Request # 19405430 **MAR 06, 2006**

Email (PDF) To: rmfmd2@cox.net

Dr. Richard Fleming
9795 Gateway Dr #105
Reno, NV 89521

MDZ

LOANSOME DOC: Journal Copy Affiliated

Title:	Angiology.
Title Abbrev:	Angiology
Citation:	1996 Sep;47(9):831-40
Article:	Assessing the independent effect of dietary counseling and h
Author:	Fleming RM;Ketchum K;Fleming DM;Gaede R
NLM Unique ID:	0203706
PubMed UI:	8810649
ISSN:	0003-3197 (Print)
Holding:	Library reports holding vol/yr
Need By:	N/A
Maximum Cost:	**Any cost**
Patron Email:	rmfmd2@cox.net ld_patron_seq=190216; patron_userid=
Phone:	1.402.639-6023
Received:	Mar 06, 2006 (11:40 AM EST)
Lender:	UNIVERSITY OF NEVADA SCHOOL OF MEDICINE/ RENO/ NV USA (NVUNEV)

Angiology
The Journal of Vascular Diseases

VOLUME 47 SEPTEMBER 1996 NUMBER 9

Assessing the Independent Effect of Dietary Counseling and Hypolipidemic Medications on Serum Lipids

Richard M. Fleming, M.D., F.A.C.A., AANC
Kristy Ketchum, R.D., L.D.*
Diane M. Fleming, R.N., B.S.N.*
and Ruth Gaede, R.N., M.S.N.*

OMAHA, NEBRASKA and CEDAR FALLS, IOWA

ABSTRACT

Determination of changes in total cholesterol (TC) and triglyceride (TG) levels has focused primarily on hypolipidemic drug effects. Changes resulting from dietary effect alone versus diet and drug effect have not yet been fully established.

Seventy subjects were enrolled into four treatment groups to determine the impact of diet and drug effect upon TC and TG. Group 1 (n = 28) served as the control group and received no dietary counseling or drug therapy. Group 2 (n = 22) received dietary counseling. Group 3 (n = 7) underwent dietary counseling for six months and drug therapy for eighteen months. Subjects in groups 1–3 were monitored for eighteen months. Patients in group 4 (n = 13) were followed up for thirty-six months. No intervention occurred during the first eighteen months, and hypolipidemic medications were used during the second eighteen-month period.

Subjects in groups 1 and 4 received no specific dietary counseling and demonstrated no significant improvement over the course of the study. Patients in groups 2 and 3 showed significant reductions in both TC and TG. The improvement in TC seen for patients in group 3 was reduced after dietary counseling ceased.

(continued on next page)

From Integrated Physicians of Nebraska, Omaha, Nebraska and the *Center for Clinical Cardiology and Research, in conjunction with Sartori Memorial Hospital, Cedar Falls, Iowa.

(Abstract continued)

Dietary intervention is necessary if patients are to statistically significantly reduce TC and TG levels. Drug therapy demonstrated the expected reductions in both TC and TG but did not statistically significantly lower lipid levels without concomitant dietary counseling. When dietary counseling and hypolipidemic medications are used together, reductions in TC and TG values are even greater than those seen with dietary effect alone. Diet control alone appears to significantly reduce TC and TG levels, resulting in reduced need for antianginal medications.

Introduction

The reversibility of coronary artery disease (CAD) by reduction of cholesterol levels was first documented[1-10] in Rhesus monkeys and cynomolgus macaques when these animals were placed on low cholesterol diets. Epidemiologic studies[11-14] have demonstrated a positive correlation between dietary intake of cholesterol and the prevalence of CAD as well as little notable effect of high density lipoprotein (HDL) cholesterol when the total cholesterol (TC) is less than 150 mg/dL.

Multiple studies[15-29] have looked at risk factor (RF) modification and the effects upon morbidity and mortality. Changes in CAD as assessed by coronary arteriography (CA) have also been studied[30-38] despite limitations[39-42] in assessing changes in percent diameter stenosis (%DS) by using visual interpretation of CAs.

