive at an objective evaluation of their strengths and weaknesses.

### CHOLESTYRAMINE — THE LRC-CPPT<sup>5</sup>

The Lipid Research Clinics (LRC) Coronary Primary Prevention Trial (CPPT) was a multicentre, randomized, double-blind study, designed to assess the effectiveness of the cholesterol-binding resin, cholestyramine, in reducing the risk of IHD in asymptomatic middle-aged men with primary hypercholesterolemia (i.e., type II hyperlipoproteinemia). A total of 3,806 participants, aged 35-49 years (mean 47.8), were selected from thousands of men who had previously been screened through twelve clinics from 1973-76. Recruits tended to be employed, better educated and less likely to be members of minority groups. Selection was based upon the following criteria: i) serum cholesterol level of 265 mg/dL (6.84 mmol/L) or greater, and a low-density lipoprotein cholesterol (LDL-C) of 190 mg/dL (4.92 mmol/L) or greater (mean pre-diet total cholesterol was 291 mg/dL in both groups); ii) asymptomatic, including being free of any manifestations of IHD and of

\*Director, Cobequid Health Unit, Department of Health and Fitness, Province of Nova Scotia, Chairman, Community Health Committee, The Medical Society of Nova Scotia.

\*\*Provincial Epidemiologist, Department of Health and Fitness, Province of Nova Scotia.



conditions associated with secondary causes of hyperlipidemia; and, iii) unresponsive to a moderate cholesterol-lowering diet. After randomization, both groups were almost identical with 1,900 and 1,906 subjects in the placebo and treatment groups, respectively. The treatment group received 24 grams of cholestyramine, either b.i.d. or q.i.d. and equivalent doses of a placebo were given to the control group. Rigorous attention was given to maintaining a uniform protocol and a high rate of compliance with the drug regimen.

The primary end-point for evaluating treatment effectiveness was the combination of definite nonfatal myocardial infarction (MI) and/or death related to CVD. An average of 7.4 years of followup was achieved in this trial, with all individuals entering the study being accounted for at its conclusion. There were 187 primary endpoints to the placebo group (diet alone) and 155 in the treatment group. Nonfatal MIs accounted for most of these events. The life-table determined event rate for the primary endpoint was 8.6% in the placebo group vs. 7.0% in the treatment group — a statistically significant difference of 1.6% ( $p < 0.05$ ), or a reduction in risk of 19% with a 90% confidence interval (CI) of 3% to 32%. Actual decline in levels of total cholesterol and LDL-C levels were highly statistically significant in the treatment group, but no significant beneficial effects were observed in the placebo group. This is not surprising in view of exclusion for dietary non-response prior to randomization. The decrease in the serum levels was also found to be correlated with the reduction of risk observed in the treatment group.

#### **GEMFIBROZIL — THE HELSINKI HEART STUDY<sup>6</sup>**

The Helsinki Heart study was similar to the design of the LRC-CPPT, and assessed the effectiveness of using gemfibrozil for reducing the risk of IHD. A total of 4,081 subjects, aged 40-55 years (mean 47) were selected from 23,531 men seen in 37 clinics in Finland and who were employed in telecommunications, railway and other industries. Participants were required to have the following eligibility criteria: i) non-high density lipoprotein serum cholesterol (HDL-C) level — i.e., total cholesterol minus HDL-C — of 200mg/dL (5.2 mmol/L) or greater; ii) free of signs or symptoms of IHD, including an abnormal ECG; and iii) free of other disease that could influence the study outcome. Subjects with hypertension and non-insulin dependent diabetes, however, were accepted.

Following randomization, the subjects were almost evenly allocated, with 2,051 and 2,030 in the treatment and the placebo groups, respectively. The mean serum cholesterol in the treatment and placebo groups was 289.1 mg/dL (7.46 mmol/L) and 288.7 mg/dL (7.45 mmol/L), respectively. The only statistically significant difference between these two groups was that those in the placebo group had a more sedentary lifestyle — a bias that could increase the mortality differential due to

CVD, a "liberal" bias, tending to inflate the treatment effect. Gemfibrozil, and a placebo were administered in a dosage of 600mg b.i.d., to the treatment and control group respectively. A cholesterol-lowering diet was recommended to all participants, and an increase in physical activity, as well as reduction in smoking was also encouraged. The principal endpoints for this study were fatal and non-fatal MI, and cardiac death. Besides rigorous attention to a uniform protocol, compliance with drug therapy was carefully monitored. All subjects were followed for the entire trial period of five years (mean 60.4 months) and included in the analyses.

Treatment with gemfibrozil induced mean reductions of 8% in total serum cholesterol, 8% in LDL-C, 35% in non-HDL-C and triglycerides, and an increase of more than 10% in HDL-C. A statistically significant decrease of 34% (95% CI 8.2% to 52.6%) in total cardiac endpoints was observed in the treatment group with almost all of this improvement being due to a reduction in non-fatal MI.

#### **CLOFIBRATE — THE WHO COOPERATIVE TRIAL<sup>7,8</sup>**

The objective of the WHO study was to determine whether the incidence of IHD was lowered by the reduction of high and moderately high blood lipid levels in otherwise healthy men aged 30-59, using clofibrate. The study design was generally similar to the previous two trials — i.e. multicentre, double-blind, and sequentially monitored with the drug intervention being randomized. Subjects were drawn from blood donors in Edinburgh and Budapest, as well as population registers in Budapest and electoral roll registrants in Prague. Those suffering from IHD, increased blood pressure, diabetes mellitus requiring drug therapy, and other diseases with a poor prognosis, were excluded. Approximately 62% of those that were eligible, volunteered for the trial.

The intervention consisted of Clofibrate 800 mg. b.i.d. and a placebo, given to the treatment and control groups, respectively. No other risk factor manipulation took place in this trial. A high rate of compliance was achieved (84-95%). Both groups were very comparable after randomization, with 5,320 on clofibrate and 5,296 on placebo. Initial mean serum cholesterol levels were 249 mg/dL (6.44 mmol/L) and 247 mg/dL (6.39 mmol/L) in the treatment and placebo groups, respectively. All men were considered to be in the trial up to the date of withdrawal or until they were lost to followup. Virtually all those entering the trial were accounted for at its conclusion. The primary outcome measures were non-fatal MI, fatal acute IHD, and sudden death. The average period of follow-up was 5.3 years; in addition, the vital status of 99.8% of these participants was also established in a subsequent study with a mean observation period of 9.6 years.<sup>8</sup>

The mean reduction in serum cholesterol that was observed in the WHO trial was only 9% in the treatment group (much less than the 15% expected). The incidence



of primary endpoints was 20% less in the treatment group than in the control group and this difference was statistically significant ( $P < 0.05$ ); moreover, this reduction was entirely due to a decrease in non-fatal MI, while mortality from fatal acute IHD and sudden death were virtually the same in both groups. Total mortality was observed to be markedly increased in the treatment group.

## DISCUSSION

While the results of these trials imply that treatment with a cholesterol-lowering agent is efficacious for reducing CVD risk, does this approach result in overall clinical benefits? All three studies demonstrated a significant decrease in non-fatal MI in the treatment group, with positive overall results ranging from a reduction of 19% in the LRC-CPPT to 37% in the Helsinki study — a significant clinical benefit. On the other hand, none of these studies observed a statistically significant reduction in overall (all causes) mortality in the treatment group, and two of the studies indicated increased mortality in the treatment group.

In the LRC-CPPT, after a mean of 7.4 years of follow-up, 71 deaths were observed in the control group, vs. 68 deaths in the treatment (cholestyramine) group — a non-significant difference. It is possible, however, that this trend (a reduction of 7%) may have become significant with a much longer period of followup. In the Helsinki study, after a mean period of followup of 5 years, 42 deaths occurred in the placebo group, vs. 45 in the treatment (gemfibrozil) group — a non-significant difference. The mortality followup study of the participants in the WHO trial had a mean observation period of 9.6 years, and reported 317 deaths in the control group vs. 396 in the treatment (clofibrate) group — a statistically significant ( $p < 0.01$ ) increase of 25% more deaths in the treatment group. These latter findings were consistent with the first report of this trial which covered a mean period of 5.3 years. The findings from the WHO trial also showed a significant increase in diseases of the liver (including malignancy), gall bladder, and intestines, in the treatment group. This has led to some concern about the possible deleterious consequences of reducing body cholesterol pools, and the long-term toxic effects of Clofibrate.<sup>8</sup> Obviously, overall mortality is an important indicator of the potential long-term safety of a particular drug therapy.

Besides evaluating the potential for adverse effects on life expectancy, these trials also provide some insight into possible side-effects. In the LRC-CPPT, these consisted of GI upset and an increase in various GI malignancies (21 vs. 11) in the treatment group. There was also an increased number of gallstones (16 vs. 11) and gallbladder operations (36 vs. 5) in the treatment group. None of these differences was statistically significant, however. In the Helsinki heart study, a non-significant increase was observed in gallstone (18 vs. 12) and cataract (7 vs. 3) operations, while significant ( $p < 0.02$ ) increase was seen in GI operations (81 vs. 52) in

the treatment group. In the WHO trial, the treatment group experienced more deaths from diseases of the liver, gall bladder and intestines, as well as a significantly ( $p < 0.001$ ) increased number of cholecystectomies (59 vs. 24), confirming other reports in the literature concerning the lithogenicity of clofibrate.<sup>9</sup> The structural similarity of Clofibrate and Gemfibrozil is worthy of note at this point.

Finally, if we assume a clinical benefit due to decreased non-fatal MI, how do these interventions apply to the clinical setting, especially in Nova Scotia? To address this question, one should examine what treatments were used and who the patients were. It is tempting to extend the results of these trials to the entire patient population; for example, in the LRC-CPPT the authors concluded that "the trial's implications, however, could and should be extended to other age groups and women and, since cholesterol levels and CHD risk are continuous variables, to others with more modest elevation of cholesterol levels." While the results provide evidence for the role of lipid reducing in the prevention of heart disease, it should be noted, however, that the patients who participated in these trials were middle-aged males with relatively high serum cholesterol and atypical demographic characteristics. As a result, one cannot reliably apply their findings to women, other racial groups, or men with lower levels of hypercholesterolemia. This lack of generalizability is often a major limitation of randomized controlled trials.

## CONCLUSIONS

As the recommendations of the recent Canadian Consensus Conference on cholesterol become more widely known, and given the increased promotion of newer and more easily tolerated cholesterol-lowering agents, there will undoubtedly be a risk of overgeneralizing the results from various studies. Many of these agents are useful for the treatment of specific lipid disorders, but their long-term safety is questionable, and thus their use should be limited to situations that are unresponsive to diet modification alone. A recent gathering of public health and clinical experts in Halifax has led to the conclusion that currently, adequate resources do not exist in Nova Scotia for optimal dietary management. It is the hope of the authors that this deficiency will not lead to increased drug usage in an effort to "bypass" dietary intervention.

Whereas the three trials reviewed provided evidence for the lipid reduction in the prevention of IHD, they were unable to show that the pharmacological treatment of moderate to severe hypercholesterolemia led to an overall increase in life expectancy — except for reduced mortality from IHD. This article points out some of the difficulties in the interpretation and application of the results from randomized controlled trials, despite their inherent methodological advantages, especially when dealing with a multi-factorial condition such as IHD. □

References on page 163.



# Management of Hyperlipoproteinemias

## DIETARY CONSIDERATIONS

K. Travers, Pdt, BSc, MA, and M. H. Tan, MD, FRCP(C), FACP,

Halifax, N.S.

Although cardiovascular disease continues to be the number one cause of death in Canada, mortality rates have been declining over the past twenty years.<sup>1</sup> The decline has coincided with beneficial changes in lifestyle and risk factors; Canadians are smoking less, exercising more and eating more wisely.<sup>1</sup> Diet cannot be given all of the credit for improvements in the heart health of Canadians, but it is well accepted that changes in diet can lower blood lipid levels, and ultimately, cardiovascular risk.<sup>1</sup> The purpose of this paper is to highlight recent developments in the nutritional management of hyperlipoproteinemias, with an emphasis on practical considerations for patient education and care.

### GOALS FOR NUTRITIONAL MANAGEMENT

From a medical perspective, the purpose of dietary modifications are: 1) to decrease elevated blood lipid levels; 2) to decrease cardiovascular risk; and, ultimately 3) to decrease the morbidity and mortality from cardiovascular disease. Nutritionally, balance and adequacy must also be considered to ensure overall health status is not compromised. To the patient, variety and quality of life are of the highest priority and worthy of full consideration by health care providers.

Reduction in lipid levels are associated with decreased risk only if maintained over the long-term; therefore, temporary changes in lifestyle are of limited value. Priority must be given to continuing patient education; ensuring nutrition recommendations are individualized to meet the medical, nutritional, social and psychological needs of each patient. Referral to a professional dietician for counselling and follow-up is recommended.

