Cardiovascular
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I-1960

Selected from World Literature

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Cardiovascular Abstracts I 1960 Selected from World Literature

Edited by
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Cardiovascular Abstracts I 1960

Selected from World Literature

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Foreword

FOR many physicians, the abstracts of current cardiovascular literature have always been an important feature of Circulation. Written by the Abstract Editors, they represent an authoritative summary of selected papers published in the field throughout the world.

The Publications Committee of the American Heart Association has long felt that they should be gathered regularly into a single reference book. In this way a physician could quickly find under each of the twenty-three categories a brief résumé of significant work in that area.

Abstracts I-1960 is the first attempt by the American Heart Association to perform this service. It is an experiment, and its continuation as an annual monograph will depend upon the response of physicians. Should this series be continued, each annual volume would become part of a uniform set for easy reference.

One final comment: These abstracts represent a *selection* of what the editor and his associates have considered most significant. It is by no means an attempt to record every paper in the field, a task already undertaken by other publications. Rather, it represents editorial judgment of what is important by the editors of *Circulation* who must exercise such judgment daily in selecting or rejecting papers for the journal. It is hoped that the result, one more aspect of the professional education program of the American Heart Association, will prove useful.

J. Scott Butterworth, M.D. President-Elect,
American Heart Association.

Atherosclerosis

Altschul, R.: Influence of Cytochrome C and Hematoporphyrin on Serum Cholesterol. Ztschr. Kreislaufforsch. 48: 844 (Sept.), 1959.

Injection of 0.02 to 0.04 Gm. of cytochrome C in rabbits caused a highly significant decrease in serum cholesterol, which usually returned to previous values within 24 hours. This was attributed to increased oxidation of cholesterol due to cytochrome C. Intramuscular injection of 1 to 20 mg. of hematoporphyrin, which is contained in the nucleus of cytochrome, also caused a highly significant decrease of cholesterol persisting also after 24 hours. Oral medication was without effect.

LEPESCHKIN

Berkowitz, D., Likoff, W., and Sklaroff, D.M.: The Effect of Sitosterol on Radioactive Fat Absorption Patterns. Am. J. Cardiol. 4: 282 (Sept.), 1959.

The administration of a single 30-ml. dose of sitosterol (Cytellin) or of 45 ml. daily for periods of 4 to 6 months was found not to change the enteric absorption curve of radioactive triolein in 15 patients with coronary atherosclerosis and an elevated serum cholesterol and in 5 healthy individuals, all on normal diets. Serum cholesterol values in the chronically treated group showed no striking changes.

ROGERS

Boyer, P. A., Jr., Lowe, J. T., Gardier, R. W., and Ralston, J. D.: Effect of a Practical Dietary Regimen on Serum Cholesterol Level. J.A.M.A. 170: 257 (May 16), 1959.

Three hundred institutionalized patients under conditions permitting rigorous control of diet were put on a regimen tending to lower blood cholesterol levels. The significant feature was the use of a margarine containing 64.2 per cent of nonhydrogenated corn oil. During the 9-month study this diet was effective in achieving and maintaining a reduction of blood cholesterol levels. The diet raised the percentage of linoleic acid by about 300 per cent. The transition to the test diet went unnoticed by the majority of patients and by many members of the staff. A 13 per cent drop in serum cholesterol was found in 301 patients within 3 weeks. After 5 months the

fall of cholesterol was about 23 per cent. The maximum change in weight was less than 1 Kg. during the test period. With resumption of usual diet, the serum cholesterol levels rose 19 per cent over a 3-month period. It was obvious that dietary alteration could be accomplished simply, easily, inconspicuously, and with an excellent degree of patient acceptability.

KITCHELL

Carlson, L. A., and Pernow, B.: Studies on Blood Lipids during Exercise. I. Arterial and Venous Plasma Concentrations of Unesterified Fatty Acids. J. Lab. & Clin. Med. 53: 833 (June), 1959.