Recent work[43] has demonstrated reversibility/remodeling of CAD by use of quantitative coronary arteriography (QCA) and positron emission tomography (PET). The primary author (RMF) was involved in later components of this work, which attempted to place subjects on vegetarian diets along with hypolipidemic medications. Little work has been done to determine the effect of changes in diet versus hypolipidemic medications and the interactions of the two upon TC and triglyceride (TG) levels.[44-47] This longitudinal study was designed to answer the following questions: (1) What is the impact on TC and TG levels when patients are advised by their cardiologist to reduce dietary intake of foods high in cholesterol and fat but receive no formal counseling? (2) What is the impact on TC and TG levels when patients undergo dietary counseling by either a dietitian or cardiologist trained in hyperlipidemia? (3) What is the effect of hypolipidemic medications on reducing TC and TG levels when patients receive dietary counseling, and what are the ramifications once dietary counseling is withdrawn? The study was not designed to assess differences between various hypolipidemic medications since multiple studies have already addressed this issue.

Methods

Patient Population

Seventy subjects were divided into four groups as noted in Table I. Thirteen subjects were observed for thirty-six months and 57 for eighteen months. Group 1 included 28 individuals who served as the "control" group and were told by their cardiologist to reduce dietary intake of cholesterol and fats but received no specific dietary instruction except for dietary brochures made available to them. Group 2 consisted of 22 people who were advised by their cardiologist to make dietary changes and follow either step I or step II American Heart Association (AHA) guidelines (Table II) or, if possible, a vegetarian diet. Subjects received instruction from a cardiologist (RMF) experienced in treating hyperlipidemia and risk factor (RF) modification and/or a registered dietitian (KK) on each of the scheduled (Table I) office visits.

A third group of patients consisted of 7 individuals who received dietary counseling during the first six months and hypolipidemic medications for the full eighteen months of the study. Groups 1–3 were followed up for eighteen months, and subjects in group 4 were followed up for (Table I) thirty-six months. Group 4 was composed of 13 people who were advised to reduce cholesterol and dietary fat intake for the first eighteen months, using the same approach as the

Table I

Scheduled Visits in Months for Evaluating Fasting Lipoproteins

	−18	−12	−9	−6	−3	Base-line	+3	+6	+9	+12	+18
Group 1	–	–	–	–	–	+	+	+	+	+	+
Group 2	–	–	–	–	–	+	+	+	+	+	+
Group 3	–	–	–	–	–	+	+	+	+	+	+
Group 4	+	+	+	+	+	+	+	+	+	+	+

"–" indicates not applicable, "+" indicates scheduled monthly visit.

Table II

Suggested Daily Dietary Guidelines for Patients in Groups 2 and 3

Constituent	Current American Diet*	Step I AHA Diet*	Step II AHA Diet*	Vegetarian Diet*
Total fat	42	< 30	< 20	< 10
Saturated	14–19	< 10	< 7	
Monosaturated		10–15	10–15	
Polysaturated		< 10	< 10	
Carbohydrate		50–60	50–60	75
Protein		15–20	15–20	15
Cholesterol	500 mg	< 300 mg	< 200 mg	5 mg

*Percent of daily calories.

"control" group. After completion of the first eighteen months subjects were then given hypolipidemic medications designed to reduce TC and/or TG levels for the next eighteen months.

Subject Enrollment

Patients were enrolled in the study if they had type IIa, IIb, or IV hyperlipidemia. Forty-three men and 27 nonpregnant women participated in the study. Subject participation was voluntary. Patients who demonstrated ischemic changes on nuclear imaging[48] requested specific dietary counseling, which placed them by definition into Group 2 or 3. Subjects were excluded from the study if they had hypercholesterolemia secondary to hypothyroidism, nephrotic syndrome, diabetes mellitus, obstructive liver disease, or a drug ef-

fect caused by beta antagonists, thiazide diuretics, progesterone, or anabolic steroids.

