American Heart Association Monograph

Abstracts II-1961

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Selected from World Literature

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Atherosclerosis

Alekseeva, A. S.: A Study of Elastase Inhibitor in Patients with Atherosclerosis and Hypertensive Disease. Cor et Vasa 2: 215, 1960.

Levels of elastase inhibitor in the serum of patients with essential hypertension and of those with arteriosclerosis showed no significant difference from those in normal blood donors.

LEPESCHKIN

Barrow, J. G., Quinlan, C. B., Cooper, G. R., Whitner, V. S., and Goodloe, M. H. R.: Studies in Atherosclerosis. III. An Epidemiologic Study of Atherosclerosis in Trappist and Benedictine Monks: A Preliminary Report. Ann. Int. Med. 52: 368 (Feb.), 1960.

The outline of a prolonged longitudinal epidemiologic study of atherosclerosis in 2 unique population groups is presented. An analysis of the diet reveals that the 2 groups differ in their dietary habits. One group, the lacto-ovo-vegetarian Trappist group, derive 26 per cent of their total calories from fat, and 43 per cent of their fat is of animal origin. The other group, a Benedictine community, derive 45 per cent of their total calories from fat and 75 per cent of this fat is of animal origin. The Trappist group appears to have significantly lower levels of most serum lipid constituents, but on an individual basis, serum lipids cannot be correlated with fat intake alone. It is concluded, on the basis of the preliminary report, that most serum lipids vary on a group basis with age and dietary fat intake, but that on an individual basis there appear to be factors other than age and dietary fat that affect serum lipids.

KAYDEN

Berge, K. G., Achor, R. W. P., Barker, N. W., and Power, M. H.: Comparison of the Treatment of Hypercholesteremia with Nicotinic Acid, Sitosterol, and Safflower Oil. Am. Heart J. 58: 849 (Dec.), 1959.

Among 10 patients with hypercholesteremia on an unrestricted diet, large doses of nicotinic acid were found to be more effective in lowering plasma cholesterol than either safflower oil or sitosterol. When nicotinic acid and sitosterol were combined in treatment, the observed effects were nearly additive. It is pointed out that from a practical point of view nicotinic acid is inexpensive, simple to administer, and does not require alterations in the patient's dietary habits. This drug may therefore prove to be of value in hypercholesteremia when the safety of its long-term use has been established.

SAGALL

Clarke, N. E., Sr, Clarke, N. E., Jr., and Mosher, R. E.: Treatment of Occlusive Vascular Disease with Disodium Ethylene Diamine Tetraacetic Acid (EDTA). Am. J. M. Sc. 239: 732 (June), 1960.

Arguments are presented against the importance of fat and cholesterol in the pathogenesis of atherosclerosis and in support of a biological aging process stressing the importance of trace elements, calcium, and magnesium. Chelation of calcium and other minerals in the human body was attempted in the hope of alleviating the manifestations of occlusive vascular disease. EDTA (disodium ethylene diamine tetraacetic acid) was administered as follows: 3 Gm. in 500 ml. of 5 per cent glucose or normal saline was given intravenously over a 2- to 3-hour period. This was administered on each of five consecutive days each week. There were two series of infusions of 15 each with a rest period of 1 week between them. In addition, pyridoxine, 25 mg. three times daily, was also administered during the period of the infusions. Short booster series of five daily infusions were given at intervals from 6 to 12 months. This therapy was given to 76 patients with angina pectoris (some of whom had had myocardial infarction), to 31 patients with intermittent claudication, rest pain, and pre-gangrene; and to 25 patients with cerebrovascular disease (including senility and tinnitus). Spectacular improvement was found in all three groups. With the exception of references to large series in the literature, no controls were utilized. The authors mention that the double-blind test is "far from infallible" and, with this, they dismiss comparative statistical analyses. In addition it was found that this therapy also produced prolonged lowering of the serum cholesterol.

SHEPS

Day, A. J.: Removal of Cholesterol from Reticulo-Endothelial Cells. Brit. J. Exper. Path. 41: 112 (Apr.), 1960.

Suspensions of cholesterol and of various cholesteryl esters were injected intraperitoneally

into male albino rats and the uptake of these substances in the sternal lymph nodes and their subsequent removal was observed. Almost all of the cholesterol which was taken up was removed from the nodes within 10 days, but there was no difference in the rate of removal of cholesterol with the different preparations. Cholesterol emulsified in corn oil appeared to be removed more rapidly initially than the other preparations. The ingestion of unesterified cholesterol by the nodes was followed by an increase in the ester, while the ingestion of cholesteryl esters was followed by an increase in free cholesterol. The uptake of both cholesterol and cholesteryl oleate resulted in the accumulation of phospholipids and total fatty acids in the lymph nodes. These substances may be derived from the blood or lymph. It was considered that these metabolic changes may influence the removal of cholesterol from reticuloendothelial cells.