### NUTRITION RECOMMENDATIONS AND RATIONALE

#### 1. Achievement and Maintenance of a Healthy Body Weight

Obesity is a well-established risk factor for cardiovascular disease.<sup>1</sup> Its influence is exerted primarily through its association with hyperlipidemia, hypertension and diabetes mellitus<sup>1</sup>, but recently has been indicated as an independent risk factor.<sup>2</sup> The biggest question in the minds of many practitioners is, at what weight is my patient at risk?

The body mass index (BMI) is an easy to calculate measure of obesity highly correlated with health risk. The BMI is calculated from measures of height and weight using the following formula;

$$\text{BMI} = \frac{\text{weight (in kilograms)}}{[\text{height (in meters)}]^2}$$

A BMI of 20-25 kg/m<sup>2</sup> is associated with the lowest health risk, 25-30 kg/m<sup>2</sup> a low relative risk, but over 30 kg/m<sup>2</sup>, risk rises sharply.<sup>3</sup>

Beneficial effects of weight reduction on serum lipids include: 1. a reduction in total cholesterol primarily due to a reduction in LDL cholesterol; 2. a reduction in triglycerides and VLDL cholesterol; and 3. an increase in the antiatherogenic lipoprotein, HDL cholesterol.<sup>4</sup>

Weight loss is best achieved by use of a nutritionally balanced hypocaloric diet combined with moderate increases in activity levels. Reduction in energy content of the diet should come primarily from a reduction in fat due to fat's hyperlipemic effects and high caloric density. Diet composition is as important as energy level in the treatment of obese patients with hyperlipidemia. Therefore it is extremely important to guard against the use of unorthodox means of weight reduction, particularly low carbohydrate, high protein, high fat diets, which may be detrimental to cardiovascular health. Once again, success in maintaining healthy weights and diminishing cardiovascular risk requires long-term lifestyle change, not temporary modifications in diet. The importance of continuing patient education cannot be overemphasized.

#### 2. Reduction of Dietary Saturated Fat

The role of dietary saturated fats in raising blood levels of total cholesterol, LDL-C and triglycerides is well established and the basis for recommending a decrease in dietary fats, particularly saturated fats, in hyperlipidemias.<sup>4</sup> Practical means of reducing intake of saturated fats are as follows:

- substituting low-fat or skim dairy products for creams, whole milks, and cheeses.
- use of lean, well-trimmed meats, skinless poultry and fish in place of high fat processed meats such as bacon or bologna.
- reduction in quantities of products fried in or baked with animal fats or saturated vegetable fats such as palm, coconut or hydrogenated vegetable oils.

Cardiovascular Risk Factor Clinic, Department of Medicine, Halifax Infirmary Hospital, and Division of Endocrinology and Metabolism, Department of Medicine, Dalhousie University, Halifax, N.S. Correspondence: Dr. M. H. Tan, Halifax Infirmary Hospital, 5303 Morris Street, Halifax, N.S. B3J 1B6



- discriminate use of table fats such as butter or hard, saturated margarines.

The hypolipidemic effect of such dietary practices is frequently augmented by weight loss due to the high caloric density of fats. In the obese, weight loss without a "reducing diet" per se is advantageous, but in persons of normal weight, caloric substitution of unsaturated fats and carbohydrates is necessary.

### 3. Substitution of Unsaturated Fats

The cholesterol-lowering effects of polyunsaturated fatty acids are well documented and have in the past been the basis of recommendations for liberal use.<sup>4</sup> However, high intakes of polyunsaturated vegetable oils have been linked with gallstones, some cancers, and temporary reduction of HDL cholesterol and therefore, current recommendations suggest more prudent use.<sup>4</sup> Substitution of polyunsaturated fats such as safflower, sunflower, soy and corn oils for reductions in saturated fat intake is preferable to dietary supplementation.

Monounsaturated fats, originally thought to have little lipemic effect, have recently gained attention as effective hypocholesterolemic oils which do not lower HDL cholesterol.<sup>5</sup> In addition, since monounsaturated fats are synthesized by the human body, the potential for "toxicity" is lower than with polyunsaturates. High levels of monounsaturates from olive oil are consumed in Mediterranean cultures with no adverse effect.<sup>6</sup> However, all fats, saturated, polyunsaturated and monounsaturated are calorically dense; indiscriminate use is likely to lead to undesired weight gain. Therefore, current recommendations suggest a reduction of total fat. Unsaturated fats can be substituted for part of the reduction in saturates to improve diet palatability.

### 4. Reduction of Dietary Cholesterol

High levels of dietary cholesterol are associated with hypercholesterolemia due to elevations of LDL-C, and hypertriglyceridemia due to elevated VLDL-C. However, the link between dietary cholesterol and serum lipids does not appear to be as strong as that between saturated fat and serum lipid levels.<sup>4</sup> Prudent consumption of high cholesterol foods is therefore recommended. A decrease in total cholesterol intake is usually associated with a decreased intake of saturated fat and therefore, emphasis is placed on moderate use of foods very concentrated in dietary cholesterol: egg yolks and organ meats. Shellfish, originally thought to be high in cholesterol is now believed to be acceptable. New methods of analysis using gas chromatography have revealed the sterols previously believed to be cholesterol are to a large extent plant sterols which do not have atherogenic effects.<sup>7</sup> As shellfish are low in saturated fat (provided they are not dipped in butter!) and are usually consumed infrequently, their restriction is not warranted.

From a patient's perspective, controlling intake of dietary cholesterol is much more straightforward and

easy to accomplish in comparison to restrictions of dietary fat. It is very important to address misconceptions early in the education process and identify a diet low in dietary cholesterol but still potentially atherogenic due to a high concentration of fat and energy.

### 5. Increase Dietary Carbohydrates

Reduction in total fat concentration in the diet necessitates energy replacement with carbohydrates. Preference is given to complex carbohydrates found in breads, cereals, beans, vegetables and some fruits. Complex carbohydrates are preferable to simple sugars because they do not stimulate surges of hyperglycemia, and due to the presence of dietary fibres, particularly water-soluble fibres found in vegetables, beans and oats, which have hypocholesterolemic effects.<sup>6</sup>

Traditionally, diets high in carbohydrate have been discouraged in hypertriglyceridemia and diabetes mellitus due to observed triglyceride and glucose raising effects. However, such effects are minimized when complex carbohydrates are emphasized. In fact, high carbohydrate-fibre diets may actually improve glycaemic control while helping to lower cholesterol and LDL levels, decreasing cardiovascular risk in diabetic patients. The effect on triglycerides is usually only transient and offset by the reduction in both cholesterol and triglycerides due to the decrease in dietary fat.<sup>6</sup> Overall, substituting complex carbohydrate for total dietary fat is the preferred approach to diet therapy for all hyperlipidemias.

In summary, nutrition recommendations are similar for all types of hyperlipoproteinemias due to the interrelated nature of dietary changes on lipid levels. Recommendations include:

1. Achievement and maintenance of healthy body weight.
2. Reduction in dietary saturated fats.
3. Substitution of dietary unsaturated fats.
4. Reduction in dietary cholesterol.
5. Increase dietary carbohydrates, particularly fiber-rich complex carbohydrates.

## CURRENT RECOMMENDATIONS FOR DIETARY MANAGEMENT OF HYPERLIPOPROTEINEMIAS

The nutritional recommendations previously described are only of value to the person with hyperlipidemia if incorporated into a practical, individualized dietary plan. It is important to consider not only the patient's lipid levels, but any other contributing health problems, overall nutritional status, and social and psychological well-being.

An assessment of the patient's usual diet is a logical place to start the counselling process. A thorough dietary history helps to highlight habits most in need of improvement, may identify potential barriers to change



(such as frequent traveling/restaurant eating or lack of support systems), and may even provide an indication of expected response to dietary recommendations. For example, a more dramatic hypolipemic effect would be expected in response to dietary changes made by someone with very poor initial habits. However, a person who follows a relatively low fat diet may be sufficiently motivated to increase the restriction for potential hypolipemic effect. Because of such individual variability in diet and motivation levels, a progressive approach to dietary change is recommended (Table I).

**TABLE I**  
PROGRESSION OF DIETARY RESTRICTION FOR  
HYPERLIPOPROTEINEMIA

Dietary Component	Phase I	Phase II	Phase III
<b>Energy to achieve and maintain healthy weight</b>			
Fat (% energy)	30	25	20
Carbohydrate (% energy)	55	60	65
Protein (% energy)	15	15	15
Cholesterol (mg/day)	300	200-250	100-150
Polyunsaturated fat to saturated fat (P/S) ratio	1	1	1

The average Canadian consumes a diet which comprises approximately 40% of energy from fat, primarily from saturated fat, and approximately 450-500 mg cholesterol per day.<sup>6</sup> Current recommendations for the general population suggest a decrease in fat intake to approximately 30% of energy, with equal contributions from saturated, monounsaturated and polyunsaturated fats. Cholesterol intake should be reduced to less than 300 mg/day.<sup>4</sup>

This first phase (Phase I) of dietary restriction is not difficult to achieve (Table II). The diet is not radical and poses no potential harm, but its potential benefit to the public's health justifies its widespread recommendations. More widespread social acceptance of the "heart-healthy" approach to eating also helps to facilitate development of an environment more conducive to prudent choices, particularly for those who require a more restrictive approach.

Following initiation of the Phase I diet, follow-up should be arranged to assess 1. lipemic response to dietary intervention, and 2. the patient's ability to implement the recommendations. Lack of response could be attributed to either dietary non-compliance or a metabolic resistance to dietary modifications.

If dietary non-compliance is the problem, additional counselling is in order to help the patients overcome the barriers encountered in day-to-day situations. It is important to recognize that although the Phase I diet is not radical, it may still represent a dramatic departure from the usual eating habits of some individuals; a workable plan will take time to achieve.

**TABLE II**  
PROGRESSIVE DIETARY MODIFICATIONS

Food Group	Phase I	Phase II (Phase I plus . . .)	Phase III (Phase II plus . . .)
Cholesterol-dense foods	limit to 3 servings/week	limit to 2 servings/week	limit to 1 serving/week
Meat, fish, poultry and alternates	choose lean meats, remove poultry skin, limit portions to 8 oz (240g) per day	limit portions to 4-6 oz (120-180) per day	limit portions to 4 oz (120g) per day, substitute vegetarian-type alternates
Milk and Milk Products	replace whole milk and cream with skim or low fat (1% or 2% M.F.) milk, choose low fat (less than 2% M.F.) dairy products, choose low fat (less than 20% M.F.) cheeses	choose only skim or 1% M.F. milk	use low fat cheese as part of meat allowance
Fruits and Vegetables	avoid high-fat choices; coconut, olives, avocados; avoid preparing with added sauces (eg. cheese or cream sauce) avoid frying as a means of preparation		
Breads and Cereals	limit use of high fat snack crackers, bakery products (donuts, muffins, croissants, pastries etc.)	account for all fat used in baked goods as part of fat allowance	
Fats and Oils	substitute a polyunsaturated margarine (min 40% PUFA) for butter/hard margarines, substitute vegetable oils for shortening or lard in cooking, limit total fat intake to 3-6 tsp. per day	account for fats/oils used in cooking/baking as part of allowance (3-6 tsp. per day)	limit allowance to 3-4 tsp./day



If no hypolipemic response is observed despite adherence to the Phase I diet, further restriction of fat and cholesterol is warranted. Progression to Phase II, and if necessary, Phase III (Tables I and II) is realistic for those patients motivated to decrease their risk by lifestyle means only, but will require intensive education to help patients to recognize foods appropriate for them when shopping or eating away from home. Food labels, cookbooks and restaurant menus are indispensable during the counselling process at this stage of dietary modification.

#### SUMMARY

A progressive individualized approach to dietary change is recommended for the following reasons:

1. The patient is given a transition period to allow a natural adjustment to new eating patterns.
2. Response to dietary change can be monitored as an indication of the level of restriction required to achieve desirable lipid levels.
3. The patient, nutrition counsellor, and physician can evaluate together the level at which further lifestyle change becomes impractical and when a medication may be an appropriate adjunct to dietary therapy.

It is important to note that throughout all stages of counselling, family changes are recommended to

decrease the patient's burden of being on a "special" diet and to help decrease the risk in family members who may have a hereditary predisposition to hyperlipidemia. In addition, other lifestyle-related risk factors such as smoking and lack of exercise should be considered as part of the total lifestyle plan. □

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1. AHA Special Report. Optimal resources for primary prevention of atherosclerotic disease. *Circulation* 1984; **70**: 157A-205A.
2. Hubert HB, Feinleik M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: A 26 year follow-up of participants in the Framingham heart study. *Circulation* 1983; **67**: 968-77.
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5. Mattson FH, Grundy SM. Comparison of effects of dietary saturated, monounsaturated, and polyunsaturated fatty acids on plasma lipids and lipoproteins in man. *J Lipid Research* 1985; **26**: 194-202.
6. Grundy SM, Bilheimer D, Blackburn H *et al.* Rationale of the diet-heart statement of the American Heart Association. *Circulation* 1982; **65**: 839A-54A.
7. Krzynowek J. Sterols and fatty acids in seafood. *Food Technology* 1985; **39**: 61-68.