Dietary Counseling

Patients in group 2 (eighteen months) and 3 (first six months) received dietary counseling from a registered dietitian (KK) and/or cardiologist (RMF). Subjects were counseled individually for one hour during their first session. Follow-up sessions ranged from fifteen to thirty minutes depending upon the needs of the patient. Patients were advised to change their dietary habits to that of a vegetarian lifestyle. If this could not be accomplished, they were encouraged to follow step II AHA standards or at least step I AHA guidelines. Since the study was designed to investigate what could realistically be accomplished, patients and their families made the final decisions about which dietary guidelines they would follow.

During each of the follow-up visits patients in groups 2 and 3 were able to review their progress, assess individual dietary concerns, and set their own future goals. Patients were encouraged about the progress they had made with criticisms limited to constructive comments.

Medications

Since the purpose of the study was not to compare specific hypolipidemic agents, selection of these medications was independently made by the cardiologist(s) taking care of the patient. Selection consisted of hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase inhibitors, bile acid sequestrants, fibric acid derivatives, and nicotinic acid. Combination regimens were used at the discretion of the primary cardiologist and were not influenced by the investigators. Medications were used according to physician preferences and guidelines established for each of the agents in the current physician desk reference (PDR), with appropriate monitoring of drug effect and side effects.

Lipoprotein Analysis

Subjects were asked to fast for a minimum of twelve hours prior to having blood drawn for serum total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG) levels. The Paramax reagent methods were used to determine TC and TGs. HDL-C was measured by means of magnesium phosphotungstate precipitation and centrifugation methodology. Low-density lipoprotein cholesterol (LDL-C) was calculated as follows:

$$\text{LDL-C} = \text{TC} - (\text{HDL-C}) - (\text{TG}/5)$$

Statistical Analysis

Each lipoprotein was measured on scheduled visits as outlined in Table I. Results for each group were determined and described as mean ± standard deviation. Differences between groups and for differences within groups over time were analyzed by unmatched two-tailed t tests. Results of group differences are graphically depicted. Other statistical analyses of TC and TGs, including range, confidence intervals, and correlation between changes in weight, TC, and TG values, were done but yielded no additional useful information.

Results

Each individual's age and weight were recorded at entry and throughout the study. No significant differences existed between groups, as shown in Table III. Baseline TC and TG levels, as noted in Tables IV and V, were comparable for each of the groups. Changes in weight over time did not appreciably correlate with changes in TC or TG.

Changes in TC and TGs over the course of the study are shown in Tables IV and V respectively. Subjects in the "control" group demonstrated an increase in both TC and TG values by the end of the eighteen months. These increases in TC and TG levels, while notable, were not statistically significant.

Subjects in group 2 demonstrated a statistically significant reduction in TC ($P < 0.005$) and TG ($P < 0.005$) levels following eighteen months of dietary counseling without the use of hypolipidemic medications. These results are shown in Tables IV and V and graphically depicted in Figures 1 and 2. Changes in dietary habits were anecdotally better if a supportive family group existed. Subjects in the second group of patients, with recent-onset exertional angina, required only "low-dose" nitrate therapy for control of angina

Table III

Patient Group Characteristics on Entry into the Study

	Number in Group	Age (Years)*	Weight (Pounds)*
Group 1	28	64 ±9	184 ±38
Group 2	22	59 ±11	190 ±34
Group 3	7	60 ±10	186 ±61
Group 4	13	58 ±7	180 ±34

*Results shown as mean ± standard deviation.

Table IV

Results for Total Cholesterol (mg/dL)

Month	Group 1	Group 2	Group 3	Group 4
-18	—	—	—	263
-12	—	—	—	273
- 9	—	—	—	266
- 6	—	—	—	260
- 3	—	—	—	278
Baseline	238	239	250	270
+ 3	254	193	216	241
+ 6	256	207	183	225
+ 9	264	234	146	237
+12	254	183	236	247
+18	273	169	218	235

"–" indicates not applicable.