KALMANSOHN

Friedman, M., and Byers, S. O.: Deposition and Fate of Cholesterol in Ocular Aortic Implant and in the Aorta in Situ. Am. J. Physiol. **197**: 1019 (Nov.), 1959.

Aortic implants were placed in the anterior eye chamber of 30 rabbits subsequently fed excess cholesterol and cottonseed oil. After 3 months of such feeding, 7 of these animals were sacrificed, and their implants and also segments of their own aorta were analyzed for cholesterol. Two more groups of these rabbits were sacrificed 2 and 3 months, respectively, after their return to a cholesterol-free diet. It was observed that the aortic implant gained almost twice as much cholesterol as the host's own aorta at the end of the cholesterol feeding period. This difference became even greater in animals that were sacrificed 2 months after cessation of excess cholesterol feeding, but were still hypercholesteremic. However, the ocular implants of rabbits examined 3 months after cessation of cholesterol feeding were observed to have lost almost all of their cholesterol, whereas the animal's own aorta continued to exhibit an unchanged excess of cholesterol. The findings suggest that the ocular aortic implant differs markedly from the aorta in situ in regard to its penetration and retention of cholesterol.

KAYDEN

George, E. P., Hall, G. V., and Farkas, G. S.: Lipaemic Clearing Action of Artificial Anticoagulants. Nature **187**: 782 (Aug. 27), 1960.

The authors investigated the in vivo clearing action of several anticoagulants using isotopically labeled fats. Heparin administered in a dose of 7,500 units every 4 hours trebled the rate of removal of alimentary lipemia; the artificial anticoagulants, phenindione, diphenadione, and 3(1-phenylpropyl)-4-hydroxycoumarin, were given to maintain the prothrombin time between 40 and 60 per cent with approximate doubling of the rate of removal of alimentary lipemia.

KALMANSOHN

Hamilton, R. E., and Pilgeram, L. O.: Lipid Bound Glutamic Acid Deficiency in Aging Arteriosclerotic Subjects. Proc. Soc. Exper. Biol. & Med. **103**: 574 (Mar.), 1960.

This study demonstrates that the lipid-bound, ninhydrin-positive constituent identified as glutamic acid is present as a constituent of human plasma. The lipid factor is deficient in the aged, arteriosclerotic human subject; these individuals have about half the "normal" average plasma concentration. The change in distribution ratio of glutamic acid between alpha and beta lipoprotein fractions favors the beta fraction and appears to be a part of a defective mechanism for metabolism of these lipoprotein moieties. The normal subject has 47 per cent in the alpha fraction compared to 35 per cent in this fraction for the arteriosclerotic patient. This deficiency of lipid-bound glutamic acid may be related to a defective blood coagulation system in the human arteriosclerotic individual.

KRAUSE

Hashim, S. A., Arteaga, A., and Van Itallie, T. B.: Effect of a Saturated Medium-chain Triglyceride on Serum-lipids in Man. Lancet **1**: 1105 (May 21), 1960.

A synthetic fat, medium-chain triglyceride (MCT), was used as the sole source of dietary fat in formula feeding experiments on human subjects. It is almost devoid of linoleic acid. The serum-lipid responses obtained with MCT were compared with those obtained when corn oil or butter was substituted in the formula diet in isocaloric amounts. Whenever a subject's regime was changed from an ad-libitum hospital diet to a formula diet, serum lipids fell regardless of the type of fat in the formula. When MCT was substituted for corn oil, serum lipids rose transiently to a significant extent and then returned to only a slight elevation. When compared with butter, serum lipids increased appreciably when butter followed MCT and decreased appreciably when MCT followed butter. Thus, the cholesterol raising properties of butter cannot be ascribed to medium-chain triglycerides nor the cholesterol lowering properties of MCT to linoleic acid. The results of the study are most consistent with the hypothesis that the effect of a dietary fat on serum-cholesterol can be related to certain of its physical characteristics such as melting point or miscibility with water.

KURLAND

Herdenstam, C. G.: Serum Polyunsaturated Fatty Acids in Coronary Heart Disease. Acta med. scandinav. **166**: 475 (May 5), 1960.