The effect of muscular work on unesterified fatty acids (UFA) in man was studied by determining plasma concentrations in arterial blood and femoral veins at rest and during exercise to the point of exhaustion of the exercising leg. Six healthy subjects were studied. The exercising legs extracted UFA from plasma, and the arterial plasma concentration decreased or remained fairly constant during exercise, increasing again during a resting period of 30 minutes. The method is described in detail. The differences in concentration between the arterial and venous blood indicate that UFA were extracted from the blood perfusing the exercising leg at the different work loads up to the maximal. At rest the arterial and venous hematocrit values were equal, but during exercise they sometimes differed, with the venous values at times 1 to 5 per cent higher than the arterial. In discussing the findings in relation to the energy metabolism of exercising muscular tissues, the authors find support for the theory that UFA is one of the major transport forms for fat needed for immediate energy metabolism and that extraction of UFA during exercise may well be due to the metabolism of fatty acids to yield energy via the Krebs cycle.

MAXWELL

Davies, D. F.: A Comparison of Erythrocyte and Chylomicron Electrophoretic Migration Times and Serum Cholesterol Levels in Atheroma. Clin. Sc. 18: 263, 1959.

The serum cholesterol was compared with the erythrocyte migration time in patients with and

without evidence of coronary artery disease. A close correlation was found between the chylomicron and erythrocyte migration times. The erythrocyte migration time was significantly prolonged in subjects with coronary occlusion compared to a control group. No significant difference was found in this study between the cholesterol level of the coronary group and of the control group; no correlation could be demonstrated between serum cholesterol level and erythrocyte migration time. It is concluded that the migration times are a measure of plasma surface activity and the colloidal stability of plasma fat.

KURLAND

de Soldati, L., Stritzler, G., Balassanian, S., and Bourguet, M. D.: Effect of Nicotinic Acid on Blood Lipids in Arteriosclerotic Patients. Cardiologia 35: 84, 1959.

In 37 arteriosclerotic patients, aged 36 to 75, the total blood lipids and fatty acids were found to be elevated in all. Cholesterol levels were beyond normal limits in 26, lipid phosphorus was increased in 2, phospholipids were elevated in 4 patients, and mean beta-lipoproteins and beta/ alpha lipoprotein index were increased. These patients were given 1 to 4 Gm. of nicotinic acid by mouth daily during periods of 5 days to 4 months with the dietary habits unchanged during the time of study. Striking reductions of blood lipid levels were observed in patients with high cholesterol levels prior to treatment, with particular reduction of the total cholesterol, cholesterol esters, and fatty acids. In patients with normal cholesterol levels there was no significant reduction of blood lipids. The mean beta/ alpha lipoprotein index was moderately reduced. Side effects, notably flushing and itching on the face and upper extremities, led to the suspension of the drug in 10 per cent of patients but actual harmful effects were never seen. The interruption of treatment was generally followed by an increase in the blood lipid levels. The administration of large doses of nicotinic acid seemed to be effective in reducing high blood lipid levels in arteriosclerotic patients without dietary restrictions. BRACHFELD

Dodds, C., and Mills, G. L.: Influence of Myocardial Infarction on Plasma-lipoprotein Concentration. Lancet 1: 1160 (June), 1959.

The lipoprotein patterns in men at various intervals after acute infarction (24 hours to 8 weeks) were compared with the values for healthy men as estimated by ultracentrifugation, Cohn fractionation, and paper electrophoresis. In general, the younger patients with coronary