Table V

Results for Triglycerides (mg/dL)

Month	Group 1	Group 2	Group 3	Group 4
-18	—	—	—	266
-12	—	—	—	266
- 9	—	—	—	160
- 6	—	—	—	162
- 3	—	—	—	259
Baseline	198	186	242	278
+ 3	206	178	137	241
+ 6	161	137	147	193
+ 9	195	213	86	183
+12	198	118	148	218
+18	391	102	110	226

"–" indicates not applicable.

once their cholesterol levels had appreciably decreased following initial dietary changes.

Patients in group 3 demonstrated a statistically significant reduction in TC ($P < 0.005$) by reducing serum levels from 250 to 183 mg/dL by the end of the sixth month (Table IV) of combined dietary counseling and hypolipidemic medication. While this overall reduction in TC for group 3 (Figure 1) was greater than that seen in group 2, the differences were not statistically significant. By the end of six months, TG levels for group 3 were significantly ($P < 0.025$) reduced from baseline values as shown in Table V and Figure 2. The difference in TG reductions (Figure 2) seen at the end of six months of treatment was not statistically different for groups 2 and 3.

After completion of the first six months, subjects in group 3 were withdrawn from participation in the dietary counseling component of the study but continued with hypolipidemic medication(s). The effects of dietary counseling persisted during the nine-month follow-up but had disappeared twelve months into the study. Patients in group 3 continued to display beneficial reductions in TC at the end of the study, although they had regressed to values ($P < 0.025$) seen three months into the program. Reductions in TGs were maintained after cessation of dietary counseling, although further statistically significant improvement was not seen.

Patients enrolled in group 4 spent the first eighteen months of the study with elevated TC and TG levels (Tables IV and V respectively) without the input of either a dietitian or physician trained in the management of hyperlipidemia. After completion of these first eighteen months, there was no statistical difference between initial levels and that considered to be present at "baseline," as defined in Table I. Subjects continued without dietary counseling but were then given hypolipidemic medications for the next eighteen months. While TC was reduced by 10.6% and TGs by 14.8%, these improvements, which are frequently seen with the use of hypolipidemic med-

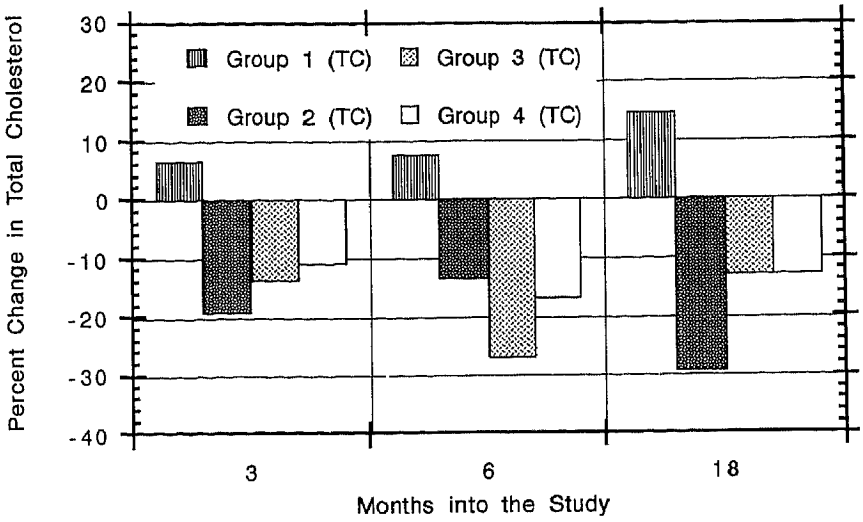
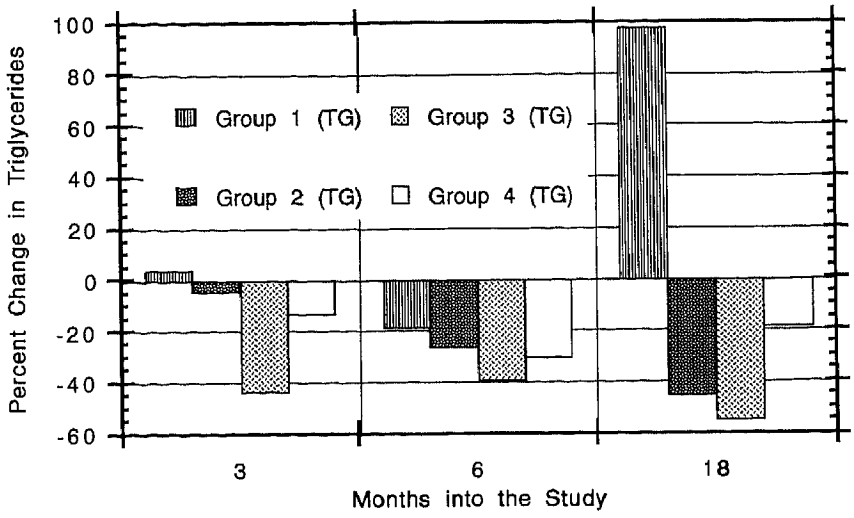