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135th Annual Meeting and  
24th Meeting of Council  
November 24-26, 1988  
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(See YOUR President's Letter of October 14, 1988)

***THE meeting of the year for YOUR profession***



## Notice Re: By-Law Amendments



# Notice Re: By-Law Amendments

The By-Laws of the Medical Society stipulate that amendments to them may be proposed at an Annual Meeting of the Society provided they are published in the Journal at least one month prior to the Annual Meeting.

The following amendments will be presented by the Executive Committee at the 1988 Annual Meeting of the Society.

(Where possible, changes/additions in the proposed are indicated by **BOLD** type.)

## EXISTING

## PROPOSED

### 1. TITLE

1.1 This Society shall be known as The Medical Society of Nova Scotia which is the Nova Scotia Division of The Canadian Medical Association, hereinafter referred to as "the Society" in these By-Laws. In these By-Laws and Rules and Regulations the singular shall include the plural and the plural the singular; the masculine shall include the feminine.

1.2 does not exist

1.3 does not exist

### 1. TITLE

1.1 This Society shall be known as The Medical Society of Nova Scotia which is the Nova Scotia Division of The Canadian Medical Association, hereinafter referred to as "the Society" in these By-Laws. In these By-Laws and Rules and Regulations the singular shall include the plural and the plural the singular; the masculine shall include the feminine.

1.2 does not exist

1.3 does not exist

6.15 Discipline of Members

6.15.1 Where, after due enquiry, a member of the Society is found by the Discipline Committee to be guilty of unprofessional conduct or of conduct unbecoming a member of the medical profession, the Executive Committee, and only the Executive Committee, may resolve to reprimand in such manner as the Executive Committee sees fit, suspend or expel the offending member from membership in the Society.

6.15.2 Should any member of the Society be convicted of any criminal offence or have his name removed from the Register of the Medical Council of Canada or the licensing body of any Province of Canada because of felonious or criminal act or disgraceful conduct in any professional respect the Executive Committee may resolve to suspend or expel such person from membership in the Society.

6.15 Suspension of Membership

6.15.1 Any member whose name is erased from the medical register or temporary medical register or who is suspended from the practice of medicine by the Provincial Medical Board, under provisions of the Medical Act, because, in either case, of unprofessional conduct or of conduct unbecoming a member of the medical profession, or who is convicted of any criminal offense or has his name removed from the Register of the Medical Council of Canada or the licensing body of any other province of Canada because of any felonious or criminal act, unprofessional conduct or conduct unbecoming a member of the medical profession, or the like, loses ipso facto his right to membership in the Society and thereby forfeits all his rights and privileges appertaining to such membership in the Society.

6.15.2 Any member losing his membership in the Society pursuant to section 6.15.1 shall, subject to conditions imposed by the Executive Committee, be restored to membership upon resolution of the Executive Committee.



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**EXISTING**

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**PROPOSED**

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6.15.3 Any member suspended or expelled by resolution as aforesaid shall thereby forfeit all his rights and privileges as a member of the Society.

6.15.3 By accepting membership in this Society under the ByLaws and Code of Ethics of the Society, every member attorns to these ByLaws and agrees to such rights of loss of membership and of forfeiture of rights and privileges in the Society and thereby specifically waives any rights of claims to damages in the event of losing such membership and forfeiture of such rights and privileges.

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8 MEETINGS

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8 MEETINGS

8.1 Time and place of Meetings

8.1 Rules of Order:

8.1.1 The time, place and format of meetings shall be decided by the Executive Committee and shall be announced as early as possible.

8.1.1 Bourinot's Rules of Order, Third Revised Edition, shall be the guide for conducting all meetings of the Society, of Council and of the Executive Committee.

8.1.2 No member shall take part in the proceedings of the Society or attend any part of the meeting until he has properly registered. Only members and specifically invited guests are eligible to register and to attend an Annual Meeting.

8.2 Presiding Officers

8.2 Notice of meetings.

8.2.1 The President shall preside at all general, scientific, business and social meetings of the Society. In his absence the President-Elect shall be the presiding officer.

8.2.1 Notice for the Annual Meeting of the Society and meetings of the Nominating Committee shall be published in *The Journal* of The Medical Society of Nova Scotia at least one month prior to the date of meeting.

8.2.2 Notice for all special and regular committee meetings of the Society, Council and the Executive Committee shall be sent out not less than ten days prior to the meeting. The agenda for the meeting shall be included in the notice.

8.2.3 Special meetings of the Society or of Council may be called by the President or upon the written request of any ten members of the Society.

8.2.4 Special meetings of the Executive Committee may be called by the President or upon the written request of any five voting members of the Executive Committee.



**EXISTING****PROPOSED**

- 8.3 Quorum:
- 8.3.1 Twenty-five members shall constitute a quorum at all meetings of the Society or of the Council. Seven members shall constitute a quorum at meetings of the Executive Committee of the Society.
- 8.4 Rules of Order:
- 8.4.1 Bourinot's Rules of Order, Third Revised Edition, shall be the guide for conducting all meetings of the Society.

- 8.3 Quorum
- 8.3.1 The quorum of the Annual Meeting of the Society and for Council shall be twenty five voting members. Quorum for all other Committees of the Society, shall be one third of the voting members.
- 8.4 Delete
- 8.4.1 Delete

## 11.7 Duties of the Executive Director

## 11.7 Duties of the Executive Director

## 11.7.1 The Executive Director

## 11.7.1 The Executive Director

- a. The Executive Director shall be appointed by the Executive Committee and shall perform such duties and functions as prescribed by the Society.
- b. The Executive Director is accountable to the President and the Chairman of the Executive Committee. He may delegate portions of Society staff functions to members of the staff but may not delegate his overall responsibility or accountability for the proper conduct of the delegated responsibilities.
- c. The Executive Director will see that Society decisions are effected. He will administer the affairs of the Society. Where appropriate and as authorized he will co-ordinate Society programs with other agencies, Government and the community generally, serving as Official Representative of the Society.
- d. The Executive Director will co-operate with the Treasurer in preparation of the annual financial report and budget. He will administer the funds allotted by Society approved budget. He will ensure that an adequate financial system is established to safeguard Society funds.
- e. The Executive Director will ensure that adequate arrangements are made for maintaining a reporting system to record and preserve a record of Society business, and that necessary arrangements are made for Society meetings. He shall ensure that Annual Reports of Committees, Sections and Representatives are circulated to Council two weeks in advance of Council meetings.
- f. The Executive Director will communicate with and assist Branch Society Officers.
- g. The Executive Director is a member ex-officio of all committees of the Society (except during discussion of staffing matters relating to him personally) and he or his delegated staff member shall attend such committee, Branch or Section meetings as directed or requested.
- h. The Executive Director shall report annually to Council.

- a. The Executive Director shall be appointed by the Executive Committee on recommendation of the Officers. A committee of the President, President-Elect and Past President shall determine the salary and benefits of the Executive Director.
- b. The Executive Director shall be accountable to the President and the Chairman of the Executive Committee. He may delegate portions of Society staff functions to members of the staff, but may not delegate his overall responsibility or accountability for the proper conduct of Society affairs.
- c. The Executive Director shall be responsible for the administration of the Society and shall ensure that proper accounts be kept of the Society's finances. He shall also ensure that Society decisions are effected and, where appropriate, shall serve as a representative of the Society and co-ordinate Society programs with other agencies, government and the community generally.
- d. It shall be the responsibility of the Officers to develop the terms of reference for the position of Executive Director. These shall encompass the conditions set out above and shall constitute part of the terms of his appointment.



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**EXISTING**

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**PROPOSED**

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12.4.6 The Executive Committee may meet when and where it may determine. It shall report to the Council at the Annual Meeting of the Society and to any Special Meeting called for that purpose or on such occasions as may be required by Council. At any meeting of the Executive Committee seven shall constitute a quorum for the transaction of business.

12.4.7 Special Meetings. On the request in writing of any five members (with voting power) of the Executive Committee the Chairman shall call a Special Meeting.

12.4.8 to 12.4.11

12.4.6 The Executive Committee shall report to Council at the Annual Meeting of the Society and to any Special Meeting called for that purpose or on such occasions as may be required by Council.

12.4.7 Delete

Renumber 12.4.7 to 12.4.10

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15. **THE OFFICE**

15.1 Until changed by resolution at an Annual Meeting of the Society the Office of the Society shall be located at Halifax/Dartmouth as defined in the Hfx/Dart. Regional Development Plan.

16, 16.1, 16.2, 16.3, 16.4 & 16.5

15. Delete

15.1 renumber as 1.2 (reads the same)

renumber as: 15, 15.1, 15.2, 15.3, 15.4 & 15.5



Council in 1987 renamed The Nova Scotia Medical Bulletin to The Nova Scotia Medical Journal. The following are related By-Law amendments.

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**EXISTING**

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**PROPOSED**

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|---------|--|---------|--|
| 11.9.1  | The official Journals of the Society are " <i>The Bulletin</i> " of the Society and " <i>The Canadian Medical Association Journal</i> ". The " <i>Bulletin</i> " shall be published under the direction of the Board of Editors. | 11.9.1  | The official Journals of the Society are <i>The Nova Scotia Medical Journal (The Journal)</i> and <i>The Canadian Medical Association Journal (The CMAJ)</i> . <i>The Journal</i> shall be published under the direction of the Editorial Board. |
| 9.1.1   | delete: <i>The Nova Scotia Medical Bulletin</i>  | 9.1.1   | insert: <i>The Journal</i>   |
| 9.4.1   | delete: the <i>Bulletin</i>  | 9.4.1   | insert: <i>The Journal</i>   |
| 10.1 b. | delete: the <i>Bulletin</i>  | 10.1 b. | insert: <i>The Journal</i>   |
| 11.9.1  | delete " <i>The Bulletin</i> ", and " <i>Bulletin</i> "  | 11.9.1  | insert: in two places: <i>The Journal</i>  |
| 11.9.2  | delete: " <i>The Bulletin</i> "  | 11.9.2  | insert: <i>The Journal</i>   |
| 12.4.5  | delete: the <i>Bulletin</i>  | 12.4.5  | insert: <i>The Journal</i>   |
| 12.9.1  | delete: The <i>Bulletin</i>  | 12.9.1  | insert: <i>The Journal</i>   |
| 14.1    | delete in two places: the <i>Bulletin</i>  | 14.1    | insert in two places: <i>The Journal</i>   |
| 14.2    | delete in two places: the <i>Bulletin</i>  |         |  |
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# Why bother?

Why bother attending The Medical Society's Annual Meeting?

Let me count the why's:

- it's "the" meeting of the year for the medical profession
- it's where your representatives report their activities
- it's where your membership dues are established
- it's where your new representatives are chosen
- it's where your new President will be installed
- it's where the profession can speak it's mind
- it's where you mix business and pleasure
- it's where you communicate your views
- it's where your future plans are made
- it's where your policies are adopted
- it's where your colleagues will be

There are countless other reasons to attend your Society's Annual Meeting.

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# Cholesterol Testing and Laboratory Standards

W. Carl Breckenridge,\* PhD,

Halifax, N.S.

In recent years considerable evidence has been accumulated to show that elevated serum cholesterol and certain lipoprotein fractions, such as low density lipoprotein (LDL), are associated with an increased risk of coronary heart disease (CHD) while low concentrations of high density lipoprotein (HDL) are also associated with a high risk. Furthermore, several primary prevention trials have indicated that lowering blood cholesterol, and in particular LDL, reduce the risk of developing CHD. Thus, there are now several recommendations from consensus conferences which propose a relatively aggressive intervention, primarily through dietary modification to lower cholesterol in subjects with moderately elevated cholesterol concentrations.

For example, the Canadian Cholesterol consensus conference recommended, in particular, that men and women over the age of 30, with a family history of CHD or other risk factors for CHD and who have cholesterol levels in excess of 240 mg/dL (or 6.2 mM/L), should be treated initially by diet, and if necessary for high elevations, with drugs. Individuals in the range of 200-240 mg/dL should be considered for treatment if the LDL cholesterol is greater than 130 (3.4) or HDL cholesterol is below 35mg/dL (0.9). A value of 240 mg/dL is approximately the 75th percentile of cholesterol frequency distribution in adult subjects. Thus treatment or management of subjects with elevated cholesterol is somewhat different than for an individual who presents with a clinical chemistry which is well outside the 95 or 5 percentile of the normal distribution for an analyte.

If the sampling techniques and laboratory technology are not standardized, reproducible and accurate, the potential true value of 240 mg/dL may cover a large range. If, for example, the C.V. of the entire analytical process, which would involve biological variation, analytical variation and analytical bias, amounts to 10%, in statistical terms one analysis for a particular person may occur across a wide range. Inherent bias in the analytical system may result in a precise but inaccurate value. For example the data which are used as a basis for consensus conference statements are based on analytical methodology which is both precise (C.V. usually less than 3%) and accurate (bias usually less than 1% from reference and definitive methods for cholesterol). This level of analytical technology does not exist in many routine clinical laboratories.