artery disease had higher lipoprotein levels than the elderly. The latter tended toward normal. Following an infarction there was a profound disturbance of the equilibrium of lipoprotein metabolism, which caused the lipoprotein levels to vary widely at different times. There was a slight decrease in the content of cholesterol in alpha lipoprotein, which was far outweighed by an increase in the percentage of cholesterol in beta lipoproteins. There was a sharp drop in the concentration of total cholesterol and the cholesterol percentage in beta lipoprotein starting a day or so after the acute infarction. Then there was a slow climb until the previous level was reached at about 3 to 5 weeks. Detailed analysis of the lipoprotein distribution by the ultracentrifuge showed that in each Sf range there was a rise in concentration reaching a peak value at about 4 weeks. These results support the hypothesis that a lipid abnormality is associated with myocardial infarction, and makes it clear that the lipoprotein pattern during the first 2 months of illness is constantly changing and cannot be represented by a single measurement during this period. It is, therefore, unwise to base conclusions on a comparison of patterns after infarction with those of a separate group of controls until sometime after the eighth week. It is suggested that the preliminary fall in lipid levels after infarction is an immediate consequence of the "stress." The largest postinfarction variations in lipid level were observed in patients whose preinfarct level was high; those with a low level showed little or no change.

SHETS

Dole, V. P., James, A. T., Webb, J. P. W., Rizack, M. A., and Sturman, M. F.: The Fatty Acid Patterns of Plasma Lipids during Alimentary Lipemia. J. Clin. Invest. 38: 1544 (Sept.), 1959.

The plasma lipids were analyzed in a group of normal subjects in the fasting state and for a 9hour period after a single meal consisting of 100 Gm. of corn oil, coconut oil, or butter. The plasma lipids were fractionated into chylomicra, nonesterified fatty acids, triglycerides plus cholesterol esters, and phospholipids. For each of these fractions the fatty acid composition was determined with gas-liquid chromatography. In the fasting samples, the fatty acid composition of each of the fractions revealed a fairly consistent pattern in the group of normal subjects. The absorption of corn oil, coconut oil, or butter failed to alter significantly the fatty acid composition of the lipid fractions when measured at 1/2, 1, and 21/2 hours (short-term studies) or at 3, 6, and 9 hours (longer-term studies). The coconut oil had mainly saturated fatty acids, whereas the corn oil contained mostly unsaturated fatty acids (89 per cent). The stability of chylomicra in plasma was striking and suggested that they were in equilibrium with a larger pool of tissue lipids. These studies were concerned mainly with the transport of fat after an acute load. Studies in which a distinctive fat was fed for many weeks altered the composition of tissue lipids, and this change may be reflected in the plasma of the fasting subject.

Fischer, F. W.: Serum Lipoproteins. Ztschr Kreislaufforsch. 48: 517 (June), 1959.

Nearly all serum lipids exist normally in the form of lipoproteins. In young persons (18 to 35 years of age), beta lipoproteins exceed 60 per cent in less than one half of the women but in three fourths of the men, corresponding to the difference between the sexes in the clinical incidence of atherosclerosis. Of 4,546 patients with clinical atherosclerosis, 90 per cent had values exceeding 72 per cent, the upper range in young women. A value exceeding 80 per cent was found in two thirds of the patients with several myocardial infarctions but in only one third of those with a single infarction. The concentration of beta lipoproteins, expressed as a percentage of the total, seemed to be a more sensitive criterion than their absolute concentration or the concentration of total lipids. While in large statistical groups this concentration showed definite correlation to the clinical findings and life-expectancy, its individual prognostic significance was small. LEPESCHKIN

Friedman, M., and Byers, S. O.: Evaluation of Nicotinic Acid as an Hypocholesteremic and Anti-Atherogenic Substance. J. Clin. Invest. 38: 1328 (Aug.), 1959.