Figure 1. Results of Changes in Total Cholesterol (TC) for Each of the Four Treatment Groups. Group 1 represents the control group and is noted by a bar with vertical lines. Subjects in this group showed an increase in TC during the study. Subjects in group 2 are represented by small squares in a vertical bar. There was an overall improvement seen in this group throughout the study. Group 3 is represented by diagonal lines within the bar, while group 4 is represented by a white vertical bar.

Figure 2. Results of Changes in Triglycerides (TG) for Each of the Four Treatment Groups. Group 1 represents the control group and is noted by a bar with vertical lines. Subjects in this group showed an increase in TG during the study. Subjects in group 2 are represented by small squares in a vertical bar. There was an overall reduction in TG seen for this group. Group 3 is represented by diagonal lines within the bar, while group 4 is represented by a white vertical bar.



ications, do not represent statistically significant reductions for either TC or TG levels.

Discussion

Seventy subjects were enrolled into four different treatment groups, with a longitudinal study design. The effects of dietary counseling, hypolipidemic medications, combination effect, and the effect of neither dietary counseling nor medical management were assessed to determine the effects of each upon TC and TG levels.

When patients received no specific dietary counseling (group 1) but were given dietary brochures and told by their cardiologist to decrease dietary intake of cholesterol and fats, there was an actual increase in serum levels for both TC and TG. While these changes were not statistically significant, they clearly represent an increased risk for CAD. Subjects in group 4 demonstrated slightly increased TC and TG values during the first eighteen months, before the addition of hypolipidemic medications. Eighteen months after treatment with hypolipidemic medications, subjects in group 4 showed the expected reductions in TC and TG levels. While these improvements are considered significant, they are not statistically significant and fell short of the improvement seen by patients in groups 2 and 3, during dietary counseling. These results suggest that significant reductions in lipoproteins require dietary changes.

Subjects in group 2 demonstrated significant reductions in both TC and TGs as a result of dietary counseling alone. While motivation may play a role in the overall reduction of TC and TGs seen for subjects receiving dietary counseling, the results clearly show that many patients who wish to reduce TC and TG levels and who undergo dietary counseling on a regular basis are frequently able to reduce and maintain lower levels of serum lipids. The effect is possibly influenced by a supportive family and requires further investigation.

When subjects in group 3 were receiving both dietary counseling and medical management, the reductions in TC and TGs were even greater than that seen in group 2. If the patients had continued to receive dietary counseling, the results seen at six months suggest that even greater improvements in TC and TG levels would have been seen, resulting in even further reductions in CAD risk. Supporting evidence for this comes from the continued reductions in TC and TG levels seen at nine months. This probably represents some residual effect from earlier dietary counseling that was not lost until the twelfth month. While some of the improvement in TC for patients in group 3 was lost by the end of the study, little effect was lost for control of TGs. This suggests some retained impact from earlier dietary teaching when results of groups 3 and 4 are compared.