The important point is that cholesterol values may

vary in an individual. It is important that the physician and the patient understand this aspect and try to minimize sources of variation. I would like to deal with some of the problems associated with the variation in cholesterol values and recommend ways to try to minimize variation through control of variation in sampling procedures, in analytical methodology and biological variation in the individual.

## VARIATION IN SAMPLING PROCEDURES

Considerable variation may occur in cholesterol values depending on how one takes a blood specimen. The plasma volume increases and the concentration of non-diffusible plasma components decreases when a standing subject assumes a recumbent position due to redistribution of water between the vascular and extra vascular compartments. A significant reduction in total plasma cholesterol occurs after a 5 min period of recumbency and changes of up to 10-15% occur after 20 min. A standing subject who assumes a sitting position will have a 6% decrease after 10 min.

Prolonged strenuous exercise in the preceding 24 hr. will lower plasma triglycerides acutely. Prolonged venous occlusion also causes an increase in the apparent concentration of non-diffusible components in plasma. Cholesterol concentrations increase an average of 2-5% after 2 min and up to 15% after a 5 min. period of occlusion. An overnight fast has relatively little influence on cholesterol concentrations but lowers triglyceride concentrations significantly. Thus the recommended procedure for collection of blood in the LRC program is to fast the subject for 12-16 h. The patient is allowed to sit quietly for about 10-15 min. and is seated during venipuncture. A tourniquet is used but should be released prior to withdrawal of the blood sample if possible.

The nature of the blood sample taken has a significant effect on cholesterol concentrations. Oxalate based anticoagulants give values about 10% lower than serum values while values from EDTA plasma are 3% lower than serum. Heparin has no effect but has other effects on lipoproteins. The LRC study used EDTA for all samples since this anticoagulant also protects the lipoproteins from degradation. Thus from this review it can be observed that very significant differences may occur in a patient sample if a standardized procedure is not established for collecting the sample.

## ANALYTICAL VARIATION

Two important factors must be considered in analytical variation: a) *accuracy*, which is an estimate of

\*Carnegie and Rockefeller Professor and Head, Dept. of Biochemistry, Dalhousie University, Halifax, N.S.



any inherent bias in the methodology in relation to a gold standard for estimation of cholesterol; and b) *precision*, which is an estimate of the ability of the analytical technology to reproduce a result regardless of the inherent bias in relation to some other methodology.

Prior to the widespread use of enzymatic methods for estimating cholesterol some colorimetric techniques carried a substantial bias (10%) in relation to other procedures. The methods used reagents which had different extinction coefficients for cholesterol and cholesteryl esters, especially when the reaction was carried out on serum or plasma. Recently, definitive methods have been set up to measure cholesterol using stable isotopes and mass spectrometry. These techniques are very specific, accurate and have high precision but they are extremely expensive. In turn these methods are used to assess reference methods which are highly specific colorimetric techniques. Finally, reference methods are used to assess routine procedures and set target values on quality control pools and reference sera.

These developments will have a positive impact on accuracy. The introduction of well-calibrated reference sera combined with enzymatic methods should go a long way to improving accuracy. In the past, it has been found that the enzymatic technology when combined with automated enzyme analyzers gave very good precision but the accuracy was influenced by the manufacturer's ability to set an accurate target value on their reference sera.

*Precision* is related to the ability of the laboratory and the instrumentation to yield a reproducible result. In the past, this variation was influenced by the technician. With the introduction of automated technology precision is improving. The Center for Disease Control (CDC) has found a steady improvement in precision in recent years. They have also found a substantial improvement in intralaboratory comparability in the past 10 years.

However there is still a great deal of improvement possible. For example, a recent survey of a large group of laboratories on a pool of serum cholesterol of 262.2 mg/dL showed that 47% of the laboratories deviated by more than 5% from the target value. Of these 16% deviated by 10% and 8% deviated by greater than 15%. A substantial part of this result is increasingly due to poorly calibrated reference sera or poor set up of the instrumentation for calibration, as laboratories increasingly use reference sera in place of chemical standards. A clear documentation of how cholesterol values are established is now a major priority. Similar data are available for proficiency testing in Ontario. In general the data suggest that accuracy is becoming a greater problem than precision.

In the past each clinical laboratory set up a method, and then analyzed a group of "healthy subjects" and devised a normal distribution with 95 percentile limits. This approach is no longer suitable because, a) the

normal population probably has cholesterol levels that are too high and, b) the epidemiologic data are derived from a very standardized methodology which may give very different values from the laboratory methodology. It is difficult for the physician to know whether a particular laboratory has a high cholesterol distribution because of its methodology or the population. It is important for physicians to ask clinical laboratories how their methodology relates to reference laboratories using methods such as the Abel Kendal procedure. If the methodology yields values which are very similar the physician may then use the limits suggested by the consensus conferences.

Although the laboratory may claim that it is functioning well in quality assurance surveys for a particular methodology and analysis, it is now imperative to know how it is performing in relation to the reference methodology. With continued pressure and assistance from governments, I believe it is possible for manufacturers to improve the calibration of reference sera so that the accuracy of methods will become closer to the reference methodologies. The objective of the CDC is to have precision and accuracy in routine laboratories to less than 3% within the next five years.

## BIOLOGICAL VARIATION

There is a third component of variation in serum cholesterol: *biological variation*. This component is difficult to separate from the other forms of variation. It is now reasonably well established that cholesterol levels vary during the year. Cholesterol values are highest during the winter months and lowest during the summer months. Normal and hypercholesterolemic subjects show this trend which may vary among individuals. The difference in values from winter to summer may be as high as 10%. Individual variation may also be the result of changes in life style related to weight changes, alcohol intake or smoking. These factors must be considered in the entire status of the patient.

## SUMMARY

Although considerable improvement has been obtained in the analysis of cholesterol there are many factors that must be improved further in order to obtain consistently reliable results. If precision is a problem the physician may improve this aspect by repetitive analyses on the individual. The CDC recommends that multiple specimens (2-4) should be taken about 1 month apart before the subject's lipid value is considered correct. Analyses should be performed with an underlying analytical coefficient of variation of about 3%. Continued pressure must be brought to bear on manufacturers to provide evidence for the establishment of target values on reference sera. Ideally these target values should be established by definitive or reference methods and, subsequently, by the routine method which is usually an enzymatic method.



There are a number of actions that physicians can do to improve their assessment of cholesterol values in their patients:

1. Standardize collection of samples with regard to posture, prior activity, venipuncture and type of vacutainers.
2. Ask the laboratories how their values compare with those from reference methodologies completed by the Center for Disease Control or reference laboratories. If suitable quality control material is unavailable try to convince the laboratory to carry out a fresh serum comparison with a reference laboratory. Determine how their normal values were obtained. If their methodologies are comparable to reference values, the consensus conference statements may be applied directly. Other-

wise, a correction factor may be necessary in order to equate the data of a particular laboratory to the data used for consensus documents.

3. Urge regulatory agencies and interested professional groups to develop mechanisms for quality assurance which stress methodology bias in addition to precision.
4. Realize that cholesterol values will vary in an individual. Treatment may be a long term project. □

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## CANADIAN GROWTH HORMONE ADVISORY COMMITTEE

### GROWTH HORMONE TREATMENT AND LEUKEMIA

The Lawson Wilkins Pediatric Endocrine Society and the Human Growth Foundation convened a workshop in Bethesda, Maryland, May 4th and 5th 1988 to discuss a possible increased incidence of leukemia in patients with hypopituitarism treated with human growth hormone (GH). The workshop was prompted by recent reports of leukemia in five Japanese hypopituitary children who had received GH. The meeting was attended by experts in the field of growth, growth hormone and cancer, and included representatives from Canada, the United States, European countries, Japan and Australia.

Fifteen cases of leukemia have occurred in patients with hypopituitarism treated with GH between 1963-1987. These patients had received pituitary-derived GH or biosynthetic GH or both. In four of the 15 cases, leukemia occurred after 2-3 months of GH therapy, or there were reasons to suspect other causes for the leukemia. Thus, there are 11 suspect cases among 22,619 patients world-wide who have been treated with GH and who account for approximately 150,000 patient years of risk including treatment and follow-up. Thus, the incidence of leukemia in this group to date is 1/14,000 patient years of risk. A reasonable, although not necessarily precise, estimate of annual expected incidence of leukemia in the age range of the patients treated is 1/42,000. Thus, the observed incidence of leukemia in GH treated patients represents a three-fold increase over the expected rate.

Among the 11 suspect cases, there were an additional four patients who, prior to any GH injections, had brain tumours, and who received cranial irradiation treat-

ment. Currently, cranial irradiation is a controversial risk factor for leukemia.

The rate of leukemia in Japanese hypopituitary patients treated with growth hormone is 1/6,000 patient years as compared to 1/35,000 patient years in other geographic areas. Isolated clusters of leukemia such as this have occurred several times in the past in the general population without explanation despite careful epidemiological investigation. Thus, whether any relationship between growth hormone deficiency, growth hormone therapy and leukemia exists is unclear at present. The incidence of leukemia in hypopituitary patients who have not received growth hormone is unknown. There is no evidence of increased frequency of relapse of leukemia in children with previous leukemia and GH deficiency.

In Canada, 1047 children have received human or biosynthetic growth hormone during the past 22 years accounting for approximately 8,000 patient years of exposure and follow-up. No cases of leukemia have been reported de novo while on therapy. The Canadian Growth Hormone Advisory Committee recommends that all persons who have received growth hormone be advised that there may be a possible increase of leukemia in growth hormone deficient patients treated with growth hormone.

Physicians are requested to report any case of leukemia in a hypopituitary person regardless of age and treatment status. Please call the National Growth Hormone Advisory Committee office at 204-787-4553.



# Nova Scotia Cholesterol Results for Nova Scotia Clinical Labs

Fred Lays,\* A.R.T. and W. Carl Breckenridge,\*\* PhD,

Halifax, N.S.

## QUESTIONS:

Do laboratories in Nova Scotia provide precise and accurate cholesterol results?

Should Nova Scotia laboratories standardize their cholesterol methods with a lipid reference centre?

## RESPONSE:

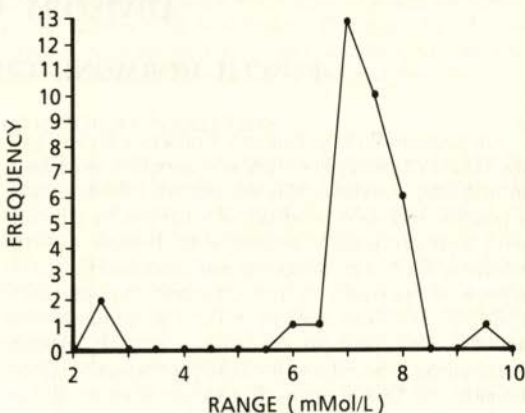
Many clinical laboratories in Nova Scotia participate in quality control programs such as the CAP basic survey. The data discussed below provide some preliminary results concerning the above questions. Results from the analysis of two pools (C-18 and C-19 from the Center of Disease Control, (CDC), Atlanta, Georgia), are shown in Table I and Figure 1 for 34 laboratories from Nova Scotia. This is a summary of only one CAP survey and should not be taken as the standard in this Province. Bias indicates the deviation of the mean result obtained by the laboratories from the value established by CDC. About 50% of the laboratories had a deviation of less than 5% from the reference value. Thus, if these labs repeated an analysis several times on a sample with a cholesterol value of 6.47 mmol/litre (250 mg/100 ml) the mean value should lie between 6.15 and 6.75 mmol/litre. Some laboratories will be much better than others since some of them have a rather small bias. About 30% of the laboratories have a large bias. On the basis of this one test the latter group of laboratories are not providing a value for cholesterol with any relationship to the values of the Lipid Research Clinic program that have been under discussion in the Cholesterol Consensus Conferences. The mean bias for the province is very good. However, this value masks biases which range from -69.7% to +32%. The implications of sending a patient to some of these laboratories are obvious.

Bias is not the complete story with regard to cholesterol analysis. At any given time a laboratory will analyze a specimen once. There is an inherent error which is determined by doing several repeat analyses over a period of days or weeks. The laboratory defines this variation (approximately equal to the standard deviation as a percent of the mean value) as a coefficient of variation or the precision of the method (i.e. the ability of the laboratory to obtain the same result over a period of time on the same sample). The enclosed data do not give an estimate of precision for individual laboratories.

Let us assume that most laboratories, with a bias of less than 5%, will have a coefficient of variation of 5% or

less. 95% of the time the result will be within the range of two standard deviations of the mean value. For example, if a lab has a bias of -5% for a sample with a reference value of 6.47 mmol/litre (-5% = 6.15 mmol/litre) and a coefficient of variation of 5%, we can expect that 95% of the time a single analysis on this sample will yield a result between 5.53 and 6.77 mmol/litre. Thus, it is clear that the combination of bias and lack of precision can result in a substantial error in a single analysis compared with the true value established by a reference laboratory.