The addition of nicotinic acid to the diet of rats produced a moderate decline in serum cholesterol as compared to that of controls at the end of 12 days. The treated rats, however, failed to gain weight. They were able to absorb cholesterol and total lipid as well as control rats. The daily biliary excretion of cholesterol remained the same for the experimental and control series. There appeared to be no effect, therefore, upon the intestinal absorption of cholesterol or total lipid, or upon the hepatic synthesis of cholesterol in rats given nicotinic acid. A group of rats given nicotinic acid and a high fat-cholesterol diet in limited amount developed the same degree of hypocholesteremia as their controls, who were also fed the high fat-cholesterol diet in like limited amounts. The anoretic properties of nicotinic acid may have been responsible for the hypocholesteremic effect previously noted in animal experiments. Rabbits pair-fed on high fat-cholesterol diets with and without nicotinic acid failed to exhibit a significant difference either in their average plasma cholesterol or in their degree of aortic atherosclerosis. The authors suggest that subtle changes in quality and quantity of the foods ingested by subjects receiving nicotinic acid may, in part, be responsible for the hypocholesteremic action.

KAYDEN

Gee, D. J., Goldstein, J., Gray, C. H., and Fowler, J. F.: Biosynthesis of Cholesterol in Familial Hypercholesterolaemic Xanthomatosis. Brit. M. J. 2: 341 (Sept. 5), 1959.

Cholesterol is synthesized from acetate units in the body and the mechanism of the biosynthesis of cholesterol in a male patient with familial hypercholesteremic xanthomatosis is the basis of this report. C-labeled acetate was administered orally, and the radioactivity in the free and ester fractions of the plasma cholesterol was estimated at intervals for 144 hours. The specific activity of the free cholesterol reached a maximum within 4 hours, fell relatively rapidly between 4 and 24 hours, and then more slowly. The specific activity of the ester fraction increased slowly and became equal to that of the free cholesterol at about 21/2 days and reached a maximum in 4 days. The results are interpreted as showing an increased rate of biosynthesis of cholesterol from acetate in this patient.

KRAUSE

Groom, D., McKee, E. E., Webb, C., Grant, F. W., Pean, V., Hudicourt, E., and Dallemand, J.: Coronary and Aortic Atherosclerosis in the Negroes of Haiti and the United States. Ann. Int. Med. 51: 270 (Aug.), 1959.

The degree of coronary and aortic atherosclerosis in 128 autopsies of Haitian Negroes and 139 autopsies of American Negroes was estimated by a grading scale. Routine autopsies covering all types of mortality over age 20 were utilized as representative samples of the 2 population groups. The degree of atherosclerosis in the coronary arteries of the hearts of the American subjects was almost double that of Haitian subjects, but no such difference was noted in the corresponding aortas. This was true for both men and women, and at virtually all age levels. Coronary grades of male subjects from both countries increase similarly with age to a suggested leveling

in the fifth decade; those of the females appeared to increase uniformly from the lowest values to the highest at 60 and beyond. An attempt was made to gather data on the dietary habits of the 2 groups as well as economic and work statistics. The inaccuracy of vital statistics for comparing the incidence of coronary disease in the 2 different civilizations was stressed. The apparent predisposition of the American group to coronary but not to aortic atherosclerosis suggested that factors other than diet alone must play important roles. The authors suggest that some of these factors may be the more stressful environment, the greater complexity, mechanization, education, and competitiveness of the Negro's life in the United States.

KAYDEN

Holman, R. L., Blanc, W. A., and Andersen, D.: Decreased Aortic Atherosclerosis in Cystic Fibrosis of the Pancreas. Pediatrics 24: 34 (July), 1959.

Lipid accumulations in the aorta were studied in necropsy specimens from 18 patients with cystic fibrosis of the pancreas and from 21 control patients all between the ages of 6 and 13 years; all of the patients were Caucasians. The authors found that the average percentage of the intimal surface involved was over 4 times as great in the control group as compared to the group with fibrocystic disease. They reviewed the metabolic abnormalities found in patients with fibrocystic disease but were unable to come to any satisfactory conclusions as to the etiologic factors involved in producing such a strong relationship between this disease process and atherosclerosis.