Control of angina with lower than the expected dose of nitrates and significant reductions in TC and TGs for participants in groups 2 and 3 support the idea that significant reductions in serum lipids may result in remodeling of atherosclerotic plaques, reduction of percent diameter stenosis, and improvement in coronary blood flow, resulting in improved stenosis flow reserve[38-43] and improved exercise capacity. Reductions in medical costs are seen by patients requiring either no additional medication or lower doses of beta antagonists, slow calcium channel antagonists, and/or nitrate compounds. Subsequently, the overall cost of dietary counseling may be significantly less than the cost of the medications it reduces or replaces, with fewer potential side effects.

Conclusions

The overall results emphasize the need for dietary counseling if patients are to obtain meaningful reductions in lipid levels. Simply being advised to reduce dietary TC and fats does not have a significant impact unless supportive dietary counseling occurs. For subjects receiving hypolipidemic medications, the maximum effect of medical management is realized with the addition of dietary counseling. Withdrawal of dietary counseling can blunt if not totally nullify the benefit of medications, while medical management in the absence of any dietary counseling appears to provide little if any statistically significant benefit.

Richard M. Fleming, M.D.
Medical Director,
Integrated Physicians of Nebraska
11906 I-Street
Omaha, NE 68137

References

1. Tucker CF, Catsulis C, Strong JP, et al: Regression of early cholesterol induced aortic lesions in Rhesus monkeys. Am J Pathol 65:493-514, 1971.
2. Eggen DA, Strong JP, Newman WP, et al: Regression of diet induced fatty streaks in Rhesus monkeys. Lab Invest 31:294-301, 1974.
3. Kokatnur MG, Malcom GT, Eggen DA, et al: Depletion of aortic free and ester cholesterol by dietary means in Rhesus monkeys with fatty streaks. Atherosclerosis 21:195-203, 1975.
4. Strong JP: Reversibility of fatty streaks in Rhesus monkeys. Primates Med 9:300-320, 1976.
5. Armstong ML, Megan MB: Arterial fibrous proteins in cynomolgus monkeys after atherogenic and regression diets. Circ Res 36:256-261, 1975.
6. Malinow MR, McLaughlin P, Papworth L, et al: A model for therapeutic intervention on established coronary atherosclerosis in a non human primate. Adv Exp Med Biol 67:3-31, 1976.
7. Vesselinovitch D, Wissler RW, Hughes R, et al: Reversal of advanced atherosclerosis in Rhesus monkeys. Part I. Light-microscopic studies. Atherosclerosis 23:155-176, 1976.
8. Weber G, Fabbrini P, Resi L, et al: Regression of arteriosclerotic lesions in Rhesus monkey aortas after regression diet. Scanning and transmission electron microscope observations of the endothelium. Atherosclerosis 26:535-547, 1977.
9. Chakravarti RN, Kumar BS, Nair CR, et al: Reversibility of cholesterol adrenaline-induced atherosclerosis in Rhesus monkeys. Evaluation of safflower oil and low-fat low-calorie diet. Atherosclerosis 28:405-416, 1977.
10. Hollander W: Studies on the progression and regression of coronary and peripheral atherosclerosis in the cynomolgus monkey. Part I. Effects of dipyridamole and aspirin. Exp Mol Path 30:55-73, 1979.