**N.S. CHOLESTEROL RESULTS**  
CAP BASIC SURVEY A-G 1987, SPEC.C-18



**N.S. CHOLESTEROL RESULTS**  
CAP BASIC SURVEY A-G 1987, SPEC.C-19

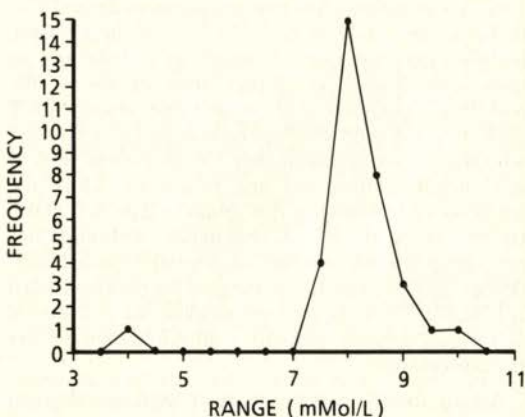


Figure 1

\*Chief Technologist, Aberdeen Hospital, New Glasgow, N.S.

\*\*Carnegie and Rockefeller Professor and Head, Department of Biochemistry, Dalhousie University, Halifax, N.S.



**TABLE I**  
**NOVA SCOTIA CHOLESTEROL RESULTS:**  
**CAP BASIC SURVEY A-G 1987**

Method	Analyzer	Pool 1		Pool 2	
		Spec. C-18	% Bias (a)	Spec. C-19	% Bias (a)
Enzymatic	ABA-200	6.99	-1.8%	7.65	-3.3%
Enzymatic	Abbott-VP	6.60	-7.3%	7.60	-3.9%
Enzymatic	Abbott-VP	6.77	-4.9%	7.49	-5.3%
Enzymatic	ASCA	6.60	-7.3%	7.50	-5.2%
Enzymatic	ASCA	6.75	-5.2%	7.55	-4.6%
Enzymatic	Centrifichem	6.93	-2.7%	7.67	-3.0%
Enzymatic	Cobas	7.26	2.0%	8.30	4.9%
Enzymatic	Cobas	7.75	8.8%	8.67	9.6%
Enzymatic	Cobas	7.54	5.9%	8.37	5.8%
Enzymatic	Cobas	7.38	3.7%	7.84	-0.9%
Enzymatic	Cobas-Mira	7.90	11.0%	8.70	10.0%
Enzymatic	Cobas-Mira	7.02	-1.4%	7.83	-1.0%
Enzymatic	Cobas-Mira	7.96	11.8%	8.14	2.9%
Enzymatic	Cobas-Mira	6.82	-4.2%	7.94	0.4%
Enzymatic	Dimension	7.16	0.6%	8.04	1.6%
Enzymatic	Gemeni	2.20	-69.1%	No Value Received	
Enzymatic	Genesis	7.20	1.1%	8.40	6.2%
Enzymatic	Gilford-400	7.42	4.2%	8.28	4.7%
Enzymatic	Hitachi-704	7.00	-1.7%	7.90	-0.1%
Enzymatic	Hitachi-704	7.10	-0.3%	8.00	1.1%
Enzymatic	Hitachi-705	6.80	-4.5%	7.50	-5.2%
Enzymatic	Hitachi-705	7.05	-1.0%	7.93	0.3%
Enzymatic	KDA	7.90	11.0%	8.50	7.5%
Enzymatic	RA-1000	5.80	-18.5%	7.98	0.9%
Enzymatic	RA-1000	6.93	-2.7%	7.82	-1.1%
Enzymatic	Seralyzer	7.80	9.6%	8.80	11.3%
Enzymatic	Seralyzer	9.40	32.0%	9.90	25.2%
Enzymatic	Seralyzer	6.90	-3.1%	8.40	6.2%
Enzymatic	SMA-12/60	7.01	-1.5%	7.81	-1.3%
Enzymatic	Spectrum	6.90	-3.1%	8.00	1.1%
Enzymatic	Srealyzer	7.50	5.3%	9.20	16.3%
LEIB-BUR	ASCA	6.70	-5.9%	7.80	-1.4%
LEIB-BUR	Cobas	2.16	-69.7%	3.77	-52.3%
LEIB-BUR	Manual	6.50	-8.7%	7.10	-10.2%
All methods	Mean	6.87		7.95	
	Std. Dev.	1.33		0.93	
	Coeff. Var.	19.4%(b)		11.7%(b)	
	Data Range	2.2 to 9.4		3.77 to 9.9	
	Deg. of Freq.	34		33	
Reference results (c)		7.12		7.91	
N.S. mean bias		-0.25 -3.5% Diff.		0.04 0.5% Diff.	
Cap all methods	MEAN	6.98		7.83	
	SD	0.37		0.41	
	CV	5.3%		5.2%	

**NOTES:** (a) BIAS = % Difference from Reference Result  
 (Acceptable BIAS  $\pm$  5% ; Ideal BIAS  $\pm$  3%)  
 (b) Acceptable CV 5% ; Ideal 3%  
 (c) CDC reference method at CDC, Atlanta

While the enclosed data do not provide a good assessment of individual laboratory precision, the combined coefficient of variation of all the laboratories is quite poor (12-19%). If outliers are removed this combined coefficient of variation is about 5-6%. These data explain why individual cholesterol results may vary from one patient within a laboratory and, particularly, between laboratories. If conditions of sampling are not standardized there will be even greater variation for a particular individual. As more

and more people are analyzed for serum cholesterol and there is increased emphasis on intervention to lower modestly elevated cholesterol values, the physician must be aware that it is important to use a laboratory with good accuracy in relation to a reference laboratory and very good precision.

In order to make the best decision regarding a patient, it is also important to standardize the conditions of sampling and carryout at least two, and preferably more, analyses of serum cholesterol before deciding on a course of therapy. Initiatives should also be undertaken in the province to improve accuracy and precision in all clinical laboratories. The involvement of routine labs with a reference laboratory would facilitate this process.

### THE BENEFITS Vs. RISKS OF PHARMACOTHERAPY OF HYPERCHOLESTEROLEMIA

Continued from page 154.

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# Coronary Heart Disease and its Risk Factors in Halifax County

R. D. Gregor\*, MD, FRCP(C), B. R. MacKenzie\*, MD, FRCP(C), FACC, M. H. Tan\*\*, MD, FRCP(C), FACP, P. M. Rautaharju\*\*\*, MD, PhD, FRCP(C), FACC and H. K. Wolf\*\*\*, PhD,

Halifax, N.S.

A survey in a random sample of the population of Halifax County was carried out to obtain estimates for the prevalence of coronary heart disease and its risk factors. The sample consisted of 772 persons between 25 and 64 years of age. It was found that 2.7% of men and 1.8% of women suffered from angina pectoris, and 2.55% of men and 1.01% of women had one or more old infarctions. Casual blood pressure 90 mmHg (diastolic) or above was found in 11.1% of men and 3.8% of women. Either most of these persons were receiving antihypertensive treatment already or they were aware of their elevated blood pressure. Cigarette smoking was still quite prevalent, particularly in the 25 to 34 year age-group (40.4% of men and 30.1% of women in that group). Total cholesterol was significantly elevated ( $>6.2$  mM/L) in 28.4% of the population.

The major conclusions to be drawn from this study are: 1) The methods used for finding and treating hypertensives are effective and should be continued, with additional emphasis being put on encouraging known hypertensives to seek and comply with treatment. 2) The anti-smoking campaign should be improved. 3) Cholesterol is the one risk factor most seriously elevated above the desired level. Intervention with this risk factor is not uniformly supported, especially for the target level advocated by the expert panel. Therefore, careful considerations are needed before engaging in a costly intervention campaign.

In 1984 the MONICA project, sponsored by the World Health Organization, was started to monitor trends in coronary heart disease (CHD) in 27 countries. The study described in this report is part of the MONICA project and its aims were defined in an earlier article.<sup>1</sup> The local objective is the investigation of coronary heart disease trends in the population of the study area Halifax County, which consists of Halifax County and the metropolitan area of Halifax/Dartmouth. This area, together with the rest of Canada, has experienced a decline in CHD mortality for the past 15 years. In comparison with other countries in the MONICA project, the CHD mortality in Halifax County ranks about halfway between the lowest and the highest rates.

\*Associate Professor, Dept. of Medicine, Dalhousie University.

\*\*Professor, Dept. of Medicine. Head of Division of Endocrinology and Metabolism, Dalhousie University.

\*\*\*Professor, Dept. of Physiology and Biophysics, Dalhousie University, Halifax, N.S.

Correspondence: Hermann K. Wolf, Dept. Physiology & Biophysics, Dalhousie University, Halifax, N.S. B3H 4H7

There are many possible reasons for this observation, and the project described here is designed to explore the major ones. The occurrence of the disease in the population is an obvious contributing factor, and a survey in a random sample of the population was conducted to establish prevalence of CHD as well as the distribution of some of the major risk factors for CHD. This report deals with the findings on prevalence and control of CHD risk factors.

## METHODS

A random sample of persons between 25 and 64 years of age was selected from a population list, and they were invited to take part in the study. It is estimated that about 40% of the individuals who received an invitation decided to volunteer for the study. Data collection sites were set up in the Sir Charles Tupper Medical Building, the Cobequid Multiservice Center and in a mobile unit that travelled to various locations in the study area. Study participants were asked to come to one of these sites to answer a questionnaire related to their health and their risk of CHD. Their blood pressure and electrocardiogram were recorded and a blood sample was taken after a 12-hour fast.

The personnel involved in the data collection had received standardized training in questionnaire administration, blood sampling, and ECG and blood pressure recording.

The laboratory that performed the serum lipid analysis was standardized by the MONICA lipid reference center to assure international compatibility of the measurements.

## RESULTS

### 1. Risk Factors

The results are reported as values that apply to the total population of the survey area as it existed in 1984 (77,100 men and 80,000 women in the age range 25 to 64). The survey data are derived from 772 participants. Approximately the same number of persons participated in each 10-year age-group of both sexes, with the exception of men between 25 and 34 years of age who volunteered at 60% of the rate of all other age/sex groups. For the major CHD risk factors (blood pressure, smoking, and serum cholesterol), the following distributions were found.

#### 1.1 Blood Pressure

The blood pressure values were calculated for each participant as the average of three measurements, two



made in sitting and one in supine position. Since analysis of covariance showed a significant effect ( $p < 0.001$ ) of sex and age on the diastolic blood pressure, data were analyzed after stratification by these two variables.

Table I shows the percentage of cases falling into various diastolic blood pressure ranges, which have been chosen to reflect frequently advocated thresholds for intervention. None of these persons received antihypertensive medication at the time of the survey. In the group of persons with casual diastolic blood pressure 95 mmHg or higher, 88% had been told previously that they had high blood pressure.

Since there exists a strong correlation between systolic and diastolic blood pressure, the distribution in Table I would not be significantly different if it had been computed for systolic pressure. Cases of isolated systolic high blood pressure were so rare (0.15%) that it is impossible to comment on them with any confidence.

A separation of the data in Table I by age-groups shows that the chance of finding a person with elevated blood pressure increases considerably with age. The probability of finding a woman between 25 and 34 years of age who has a diastolic blood pressure 90 mmHg or higher is only 1.4%. This probability increases for each additional 10 years of age to 3.4%, 4.5%, and 6.1%. The corresponding probabilities for men are 2.0%, 8.8%, 16.2%, and 14.9%. These results show that untreated hypertension is probably more of a problem in men than in women and increases significantly with age. It should be emphasized that elevated blood pressure in this survey does not necessarily mean the presence of hypertension. This report deals only with casual blood pressures, and a diagnosis of hypertension would require a careful follow-up investigation to establish the persistent blood pressure elevation. The data of Table I give an indication of the male/female ratio of hypertensives.

TABLE I

AVERAGE DIASTOLIC BLOOD PRESSURE DISTRIBUTION (IN %) IN THE STUDY POPULATION THAT IS NOT ON ANTIHYPERTENSIVE MEDICATION.

Sex	Diastolic Blood Pressure			
	<90	90-94	95-99	≥100
men	88.9	6.6	2.8	1.7
women	96.2	2.5	1.0	0.3

A significant number of persons were taking medication for hypertension at the time of the survey. As Table II shows, the percentage of treated hypertensives increases with age. Extrapolated to the total population, it means that 6.5% of women and 8.2% of men between 25 and 64 years of age are being treated. The diastolic blood pressure was 90 mmHg or higher in 40% of treated men and 27% of treated women. A single drug was used in the treatment of 67% of hypertensives, 30% received a

combination of two and 3% a combination of three antihypertensive drugs. The single-drug treatment was based on a diuretic in 53%, a  $\beta$ -blocker in 37%, and calcium antagonists, ACE inhibitors, or antiadrenergic agents in the remainder of the cases. The combination of two drugs was a diuretic and  $\beta$ -blocker in the majority of cases (79%). All other combination regimens involved also a diuretic, a  $\beta$ -blocker or both in addition to vasodilators, ACE inhibitors, Ca-antagonists or centrally-acting antiadrenergic agents.