It has been suggested that the development of atherosclerosis may be related to a relative deficiency of polyunsaturated fatty acids (PUFA) in the diet. UV-spectrophotometric analyses were made to determine the amounts of PUFA in the serum of 30 normal Caucasian subjects, 6 normal Japanese subjects, and 30 patients with coronary heart disease. There was no significant difference between the average serum level of the different polyunsaturated fatty acids expressed as a percentage of total lipids in the coronary group and in the controls. Among the Japanese, however, there was a significantly lower triene level, but otherwise the same amount of PUFA and total lipids as in the normal material. The author suggests that this may be related to a higher proportion of unsaturated fat in the diet of the Japanese. These data do not confirm the hypothesis that deficiency of PUFA in the serum is a factor in the genesis of coronary heart disease. The PUFA level in the serum may be in a dynamic equilibrium and regulated by homeostatic mechanisms.

SHEPS

Hollander, W., Chobanian, A. V., and Wilkins, R. W.: The Effects of Triparanol (MER-29) in Subjects with and without Coronary Artery Disease. J. A. M. A. **174**: 5 (Sept. 3), 1960.

Eighty-nine patients who had had serial cholesterol determinations for more than 2 years before the institution of the study were treated with triparanol. The age range was 24 to 76 years. Fifty-one were women and 38 were men. Of these, 43 had either clinical or electrocardiographic evidence of coronary artery disease, with angina pectoris in 28. On a maximally effective dose of 250 mg. triparanol per day, 71 of 89 subjects had significant reduction of serum cholesterol, whether or not they had previously had hypercholesteremia. The decrease in serum cholesterol (Abell) averaged 45 mg. per cent and ranged from 20 to 110 mg. per cent. The serum cholesterol to serum phospholipid ratio was also favorably influenced. Radioisotopic tracer substances indicate that this therapy not only reduces serum cholesterol but also the "miscible pool" of cholesterol in man. There is also reduction in total sterol content of the blood as well as the "total sterol pool." There was an antianginal effect in 12 of 28 subjects, and electrocardiographic improvement was noted in stress tests in three of 11 subjects with angina pectoris, associated with the fall in the serum cholesterol.

KITCHELL

Lukomsky, P. E., Bobkova, B. I., and Savenkov, P.M.: The Administration of Unsaturated Fatty Acids in Patients with Coronary Atherosclerosis. Cor et Vasa **1**: 100, 1959.

Forty patients with coronary arteriosclerosis were given 20 ml. per day (total dose 400 ml.) of linetol (a mixture of fatty acids of linseed oil), as a supplement to a basic diet of 2,400 calories containing 55 to 60 Gm. of fat., for 20 days. Serum cholesterol, beta-globulin, and beta-lipoprotein fractions showed a significant lowering, while the phospholipid cholesterol coefficient and albumins showed an increase. The only side effects were loose stools in five patients. These results encourage the prophylactic and therapeutic use of linetol in coronary arteriosclerosis.

LEPESCHKIN

Mauruxas, J., and Thomas, R. G.: Treatment of Experimental Atherosclerosis in the Rabbit with L, D. Alpha (Dimyristoyl) Lecithin. J. Lab. & Clin. Med. **56**: 30 (July), 1960.

Fifteen male rabbits were used. Five, as controls, were fed only regular Purina rabbit chow. At autopsy these animals showed aortas that were completely free of arteriosclerotic change. This finding was confirmed by histologic examination. Atherosclerosis was induced in the other 10 animals by feeding them high-cholesterol rabbit chow for 11 weeks. Then five of the atherosclerotic rabbits received infusions of synthetic L, D. alpha (dimyristoyl) lecithin through cannulated external jugular veins, at the rate of 100 ml. of 0.8 per cent of the emulsion over a 4-hour period. This infusion was repeated at intervals of 4 to 6 days. Two rabbits received five infusions; another received four; and two others, three infusions each. Blood samples before and at intervals after infusion were analyzed for total cholesterol, phospholipid phosphorus, and hematocrit. After a rest of 6 to 12 days, the 10 rabbits were killed, and their aortas were examined grossly and microscopically to estimate the degree of atherosclerosis. The remaining portions of the aortas were dried and analyzed for cholesterol, phospholipid phosphorus, and total fat content. Typical atherosclerotic plaques covered 50 per cent of the intimal surface of the aortas in five non-infused rabbits, reaching nearly 90 per cent in the arches. No plaques were found in one rabbit that had received five infusions of lecithin and the vessel walls appeared normal. Striking resolution of the plaques occurred in the second rabbit that had five infusions. The other infused rabbits showed some resolution. A gradual rise in plasma cholesterol and phospholipid phosphorus and a significant drop in hematocrit value were noted after