11. Connor WE, Cerqueira MT, Connor RW, et al: The plasma lipids, lipoproteins and diet of the Tarahumara Indians of Mexico. Am J Clin Nutr 31:1131-1142, 1978.
12. McGill HC: The relationship of dietary cholesterol to serum cholesterol concentration and to atherosclerosis in man. Am J Clin Nutr 32:2664-2702, 1979.
13. Glueck CJ: Dietary fat and atherosclerosis. Am J Clin Nutr 32:2703-2711, 1979.
14. Simons, LA: Interrelations of lipids and lipoproteins with coronary artery disease mortality in 19 countries. Am J Cardiol 57:5G-10G, 1986.
15. Dewar HA, Arthur JB, Ashby WR, et al: Trial of clofibrate in the treatment of ischaemic heart disease. Five-year study by a group of physicians of the Newcastle-upon-Tyne region. Br Med J 4:767-775, 1971.
16. Alstead S, Aitchison JD, Barr JB, et al: Ischaemic heart disease: A secondary prevention trial using clofibrate. Report by a research committee of the Scottish Society of Physicians. Br Med J 4:775-784, 1971.
17. The Coronary Drug Project Research Group: Clofibrate and niacin in coronary heart disease. JAMA 231:360-381, 1975.
18. Puska P, Virtamo J, Tuomilehto J, et al: Cardiovascular risk factor changes in a three-year follow-up of a cohort in connection with a community programme (the North Karelia Project). Acta Med Scand 204:381-388, 1978.
19. Kornitzer M, Backer GD, Dramaix M, et al: The Belgian Heart Disease Prevention Project. Modification of the coronary risk profile in an industrial population. Circulation 61:18-25, 1980.
20. Shekelle RB, Shryock AM, Paul O, et al: Diet, serum cholesterol, and death from coronary heart disease. The Western Electric Study. N Engl J Med 304:65-70, 1981.
21. Kjelsberg MO: Multiple risk factor intervention trial. Risk factor changes and mortality results. JAMA 248:1465-1477, 1982.
22. Lipids Research Clinics Program: The Lipid Research Clinics Coronary Primary Prevention Trial Results. I. Reduction in incidence of coronary heart disease. II. The relationship of reduction in incidence of coronary heart disease to cholesterol lowering. JAMA 251:351-374, 1984.
23. Goldbourt U, Holtzman E, Neufeld HN: Total and high density lipoprotein cholesterol in the serum and risk of mortality: Evidence of a threshold effect. Br Med J 290:1239-1243, 1985.
24. Miettinen TA, Huttunen JK, Naukkarinen V, et al: Multifactorial primary prevention of cardiovascular diseases in middle-aged men. Risk factor changes, incidence, and mortality. JAMA 254:2097-2102, 1985.
25. Brunner D, Weisbort J, Meshulam N, et al: Relation of serum total cholesterol and high-density lipoprotein cholesterol percentage to the incidence of definite coronary events: Twenty-year follow-up of the Donolo-Tel Aviv prospective coronary artery disease study. Am J Cardiol 59:1271-1276, 1987.
26. Frick JH, Elo O, Haapa K: Helsinki Heart Study: Primary-prevention trial with gemfibrozil in middle-aged men with dyslipidemia. Safety of treatment, changes in risk factors, and incidence of coronary heart disease. N Engl J Med 317:1237-1245, 1987.
27. Carlson LA, Rosenhamer G: Reduction of mortality in the Stockholm ischaemic heart disease secondary prevention study by combined treatment with clofi-

brate and nicotinic acid. Acta Med Scand 223:405-418, 1988.