TABLE II

PERCENTAGE OF PERSONS PER AGE GROUP THAT RECEIVE ANTIHYPERTENSIVE MEDICATION.

Sex	Age Group			
	25-34	35-44	45-54	55-64
men	1.9	2.1	20.0	20.6
women	1.2	1.1	14.3	19.3

## 1.2 Cholesterol

Not all study subjects were prepared to give a blood sample and as a result, only 677 cholesterol measurements were obtained. Analysis of covariance showed that sex was not significantly related to cholesterol values; however, a strong age dependency exists. The data for men and women were therefore pooled, and the cholesterol results are summarized in Fig. 1 by age only, showing the percentage of persons with values below 5.17 mM/L (200 mg/dL), between 5.17 and 6.2 mM/L (200 and 240 mg/dL), and above 6.2 mM/L (240 mg/dL) in the different age-groups. If one extrapolates these values again to the whole population, it means that 66% of all persons in the age range 25 to 64 have cholesterol values exceeding 5.17 mM/L and 28.4% exceed 6.2 mM/L.

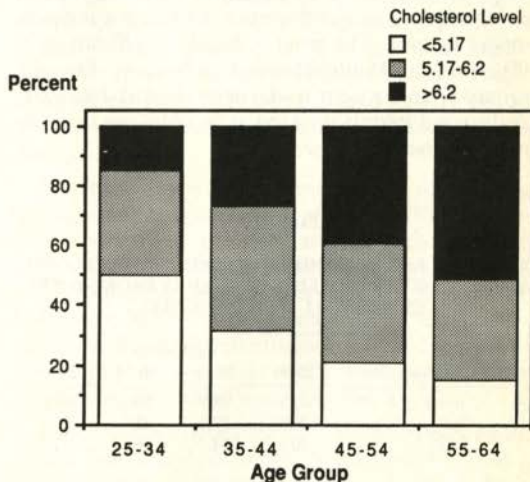


Fig. 1 Distribution of blood cholesterol levels in each age-group of the survey population. The group  $>6.2$  mM/L is recommended for treatment according to reference no. 5.



The most recent report on evaluation and treatment of hypercholesteremia recommends that patients with high blood cholesterol (above 6.2 mM/L) or with borderline-high cholesterol (between 5.17 and 6.2 mM/L) who are at risk because of definite CHD or other risk factors should undergo lipoprotein analysis.<sup>5</sup> The decision to treat and the type of treatment should then be made on the basis of LDL levels. Table III shows the prevalence of normal, borderline-high-risk and high-risk LDL levels among the group of persons whose total cholesterol exceeds 5.17 mM/L.

TABLE III

PREVALENCE (IN %) OF NORMAL (<3.4 mM/L), BORDERLINE-HIGH-RISK (3.4 TO 4.1 mM/L) AND HIGH-RISK (>4.1 mM/L) LDL-CHOLESTEROL LEVELS AMONG THE GROUP OF STUDY PARTICIPANTS WHOSE TOTAL CHOLESTEROL WAS IN EXCESS OF 5.17 mM/L.

Total Cholesterol	LDL-Cholesterol			Total
	<3.4	3.4-4.1	>4.1	
5.17-6.20	21.7	27.0	3.3	52.0
>6.2	0.9	10.2	36.9	48.0
Total	22.6	37.2	40.2	100.0

The treatment of hyperlipidemia by pharmaceutical means does not appear to be popular yet. Only three patients on lipid-lowering drugs were found, suggesting that drug therapy at the time of the survey was not yet widely used.

### 1.3 Smoking

Table IV documents the proportion of smokers, ex-smokers (quitting more than 3 months before the survey), and those who never smoked, by sex and age-group. The decline in the proportion of smokers with age is evident in men and women, although it is much stronger in men. The trend is highly significant ( $p = 0.006$ , Cochran-Mantel-Haenszel technique). Overall, there are 10% more women who never smoked than men, but the trend to quit smoking at an older age is much stronger in men than in women.

TABLE IV

PERCENTAGE OF MEN AND WOMEN WHO, BY THEIR OWN ACCOUNT, NEVER SMOKED (NEVER), QUIT SMOKING (EX), OR ARE STILL SMOKING (STILL).

Sex	Smoking Status	Age Group			
		25-34	35-44	45-54	55-64
men	never	32.7	28.1	30.5	21.7
	ex	26.9	37.5	43.2	54.6
	still	40.4	34.4	26.3	23.7
women	never	43.4	45.7	47.3	42.2
	ex	26.5	29.8	27.7	38.5
	still	30.1	24.5	25.0	19.3

### 1.4 Multiple Risk Factors

Risk factors act additively and the simultaneous presence of two or more factors elevated only into the borderline range will put a patient in the high-risk group. For the population in the study area Halifax County, the coexistence of borderline risk factors occurs with the following frequency: Smoking + borderline cholesterol = 9.4%, smoking + borderline diastolic blood pressure = 0.3%, borderline cholesterol + borderline diastolic blood pressure = 3.4%, smoking + borderline cholesterol + borderline diastolic blood pressure = 1.2%.

## 2. Coronary Artery Disease

### 2.1 Angina Pectoris

The history of angina pectoris is difficult to establish in a population survey. Two criteria for the presence of angina pectoris were used: 1. The Rose questionnaire<sup>2</sup> which has been validated<sup>3</sup> and is, in our view, the best tool available for this purpose; and 2. self-reported medication for angina pectoris in the absence of previous myocardial infarction. Persons were declared as angina cases if they met either one of the criteria. The prevalence of angina in the total population was 2.7% for men and 1.8% for women. No cases were found in the 25 to 34 year age-group. In persons 34 years and older, the prevalence increased gradually with age and reached its highest level in the 55 to 64 year age-group (15.4% in men and 5.1% in women).

The majority of angina patients received drug therapy (83%); the most common treatment regimen (42% of cases) involved a single drug, either a  $\beta$ -blocker (29%), Ca-antagonist (8.5%), or nitroglycerin (4.5%). Two drugs were prescribed in 29% and three drugs in 12% of cases. The multiple drug regimens consisted of combinations of  $\beta$ -blockers, Ca-antagonists, nitroglycerin, vasodilators, and aspirin. Even the 17% of angina cases who received no antianginal drugs were under a physician's care since they were on other prescription drugs.

### 2.2 Old Myocardial Infarction

Two criteria were used to estimate the number of persons with old myocardial infarction. Either a person must have been told by a health professional that he or she had a myocardial infarction or the ECG met the criteria for old MI. If one relied only on the ECG criteria, the prevalence in the total population would be 0.95% for men and 0.52% for women. If an old MI is defined either by ECG or by the statement of a health professional, the prevalence becomes 2.55% for men and 1.01% for women. Similarly to angina, the prevalence increased with age in both, men and women.

Drug therapy was received by 77% of these possible old infarction cases, 65% were on some cardio-active drug. The most commonly prescribed ones were  $\beta$ -blockers, followed by nitro preparations, Ca-antagonists, antiarrhythmic drugs, and aspirin; 12% received a diuretic for control of blood pressure.



## DISCUSSION

The sample for the survey population was drawn according to sound statistical principles and therefore it should be representative for the total population of the survey area. However, there was less than 100% participation and the data may no longer correctly estimate the characteristics of the population. At this point in time we have not been able to evaluate whether our results are biased and in which direction. The investigators of the Nova Scotia Heart Health Survey have recently released to us their results on the Halifax County population.<sup>4</sup> Although their sample size was smaller than ours and had a higher participation rate, their risk factor data agree in general with ours, with the exception of the serum lipid data, for which we find about 10% higher mean values. The reason for this discrepancy is under intense investigation. If one accepts our data as valid, a number of interesting conclusions can be drawn.

With regard to blood pressure, the low percentage of persons with elevated diastolic pressure is a surprise. According to the latest recommendations, pharmacological treatment should only be instituted when the diastolic blood pressure is consistently above 100 mmHg.<sup>5</sup> Only 1.7% of men and 0.3% of women had casual diastolic blood pressure of 100 mmHg or higher. According to our experience less than half of the casual pressures above 100 mmHg will remain above that level on repeat measurements. Therefore, the number of persons who are currently untreated and who should receive pharmacological treatment according to the guidelines is very small (probably less than 0.9% of men and 0.2% of women). If one contrasts these numbers with the 8.2% of men and 6.5% of women who receive treatment already, it becomes apparent that the existing system of finding and treating hypertensives functions quite well already and therefore, no elaborate new case-finding programs are needed.

Improvements would be desirable, however, in translating the awareness of high blood pressure into effective treatment. The great majority (88%) of those with diastolic pressures above 95 mmHg knew about their condition but failed to seek treatment. Of those under treatment, a significant number (40% of men and 27% of women) do not achieve a treatment goal of less than 90 mmHg; a failure to comply with the treatment regimen is suggested by the male/female ratio. Women have been shown in other studies to be more compliant with prescribed treatment.

The situation with cholesterol is quite different. According to the most recently advocated guidelines, everybody, regardless of age or sex, should have cholesterol levels below 5.17 mM/L (200 mg/dL).<sup>6</sup> According to our survey, 66% of the population in the age range 25 to 64 years do not meet these recommendations; more importantly, 28% have blood cholesterol levels above the threshold where careful medical evaluation is indicated.

The magnitude and costs of such an evaluation program are enormous. Assuming a cost per evaluation of \$150, the funds required for the evaluation program alone would be \$5.9 million just for the County of Halifax, not counting the costs of finding the persons who need the evaluation. Even more frightening is the prospect that this population group will probably not be able to lower their cholesterol levels below the target threshold by dietary means alone. The Multiple Risk Factor Intervention Trial used intensive dietary counselling and dealt with cooperative subjects and managed only a modest 6.3% decrease in total cholesterol after one year.<sup>7</sup> The Lipid Research Clinics Program used a less intensive dietary intervention and achieved a 5.6% lowering of blood cholesterol.<sup>8</sup> Most of the persons in the high range of cholesterol might therefore need an expensive and extended drug program. Obviously, implementation of the guidelines on treatment of high blood cholesterol requires very careful consideration, particularly since there is still a group of health care planners who express strong reservations about such programs.<sup>9</sup> Studies that attempt to estimate the gain in life expectancy by controlling cholesterol levels estimate benefits that range from a few days to maximally 12 months for the most severe cases.<sup>10</sup>

No controversy exists about controlling cigarette smoking and the data of this study show that there is room for continued efforts in this regard. It is a positive sign that in men the percentage of those who never smoked is highest in the youngest age-group. But it is disturbing that this age-group also has the highest proportion of smokers. It suggests that the anti-smoking campaigns have some effect on preventing young persons from starting to smoke but more effort or a different approach is needed to encourage more of the young smokers to quit.

The prevalence of angina pectoris estimated by the sample of this study — 2.7% for men and 1.8% for women — is in general agreement with other studies. The rates reported from the Health Insurance Plan of Greater New York (HIP) were 3.5% and 1.5% respectively for men and women,<sup>11</sup> and from the US National Health Survey 3.0%.<sup>12</sup>

The high percentage of individuals identified as having angina pectoris on drug therapy (83%) suggests that physicians in the study area are actively treating cardiac pain. As would be expected, nitrates,  $\beta$ -blockers, and Ca-antagonists are the most common pharmacological agents. Multiple drug therapy was used in approximately 40% of cases, reflecting the current management philosophy of aggressive medical therapy prior to committing individuals to surgical therapy.

The prevalence of old myocardial infarction is similar to the one found in other populations<sup>12, 13</sup>, but is probably an underestimate since our criteria ignore the cases where ECG signs have regressed or where the patient did not get admitted to a hospital. Although two-thirds of old MIs are on some type of cardiac



medication, this proportion ought to be improved. Both,  $\beta$ -blockers and antiplatelet agents, have been recommended by many authors as secondary prevention against recurrent myocardial infarction or cardiac death following acute myocardial infarction. This study observed that  $\beta$ -blockers are the most commonly prescribed agents in the myocardial infarction group, reflecting the acceptance of the recommendations by the prescribing physicians.

The major conclusions to be drawn from the data of this study are: 1) The methods used for finding and treating hypertensives are effective and should be continued, with additional emphasis being put on encouraging known hypertensives to seek and comply with treatment. 2) Anti-smoking campaign should be improved. 3) Cholesterol is the one risk factor most seriously elevated above the desired level. Intervention with this risk factor is not uniformly supported, especially for the target level advocated by the expert panel. Therefore, careful considerations are needed before engaging in a costly intervention campaign.

#### ACKNOWLEDGEMENT

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## Fall Symposium on Back Pain

American Back Society in association with St. Rose Hospital and the San Francisco Spine Institute presents Fall Symposium on Back Pain, December 1, 2, and 3, 1988, Hyatt Regency Hotel, San Francisco, California. The program includes a distinguished faculty, recognized nationally and internationally, including Arthur H. White, M.D.; Rene Cailliet, M.D.; William Kirkaldy-Willis, M.D., F.R.C.S.(C); Scott Haldeman, M.D.; Philip Greenman, D.O.; Donald Resnick, M.D.; Jeffrey Saal, M.D.; Arthur D. Steffee, M.D.; and William V. Glenn, Jr., M.D.