KARPMAN

Holman, R. L., McGill, H. C., Jr., Strong, J. P., and Greer, J. C.: Filtration Versus Local Formation of Lipids in Pathogenesis of Atherosclerosis. J.A.M.A. 170: 416 (May 23), 1959.

The method whereby lipids accumulate in the inner layers of the arterial wall in atherosclerosis is one of the most cogent problems of our time. Evidence suggests that the active principles governing lipid transportation and local accumulations are enzyme-hormone complexes. The active metabolic work concerned is performed by the mesenchymal cells in the inner layers of the arterial wall. There are 3 stages leading to clinical disease: fatty streaking in the first 2 decades, conversion of some fatty streaks to fibrous plaques in the second 2 decades, and local complications such as hemorrhage and thrombosis about a plaque in the third 2 decades. Much confusion

can be avoided by keeping interspecies differences in mind and recognizing the stage of atherosclerosis in man at any given age.

KITCHELL

Kuo, P. F., and Carson, J. C.: Dietary Fats and the Diurnal Serum Triglyceride Levels in Man. J. Clin. Invest. 38: 1384 (Aug.), 1959.

The serum lipids were measured in 6 patients with the following lipid abnormality: 2 patients with hypercholesteremia; 2 patients with essential hyperlipemia; 2 patients with hypercholesteremia and mild hyperlipemia. Four other patients without any known lipid abnormalities were also studied as normal controls. Diurnal variations in serum cholesterol and phospholipid levels were minimal in the 10 subjects whether on isocaloric full diet, rice and fruit, or corn oil formula diets in which corn oil constituted 50 to 70 per cent of the total daily caloric intake. In the 4 normal patients and 2 patients with hypercholesteremia, the postprandial serum triglyceride elevations were lower and briefer while on the corn oil diet than on a full diet. However, the differences in the effects of unsaturated and saturated dietary fats upon the postprandial serum triglyceride concentrations became progressively less evident in the 4 patients with increasingly severe degrees of hyperlipemia. On rice and fruit diets the fasting serum triglycerides of the nonlipemic subjects were only slightly higher than their respective fasting levels measured during the full and the corn oil dietary periods. In the hyperlipemic patients, significant increases in their fasting triglyceride concentrations were observed, following the change from high-fat diets (100 to 140 Gm. animal fat) to the rice and fruit diet (5 Gm. fat). The mechanism of the fasting lipemia with rice diet is not understood, but patients with ischemic heart disease should certainly not be placed on a rigidly restricted fat diet. KAYDEN

Malmros, H., and Wigand, G.: Atherosclerosis and Deficiency of Essential Fatty Acids. Lancet 2: 749 (Nov. 7), 1959.

A method has been devised for producing atherosclerosis in rabbits by feeding a semi-synthetic cholesterol-free diet containing only 8 per cent fat. The cholesterol-free diet without any fat produced a rise in cholesterol and the same aortic changes as in cholesterol-induced atherosclerosis. The effect of various added fats on cholesterol level and aortic atherosclerosis was studied. Milk fat and hydrogenated cocoanut fat produced hypercholesteremia, and within 3 to 4 months, gross aortic changes. Corn oil and similar oils produced only a small rise in serum

cholesterol but no gross aortic lesions. In 1 animal, the fat-free diet was followed by diet with added corn oil; there was a prompt drop in serum cholesterol. This suggests that the hypercholesteremia was due to a deficiency of fatty acids.

KURLAND

Morris, T. G.: A Comparison of Methods for the Estimation of Serum Cholesterol and Values in Random Samples of Populations in the 55-64 Age Group. J. Clin. Path. 12: 518 (Nov.), 1959.