28. Assmann G, Schulte H, Munster DR: The Prospective Cardiovascular Munster (PROCAM) Study: Prevalence of hyperlipidemia in persons with hypertension and/or diabetes mellitus and the relationship to coronary heart disease. Am Heart J 116:1713-1724, 1988.
29. Alderman JD, Pasternak RC, Sacks FM, et al: Effect of a modified, well-tolerated niacin regimen on serum total cholesterol, high density lipoprotein cholesterol and the cholesterol to high density lipoprotein ratio. Am J Cardiol 64:725-729, 1989.
30. Cohn K, Sakai FJ, Langston MF: Effect of clofibrate on progression of coronary disease: A prospective angiographic study in man. 89:591-598, 1975.
31. Kuo PT, Hayase K, Kostis JB, et al: Use of combined diet and colestipol in long-term (7 to 7 and ½ years) treatment of patients with type II hyperlipoproteinemia. Circulation. 59:199-214, 1979.
32. Nash DT, Gensini G, Esente P: Effect of lipid-lowering therapy on the progression of coronary atherosclerosis assessed by scheduled repetitive coronary arteriography. Int J Cardiol 2:43-55, 1982.
33. Levy RI, Brensike JF, Epstein SE, et al: The influence of changes in lipid values induced by cholestyramine and diet on progression of coronary artery disease: Results of the NHLBI type II coronary intervention study. Circulation 69:325-337, 1984.
34. Nikkila EA, Viikinkoski P, Valle M, et al: Prevention of progression of coronary atherosclerosis by treatment of hyperlipidaemia: A seven year prospective angiographic study. Br Med J 289:220-223, 1984.
35. Arntzenius AC, Kromhout D, Barth JD, et al: Lipoproteins and the progression of coronary atherosclerosis. The Leiden Intervention Trial. N Engl J Med 312:805-811, 1985.
36. Blankenhorn DH, Nessim SA, Johnson RL, et al: Beneficial effects of combined colestipol-niacin therapy on coronary atherosclerosis and coronary venous bypass grafts. JAMA 257:3233-3240, 1987.
37. Blankenhorn DH, Johnson RL, Nessim SA, et al: The cholesterol lowering atherosclerosis study (CLAS): Design, methods, and baseline results. Controlled clinical trails. 8:354-387, 1987.
38. Gould KL, Buchi M, Kirkeeide RL, et al: Reversal of coronary artery stenosis with cholesterol lowering in man followed by arteriography and positron emission tomography. J Nucl Med 30:845, 1989.
39. Fleming RM, Kirkeeide RL, Smalling RW, et al: Patterns in visual interpretation of coronary arteriograms as detected by quantitative coronary arteriography. J Am Coll Cardiol 18:945-951, 1991.
40. Fleming RM, Harrington GM: Quantitative coronary arteriography and its assessment of atherosclerosis. Part 1. Examining the independent variables. Angiology 45:829-833, 1994.
41. Fleming RM, Harrington GM: Quantitative coronary arteriography and its assessment of atherosclerosis. Part 2. Calculating stenosis flow reserve directly from percent diameter stenosis. Angiology 45:835-840, 1994.
42. Fleming RM, Fleming DM, Gaede, R: Teaching physicians and nurses to accurately read coronary arteriograms: A training program. (submitted to Angiology December 1994).
43. Ornish D, Brown SE, Scherwitz LW, et al: Can lifestyle changes reverse coronary heart disease? Lancet 336:129-133, 1990.
44. Fleming RM, Rater D, Ketchum K: Reducing cholesterol and triglycerides in the elderly patient by diet alone. Abstract submitted to the Council on Arteriosclerosis for the 66th Scientific Sessions of the AHA. Published Sept. 1993:127.
45. Fleming RM, Rater D: Dietary changes without medication can equally reduce cholesterol in both the young and older patient. Abstract submitted to the Council on Arteriosclerosis for the 66th Scientific Session of the AHA. Published Sept. 1993:128.
46. Fleming RM, Rater D, Ketchum K: Studying the effect of medications on cholesterol and triglycerides in subjects not receiving dietary counseling. Abstract submitted to the Council on Arteriosclerosis for the 66th Scientific Session of the AHA. Published Sept. 1993:128.
47. Fleming RM, Ketchum K: Dietary reinforcement is an integral component of cholesterol reduction. Abstract submitted to the Council on Arteriosclerosis for the 66th Scientific Session of the AHA. Published Sept. 1993:128.
48. Fleming RM, Rose CH, Feldmann KM: Comparing a high dose dipyridamole SPECT imaging protocol with dobutamine and exercise stress testing protocols. Angiology 46:547-556, 1995.