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## CANCER PREVENTION You Can Have A Hand In It

The Canadian Cancer Society reminds you to increase your intake of whole-grain breads, cereals, and grains and to decrease your intake of fat. This is part of a well-balanced diet which may reduce your risk of cancer.





## The Cholesterol Story, its Early Era and The Great Nova Scotia Diet

Dr. Bud Harlow retired Halifax physician, played a prominent part in the education of many Nova Scotia physicians in the last thirty years. He taught laboratory medicine at Dalhousie for twenty-eight years and he directed his attention to the cholesterol problem long before it became the topical issue that it is today.

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*Journal: How did you become involved in research, diets, cholesterol and heart disease?*

**Dr. Harlow:** At McGill University in 1932 while working for my PhD under J. B. Collip, co-discoverer of insulin with Banting and Best, and Dr. Hans Selye, originator of the Street Theory. They asked me to conduct an experiment to force feed 100 rats crystalline cholesterol. Since crystalline cholesterol was unable to be absorbed through the digestive system the experiment was a failure. Fortunately after this failure, I came directly under the supervision of Dr. Selye through Dr. Collip, although the latter was the overall head of the department. It was at this time that Selye began to put his theories of Stress under investigation. I became his first PhD student in that study. After my PhD in 1938 and my MD in 1941, I joined the Royal Canadian Navy as a Surgeon Lieutenant-Commander. Following my war years I was appointed Director of Laboratories at Camp Hill Veterans Hospital, and Associate Professor of Pathology and Biochemistry at Dalhousie University.

Dr. W. P. Warner, at that time Director General of D. V. A. Hospitals in Canada, encouraged me to become involved in research once again in the mid 1950s. In my reading, I came across an article in the British medical journal, *Lancet*, in which the well-known medical scientist, Prof. Bronte Stewart gave a review of a research study done on one of the South African native tribes "The Bantus". The only animal protein they received was the fish they caught from the sea. Bronte-Stewart observed that these natives experienced very little coronary heart disease or atherosclerosis, which was so prevalent among the white South African population. The diet of the well-fed whites was similar to the high fat meals of the English and North Americans where coronary heart disease was the number one cause of death.

Therefore with these observations and study, it appeared to me that this would be a highly suitable

project for a Nova Scotia doctor to explore. Nova Scotia stands high on the list of Canadians suffering from coronary heart disease. Thus my mind was made up as to where and how our research should be conducted.

*Journal: How did you go about your study?*

**Dr. Harlow:** Our plan was to recruit relatively healthy men from age 20 to age 60. These men were divided into five different age groups — 20-29, 30-39, 40-49, 50-59 and the fifth control group was between 25 to 50. The experimental control involved preliminary counselling on basic food rules and an introduction to the exchange system as developed by a joint committee of the American Diabetic Association and the Canadian Dietetic Association.

*Journal: Did you have any experience in nutritional research when you started this project?*

**Dr. Harlow:** To be more familiar with the ways of conducting nutritional research, I spent considerable time studying, observing, and interviewing individuals at leading nutritional centers in the USA and Canada. They were doing similar investigations, but were not advocating fish to the extent we were. It did not take me long to realize that we were competing with these internationally known centres where they were using teams of physicians, nutritionists, clinical psychologists, and dedicated technologists to conduct their studies.

*Journal: What were the results of your study?*

**Dr. Harlow:** Our goal was to maintain the fat content of the subject's diet within the 30 to 33 percent range. The average fat content of these men's diet had been in the 40 to 45 percent range for many years. The polyunsaturated to saturated fat became 1:1 or better instead of the 1:3 ratio that had been their standard fare. The summary of results is available. (see Table I).

*Journal: Has the successful results of this study attracted any attention?*

**Dr. Harlow:** In the early 1960s I was asked to speak in New York City before 150 food editors of various magazines and newspapers from the United States and Canada. The topic of my address was the value of fish in diets to control cholesterol levels of the blood to prevent heart disease. The editors and writers were very responsive and a four-page feature article appeared in



the *Ladies Home Journal* entitled "The Great Nova Scotia Diet". This story received a great deal of international recognition and played no little part in the increased consumption of fish in the US in recent years. Since that time there have been numerous TV and Radio interviews on the value of "The Great Nova Scotia Diet".

TABLE I

Time	Number	Age	Average Cholesterol	Average Weight
Start	53		195.0 mg%	193 lbs.
1 year later	50	20-29	183.0 mg%	182 lbs.
Start	35		265.0 mg%	211 lbs.
1 year later	34	30-39	223.0 mg%	195 lbs.
Start	50		248.0 mg%	208 lbs.
1 year later	48	40-49	209.0 mg%	201 lbs.
Start	10		242.0 mg%	207 lbs.
1 year later	9	50-59	215.0 mg%	198 lbs.
Controls start	50		219.0 mg%	192 lbs.
1 year later	42	25-59	241.0 mg%	198 lbs.

*Journal:* Do you think the public understands the cholesterol question at present?

**Dr. Harlow:** The public awareness of the cholesterol threat has changed behaviour a great deal. Since 1963 the average Canadian-American cholesterol intake has dropped from 800 mg down to less than 500 mg a day, and the consumption of milk, butter, eggs and animal fat have all dropped. However, the consumption of vegetable oils, fish, chicken have increased.

*Journal:* Did you learn anything personally from your cholesterol study and experience?

**Dr. Harlow:** Having done over 2500 autopsies over the past 50 years and read through the voluminous files before conducting the post mortem examination, one cannot help but see how life style does affect ones quality of life and longevity. In order to encourage the subjects in my study to change lifestyle, I started on a similar diet during our study and fish entered into my daily meal plan 5 to 7 times a week with increased amounts of polyunsaturated fats. My exercise program has been 30 minutes on the exercise bicycle daily, 250 skips, walking and gardening in the summer.

*Journal:* In the last three years you have become known by many public school children as the skipping doctor. Do you enjoy this activity?

**Dr. Harlow:** I am very gratified by my experience with school children. The best way of teaching is by example.

Dr. Edwin Kinley, a friend for many years, did a operation on one of the valves of my heart and an extensive examination of all my coronary arteries. Later he smilingly told me that they were like a person in his early thirties. Therefore I have no doubt in my own mind that my life style has greatly contributed to my present good health. A programme with a diet high in fruits, vegetables, fish, chicken and grains plus regular sweat producing exercise can be very worthwhile. □

## CURRENT TOPICS IN COMMUNITY HEALTH

Continued from page 172.

health services research, public health research and social and behavioural research.

The CCCC provided important information on the prevention of heart and vascular disease. Blood cholesterol is related to cardiovascular disease. Impressive evidence exists regarding the positive effect of decreasing blood cholesterol levels. Dietary modification can influence blood lipid levels. High risk individuals were defined and recommendations made for intervention. These recommendations will guide physicians and dietitians in counselling patients. A post-conference task force is now being established to define more precise guidelines for treatment of individuals at high risk.

The conference evidence and panel recommendations must now be evaluated in terms of relevance for the entire population by the Health and Welfare Canada Committees in the current review of Nutrition Recommendations for Canadians. The panel acknowledged the importance of comprehensive dietary guidelines for Canadians as fundamental to a public health approach.

Source: National Institute of Nutrition, Rapport (1988) 3, 3: 1-3.

Note: Copies of the Report of the Canadian Consensus Conference on Cholesterol are available from the Organizing Committee Chairman, Dr. Alec Little, 30 Bond Street, Toronto, Ontario M5B 1W8. □

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# Current Topics in Community Health

Selected by: Dr. Frank M.M. White  
Department of Community Health and Epidemiology  
Dalhousie University, Halifax, N.S.

## HOW CAN THE POOR AFFORD TO EAT?

Hunger and poverty are becoming increasingly common in Nova Scotia. To provide data on the actual costs of feeding a family in Nova Scotia, the Nova Scotia Nutrition Council conducted a food price survey in January 1988. Pricing of a 74 item food basket, designed to meet the nutritional needs of a reference family of four people, was undertaken in thirteen communities across Nova Scotia. Results were compared with provincial and municipal social assistance food rates.

Results of the survey show that food rates provided by most municipalities and by the province are woefully inadequate compared with what is needed to adequately feed families in Nova Scotia.

Based on its findings, the Council recommends that the following six changes be considered by the Provincial Department of Community Services and by municipalities in Nova Scotia.

1. That social assistance rates in Nova Scotia be increased to accurately reflect actual costs of living. In particular, that food rates be increased to allow for the purchasing of a nutritious diet.
2. That both the Provincial Department of Community Services and municipalities establish nutrition education programs for people receiving social assistance.
3. That food rates given reflect the actual costs of food in municipalities and be reviewed and revised if necessary on an annual basis.
4. That food allowances be given separately, not in combination with other allowances such as clothing.
5. That food allowances be established with consideration of age, sex and size of family.
6. That all pregnant and lactating women receiving social assistance be given nutrition education and free supplementary orange juice and milk tickets as well as funds to purchase a nutritionally adequate diet.

*Source:* How Can the Poor Afford to Eat? An Examination of Social Assistance Food Rates in Nova Scotia? Executive Summary. Nova Scotia Nutrition Council, 102 Glenforest Drive, Halifax B3M 1H8.

*Notes:* In the Spring of 1987, the difficulties of the poor in Nova Scotia were graphically described by the Nova Scotia Association of Social Workers in *How Will the Poor Survive? A Discussion Paper on the Current Social Assistance System in Nova Scotia*. This discussion paper indicated that the rates for all social assistance payments in Nova Scotia are 45-67% below the poverty line as established by Statistics Canada.

The Nova Scotia Nutrition Council, an interest group made up of professionals with a diversity of backgrounds, works to promote the nutritional health of Nova Scotians. The council has become increasingly concerned over the growing incidence of poverty and the effect it is having on the nutritional status of Nova Scotians.

## CANADIAN CONSENSUS CONFERENCE ON CHOLESTEROL

Development of a Canadian point of view on cholesterol and lipoproteins in coronary artery disease was the goal of the Canadian Consensus Conference on Cholesterol (CCCC), held in Ottawa from March 9 to 11, 1988. The conference was sponsored by the Canadian Atherosclerosis Society, the Canadian Heart Foundation, Health and Welfare Canada and the Heart and Stroke Foundation of Ontario. More than 400 health professionals and representatives of government, industry and the media attended the conference.

A panel (including a lawyer, a family practitioner, a pediatrician, cardiologists, biochemists, nutritionists, a pathologist and an epidemiologist) reviewed reports in advance and then listened to presentations, by international experts, of evidence relating serum cholesterol, lipids and lipoproteins to the risk of coronary heart disease (CHD). Other evidence presented included the effects of diet, dietary trends, exercise and energy balance on these parameters, as well as principles of drug management and the basis for a national strategy for prevention of CHD. After listening to the evidence, the panel met privately and prepared recommendations representing a consensus of opinion among the panelists.

The panel unanimously supported the concept that a number of modifiable risk factors play an important part in the genesis of heart attack and stroke in Canada. Noting the need for a collaborative approach, the panel cited the identification of individuals at risk, the utilization of a public health approach and a strong educational program as important strategies. The following were recommendations of the panel:

### Recommendations:

1. Government and voluntary health agencies should give high priority to the development of health promotion programs which address the range of cardiovascular risk factors including smoking, hypertension, diabetes, obesity and sedentary behaviour. Programs should enlist all relevant sectors of the economy and involve all health care



disciplines, and receive sufficient resources to be effective.

Dietary guidelines for Canadians should be developed as a strategy to reduce population risk.

2. Public health programs directed to the reduction of levels of serum cholesterol should consider a mean population value of 190 mg/dL as a feasible long-term goal.
3. The agri-food industry should continue efforts to produce foods that will make it possible for the Canadian population to achieve lower levels of blood cholesterol. Restaurants and cafeterias should be encouraged to offer meals that are low in fat and cholesterol.
4. Biochemical parameters which are strongly related to atherosclerosis (high total cholesterol, high low-density lipoprotein (LDL) cholesterol, low high-density lipoprotein (HDL) cholesterol and a high ratio of total cholesterol/HDL cholesterol) merit remedial action. Determination of lipid risk factors should include these parameters.
5. Determination of lipid risk factors should be a priority for:
  - a. individuals known to have coronary heart disease (CHD)
  - b. those with a family history of hyperlipidemia, or CHD, occurring at an early age (parent, grandparent, brother or sister with heart attack under age 60)
  - c. individuals with hypertension, diabetes, renal failure and abdominal obesity

As resources permit, determination of lipid risk factors should become part of a periodic health examination for all adult Canadians.

6. While cholesterol and LDL levels vary with age and sex, in the interests of simplicity, the blood lipid levels shown in Table I (based on a minimum of two consecutive tests, one month apart) should be regarded as elevated. Intervention using dietary therapy, and drug therapy if necessary, should be considered for levels of cholesterol above 240 mg/dL (over age 30) and 220 mg/dL (age 18-29). In the range 200 mg/dL to 240 mg/dL, dietary advice alone is advocated.