Cholesterol levels in random samples of populations in different areas were measured in the age group of 55 to 64. There is a general upward trend over the years 55 to 59 and then a fall to the age of 64. Levels were higher in women than in men. Results were consistent with findings in studies by other researchers. Six methods of estimating blood cholesterol levels were compared with a standard test solution and with each other by carrying out determinations in triplicate by each method on 10 sera. Trinder's method was the most reproducible, and those of Anderson and Keys (K.5) and Sperry and Webb were the next. Sackett's method was the least reproducible. Mean levels obtained with the methods of Sperry and Webb and Anderson and Keys did not differ; the mean by Trinder's method was 4.2 per cent higher; by Sackett's method, 7.3 per cent higher; by Pearson's method, 8.8 per cent higher; and by Zlatkis' method, 51.8 per cent higher. For routine use Trinder's method is most suitable and involves less manipulation and time. Anderson's and Keys' method is also quite suitable. There are 2 major types of technic. Pearson's and Zlatkis' methods involve adding reagents directly to the serum. In the others, the cholesterol is first extracted, either by solvents or by digitonin precipitation. In all the methods, colorimetric technics are used.

MAXWELL

Perkins, R., Wright, I. S., and Gatje, B. W.: Safflower Oil—Pyridoxine and Corn Oil—Pyridoxine Emulsions. J.A.M.A. 169: 1731 (April), 1959.

Serum cholesterol levels were studied in 22 healthy young men. An initial observation period of 5 weeks afforded a basis for forming 2 matched groups with equal mean serum cholesterol levels (221 mg. per 100 ml.). Thereafter 1 group received a supplement of safflower oil for 7 weeks. The other group received corn oil for 7 weeks followed by safflower oil for 7 weeks. A slight decrease was observed in average serum cholesterol level but was not found to be statistically significant. This study points out that if one wishes to lower significantly the serum cholesterol

level, unsaturated fats should be used only when combined with a diet sharply limited in the use of saturated fats.

KITCHELL

Pick, R., Stamler, J., Rodbard, S., and Katz, L. N.: Effects of Testosterone and Castration on Cholesteremia and Atherogenesis in Chicks on High-Fat, High-Cholesterol Diets. Circulation Research 7: 202 (Mar.), 1959.

These experiments explored the effects of androgenic activity on atherogenesis in chicks using a standardized high-fat, high-cholesterol diet. Testosterone in large doses partially inhibited hypercholesteremia but no effect was noted on aortic or coronary atherogenesis. Gonadectomy in young male and female chicks was without influence on hypercholesteremia and atherogenesis.

PAUL

Schlüssel, H., Schulte, M., Heinrich, W., and Hamacher, J.: Athletics and Atherosclerosis. Ztschr. Kreislaufforsch. 48: 734 (Aug.), 1959.

Twenty-eight guinea pigs given a dietary supplement of goose liver and cholesterol and subjected to daily exercise for 102 days showed significantly lower serum lipid and cholesterol levels and incidence of aortic atheromatosis than 28 guinea pigs given the same supplement but not exercised. The blood pressure amplitude was also lower. It is concluded that athletic activity in man has a similar preventive effect on atherosclerosis.

Worne, H. E., and Smith, L. W.: Effects of Certain Pure Long Chain Polyunsaturated Fatty Acid Esters on the Blood Lipids of Man. Am. J. M. Sc. 237: 710 (June), 1959.

The role of polyunsaturated fatty acids in the etiopathogenesis of hypercholesteremia is discussed. Various polyunsaturated fatty acids were administered to patients with and without hyperlipemia. Studies were carried out over a period of 90 days. There was a significant correlation between the number of double-bonds in the fatty acid molecule and their effect on the blood lipids. Four grams per day of the 4, 5, and 6 doublebonded fatty acids, produced significant changes in blood lipid reflected by reduced cholesterol levels and a more favorable cholesterol-phospholipid ratio. Sixteen grams of 2 and 3 doublebonded fatty acids per day produced the same effect, although 4 Gm. per day was without effect. A combination of all the polyunsaturated fatty acid esters gave rise to the same effects as the pure individual esters. In several patients with skin xanthomata, elimination of these lesions was