If other risk factors are present, intervention should be considered at lower levels of total cholesterol and LDL cholesterol. In children older than two years with a family history of risk factors, blood cholesterol, LDL and HDL should be determined.

7. Dietary modification remains the principal intervention for individuals known to have elevated blood lipids. Principles of dietary modification include:

- total fat not exceeding 30% of energy intake
- saturated fat limited to 10% of calories; such a reduction in saturated fatty acids will reduce cholesterol intake but intake of high cholesterol foods should be restricted
- polyunsaturated fatty acids limited to 10% of calories
- protein intake in the range of 10%-15% of calories
- carbohydrate to provide the remaining energy emphasizing polysaccharides and good sources providing dietary fibre
- body weight to be maintained in an acceptable range

Some individuals may require a stricter dietary therapy to achieve target levels.

8. Smoking, hypertension, diabetes, obesity and sedentary behaviour are important risk factors for CHD. Intervention on all these factors is recommended in individuals at risk for elevated lipids.
9. Hypolipidemic drug therapy should be used only after an adequate trial of rigorous diet modification. Maximal diet modification should be continued during drug treatment.
10. In order to implement these recommendations, further recommendations were made with respect to the need for expanded laboratory facilities, a national professional education campaign for physicians and other health professionals, more training positions for dietitians as well as further professional education for practicing dietitians. A national cholesterol education program should be considered.

TABLE I

BLOOD LIPID LEVELS CONSIDERED TO BE ELEVATED

	AGE			
	Over 30 Years		18-29 Years	
	mg/dL	(mmol/L)	mg/dL	(mmol/L)
Blood Cholesterol	>240	(6.2)	>220	(5.7)
Blood Cholesterol Plus LDL Cholesterol	>200	(5.2)	>180	(4.6)
LDL Cholesterol	>130	(3.4)	>115	(3.0)
Blood Cholesterol Plus HDL Cholesterol	>200	(5.2)	>180	(4.6)
HDL Cholesterol	< 35	(0.9)	< 35	(0.9)
Blood Cholesterol Plus Triglyceride	>200	(5.2)	>180	(4.6)
	>200	(2.3)	>200	(2.3)

11. Further advances in the reduction of CHD will require a balanced and coordinated research effort. Priorities were identified in areas relevant to cardiovascular disease, including basic medical research, clinical research, nutritional research,

Continued on page 170.



# An Appreciation

## DR. JOHN JAMES QUINLAN

Dr. John James Quinlan passed away at home on July 12, 1988, age 71 years, after a short illness. He was born in Holyrood, Newfoundland, and received his medical degree from Dalhousie University in 1941. He then joined the staff of the Nova Scotia Sanatorium, becoming resident surgeon, and completing his training in thoracic surgery. Following his certification in that field, he practised thoracic surgery at both the Nova Scotia Sanatorium and the Blanchard Fraser Memorial Hospital. Following amalgamation of the hospitals, he served as chief of staff of the Valley Health Services Association until he retired in 1982. Until the time of his death, he continued to serve as a consultant, and assist in the operating room.

He was a fellow of the Royal College of Physicians and Surgeons of Canada, a member of the American Association for Thoracic Surgery, and a fellow of the American College of Chest Physicians. He was appointed to the Provincial Medical Board of Nova Scotia for the term January 1, 1977 to December 31, 1979; re-appointed for the term January 1, 1980 to December 31, 1982, and was president during his final year. He was a member of the Medical Society of Nova Scotia, past president of the Valley Branch; a member of the Canadian Medical Association, having been elected for senior membership; a member of the Nova Scotia Lung Association, medical advisory board and chairman for three years; Canadian Lung Association, honorary life member; American Lung Association; International

Union Against Tuberculosis; Nova Scotia Thoracic Society; American Thoracic Surgery; Canadian Public Health Association; Public Health Association of Nova Scotia; and the Nova Scotia Surgical Society, senior member.

Dr. Quinlan served two terms as President of the Valley Medical Society and was chairman of the Medical Society of Nova Scotia, surgical section, from 1974 to 1975. He was a serving brother of the Saint John Ambulance Association. In the last two years, much of his time was devoted to work with the Valley Regional Hospital Foundation, serving on the Board of Directors, as well as being the assistant general chairman. During his lifetime, Dr. Quinlan had authored or co-authored more than fifty scientific publications, and was an avid scholar, as well as an excellent clinician and surgeon.

He is survived by his wife, Dr. Helen Holden; two daughters, Kathleen (Dr. Kathleen Landymore) Halifax; Patricia Jones, Toronto; a brother, Donald, Brampton, Ont.; two sisters, Mrs. Patricia Hawkins, Halifax, and Eileen Quinlan, Kentville; as well as five grandchildren.

He will be sadly missed by those of us who have had the privilege of knowing him, and working with him, over the past years. His expertise and advice was frequently sought.

Sincere sympathy is extended to his family.

Ralph H. Burnett, M.D.

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## Reminiscences

### JACK HARE

Jack Hare died suddenly on April 30 of a myocardial infarction. An accountant by training, his name was well known to the Medical Society Executive and Administration for over twenty five years. He was head of the Finance Division of the Hospital Insurance Commission until he became Executive Director in the late nineteen sixties. After the Medical Care Insurance Commission and the Hospital Insurance Commission amalgamated in 1973, he became Executive Director of the Health Services Insurance Commission. He held that position until his retirement in June 1986.

Jack was keenly aware of his responsibility to government, and ultimately, the taxpayer. This meant that in much of his dealing with organized medicine, we negotiated with him from the opposite side of the table.

Those of us who sat as The Medical Society of Nova Scotia representatives on the Health Services Insurance

Commission over the years, sometimes collided with Jack Hare. Yet we developed a respect for his ability, his comprehensive knowledge of the Commission records, and his open and frank dealings with the Medical Society. It is not surprising that friendships developed out of such mutual respect.

As a Society, we have always been appreciative of those who labor diligently on our behalf. As citizens of this province, we should be prepared to recognize the dedication and ability of some of those with whom we debate across the table. Jack Hare was a conscientious executive, a forceful negotiator, and when lines were drawn, a worthy adversary.

To his wife Marjorie and family, on behalf of present and past members of the Health Services Insurance Commission. I offer our sincere sympathy.

N.K.M.



# CoActifed\*

Tablets/Syrup/Expectorant  
Antitussive—Expectorant—Decongestant

**Indications: CoActifed Expectorant:** To facilitate expectoration and control cough associated with inflamed mucosa and tenacious sputum.

**CoActifed Syrup and Tablets:** The treatment of cough associated with inflamed mucosa.

**Precautions:** Before prescribing medication to suppress or modify cough, it is important to ascertain that the underlying cause of the cough is identified, that modification of the cough does not increase the risk of clinical or physiologic complications, and that appropriate therapy for the primary disease is provided.

In young children the respiratory centre is especially susceptible to the depressant action of narcotic cough suppressants. Benefit to risk ratio should be carefully considered especially in children with respiratory embarrassment, e.g., croup. Estimation of dosage relative to the child's age and weight is of great importance.

Since codeine crosses the placental barrier, its use in pregnancy is not recommended.

As codeine may inhibit peristalsis, patients with chronic constipation should be given CoActifed preparations only after weighing the potential therapeutic benefit against the hazards involved.

CoActifed contains codeine: may be habit forming. Use with caution in patients with hypertension and in patients receiving MAO inhibitors.

Patients should be cautioned not to operate vehicles or hazardous machinery until their response to the drug has been determined. Since the depressant effects of antihistamines are additive to those of other drugs affecting the CNS, patients should be cautioned against drinking alcoholic beverages or taking hypnotics, sedatives, psychotherapeutic agents or other drugs with CNS depressant effects during antihistaminic therapy.

**Adverse Effects:** In some patients, drowsiness, dizziness, dry mouth, nausea and vomiting or mild stimulation may occur.

**Overdose: Symptoms:** Narcosis is usually present, sometimes associated with convulsions. Tachycardia, pupillary constriction, nausea, vomiting and respiratory depression can occur.

**Treatment:** If respiration is severely depressed, administer the narcotic antagonist, naloxone. Adults: 400 µg by i.v., i.m. or s.c. routes and repeated at 2 to 3 minute intervals if necessary. Children: 10 µg/kg by i.v., i.m. or s.c. routes. Dosage may be repeated as for the adult administration. Failure to obtain significant improvement after 2 to 3 doses suggests that causes other than narcotic overdosage may be responsible for the patient's condition.

If naloxone is unsuccessful, institute intubation and respiratory support or conduct gastric lavage in the unconscious patient.

**Dosage: Children 2 to under 6 years: 2.5 mL 4 times a day. Children 6 to under 12 years: 5 mL or ½ tablet 4 times a day. Adults and children 12 years and older: 10 mL or 1 tablet 4 times a day.**

**Supplied: Expectorant:** Each 5 mL of clear, orange, syrupy liquid with a mixed fruit odor contains: triprolidine HCl 2 mg, pseudoephedrine HCl 30 mg, guaifenesin 100 mg, codeine phosphate 10 mg. Available in 100 mL and 2 L bottles.

**Syrup:** Each 5 mL of clear, dark red, syrupy liquid with a pineapple odor and a sweet black currant flavor contains: triprolidine HCl 2 mg, pseudoephedrine HCl 30 mg and codeine phosphate 10 mg. Available in 100 mL and 2 L bottles.

**Tablets:** Each white to off-white, biconvex tablet, code number WELLCOME P4B on same side as diagonal score mark, contains: triprolidine HCl 4 mg, pseudoephedrine HCl 60 mg and codeine phosphate 20 mg. Each tablet is equivalent to 10 mL of syrup. If tablet is broken in half, it reveals a yellow core. Bottles of 10 and 50 tablets.

Additional prescribing information available on request.

\*Trade Mark W-611



WELLCOME MEDICAL DIVISION  
BURROUGHS WELLCOME INC.  
KIRKLAND, QUE.

On behalf of

## HUMANE MEDICINE

Drs. D.G. Oreopoulos and J.O. Godden  
invite you to join a unique community

through participation in HUMANE MEDICINE, an ecumenical journal of the art and science of health care.

This work brings together physicians, nurses, other health-care professionals, lawyers, clergy, academics and concerned persons from all levels of society. Through the agency of this journal these people are banding together to

*become a network*

Thus, working together, they can ensure that we, our families, and those of our fellow citizens who wish these benefits may

*have competent and compassionate care*

Those who support this vision believe that this network will be brought into being and, thereafter, sustained only if those concerned with humane care

*engage in a continuing dialogue*

Because modern health care is an exercise in community, and because the heart of caregiving is the person-to-person contact of the healer and healed, this dialogue is essential if we are to learn to understand and value each other, if we are to grow in mutual sympathy and support, and if we are to become wise enough and determined enough to choose, to work for and to defend a system that will

*ensure caring in all health care*

All are welcome. All can participate. Further information can be had from

Dr. D.G. Oreopoulos  
Humane Medicine  
Toronto Western Hospital  
399 Bathurst Street  
Toronto, Ontario  
M5T 2S8



**Personal Interest Notes**

**1988 CONVOCATION  
DALHOUSIE UNIVERSITY  
FACULTY OF MEDICINE**

The Dalhousie University Faculty of Medicine Convocation was held on May 20, 1988, when 94 M.D. degrees were conferred. By place of residence, these graduates were from:

Nova Scotia-59; New Brunswick-18; Prince Edward Island-6; Québec-6; Ontario-4; and British Columbia-1.



President Howard C. Clark, Dr. Harold Rifkin, and Dean T. J. ("Jock") Murray.

Dr. Sarah Kirby, Halifax, N.S., was awarded the C.B. Stewart Gold Medal as the most outstanding graduate. An honorary degree was conferred on Dr. Harold Rifkin (M.D. Dal., 1941), Clinical Professor of Medicine, Albert Einstein College of Medicine, New York City, who delivered the Convocation Address.

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Dr. Sarah Kirby receiving the C.B. Stewart Gold Medal from Dr. Stewart (President Clark in the foreground).

Dr. David C. Young, Assistant Professor of Obstetrics and Gynaecology, was named Professor of the Year by the Graduating Class. This award, which is a trophy in the form of a small shovel with an inscribed silver blade, was presented during the convocation exercises.



Dr. David Young receiving the Professor of the Year award from the Class President, Dr. Jeffrey Steeves.

Photographs by *Carlos* [courtesy of the Dalhousie Medical Alumni Association].

Congratulations to **Dr. Bernard Badley**, Halifax, N.S., in being named Executive Director of the Victoria General Hospital. "Bernie" serves as a reminder to us that we still can play a part in management, and in the vital decisions concerning our profession. His example is appreciated.

**Dr. Richard Hall**, Victoria General Hospital Staff Anaesthetist became the first Nova Scotian to receive the Canadian Anaesthetists' Society Research Award. The honour was bestowed during their 45th Annual Meeting in Halifax during the summer. □