

# Abstracts of Current Literature



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## ITEMS OF GENERAL INTEREST

**Practical Diets for Lowering Serum Lipids. A Long-Term Study on Out-Patients with Ischaemic Heart Disease.** T. R. E. Pilkington, J. L. Stafford, V. S. Hankin, F. M. Simmonds and H. B. Koerselman. *Brit. M. J.*, 1: 23, 1960.

As long as it is suspected that lipemia, induced by diet, is responsible for cardiovascular disease there will be a demand for simple dietary measures to reduce lipemia. In this study fifty-eight subjects with ischemic heart disease were divided into three treatment groups. Twenty-three were treated with anticoagulants, twenty-three took an "unsaturated fat" diet in which dairy products were excluded and unsaturated fats allowed, and twelve took a "low fat" diet giving 20 to 30 gm. fat daily.

Serum cholesterol and low density lipoprotein levels were effectively reduced by dietary means for periods of more than a year. The "unsaturated fat" diet was the more effective and was better tolerated by patients than the monotonous low fat diet. F. E. HYTTEN

**The Response of Man to Dietary Cholesterol.** J. M. R. Beveridge, W. F. Connell, G. A. Mayer and H. L. Haust. *J. Nutrition*, 71: 61, 1960.

A special "butter-fat fraction," prepared from butter fat by removing cholesterol and the more volatile triglycerides, were fed to ninety-three university students at a 30 per cent calorie level, following eight days on a fat-free diet. Purified cholesterol was added to the diets in steps from nil to 1,600 mg. per 950 calories.

Serum cholesterol levels, determined at eight and sixteen days, were observed to correlate with increasing dietary intake of cholesterol up to 200 mg. per 950 calories. Larger intakes, 400, 800 and 1,600 mg.

cholesterol per 950 calories, produced no significant increases in serum cholesterol. "It is concluded that the serum cholesterol concentration in man is affected by dietary levels of this sterol but that there is a very effective control in normal young subjects that prevents the development of hypercholesterolemia even when relatively large amounts are eaten. Presumably this mechanism has broken down in hypercholesterolemic subjects and is impaired in diabetics."

FRANK E. RICE

**An Electron Microscopic Study of Experimental Atherosclerosis.** F. Parker. *Am. J. Path.*, 36: 19, 1960.

Rabbits and mature female albino rats were given from 4.8 to 20 gm. of cholesterol by stomach tube or in the form of gelatin capsules for twenty-four hours to twenty-five days. Some animals received in addition 10 to 60 cc. of cottonseed oil. The early stages of the lipid lesions forming in the coronary arteries were studied with the light and electron microscope. The lipid globules found in the subendothelial tissue during the stages of acute lipemia consisted electron microscopically of clusters and caps of dense material, probably complexes of lipids and protein. This material was superimposed on the surfaces of a few endothelial cells. Similar material was also noted in the cytoplasm of endothelial cells. Early elastic tissue changes consisted of decreased density and swelling of the internal elastic membrane with loss of the characteristic fibrillation of the elastic fibers. These changes corresponded to areas showing defects of staining quality by light microscopy.

M. SILBERBERG

**Control of Lipaemia in Children with Diabetes Mellitus. The Role of Insulin and the Effects of a Diet Rich in Unsaturated Fatty Acids.** H. B. Salt,

O. H. Wolff, A. Nestadt and J. K. Lloyd. *Lancet*, 1: 71, 1960.

It has been shown that insulin treatment of diabetes in childhood lowers the serum lipid level. But since control of diabetes can never be maintained perfectly the effect of feeding a diet rich in unsaturated fatty acids has been studied in fourteen patients aged two to fourteen.

In four previously untreated children, the administration of insulin lowered the initially high blood lipid levels; however in four already under control, blood lipid levels appeared to be relatively constant and did not fluctuate as did the blood sugar. Feeding with a diet containing unsaturated fats further lowered the blood lipid levels. It is considered that the hyperlipemia of diabetes may predispose to later vascular complications and since perfect control of diabetes is not practicable, a diet which reduced blood lipids represents a valuable additional safeguard.

F. E. HYTEN

**Serum Enzymes in Pernicious Anaemia.** D. Amelung. *German M. Month.*, 5: 334, 1960.

In severely anemic and untreated patients with pernicious anemia, the activity of lactic dehydrogenase was almost without exception more than ten times the normal value. The elevated levels fell promptly on vitamin B<sub>12</sub> therapy.

Compared to 2,500 patients in whom serum lactic dehydrogenase activity was studied, it was found that values above 75  $\mu$ M largely confirmed the diagnosis of pernicious anemia. Values as high as this were very rare in patients with other diseases. When the enzyme activity is in the range of 50 to 75  $\mu$ M in anemia, this largely confirms the diagnosis. However, the possibility of hemolytic anemia or anemia due to leukemia or carcinoma must be considered. Values below 50  $\mu$ M are found in many diseases and, therefore, are of little diagnostic value. Normal values do not exclude the existence of megaloblastic anemia. It is interesting that the lactic dehydrogenase activity of megaloblasts is about three times that of normal red cells. The rapid fall in enzyme immediately after treatment with vitamin B<sub>12</sub> is paralleled by the changes in the bone marrow. It appears that the bone marrow is very largely the source of the increased amount of enzyme protein in untreated patients with pernicious anemia.

S. O. WAIFE

**Relation of Age and Race to Serum Cholesterol Ester Fatty Acid Composition.** L. Swell, H. Field, Jr. and C. R. Treadwell. *Proc. Soc. Exper. Biol. & Med.*, 105: 129, 1960

The character of the fatty acids in the cholesterol ester fatty acid (CEFA) fraction of serum is believed to be important in the study of atherosclerosis. Children, six to ten years of age, and older subjects, sixty to eighty-seven years of age, both white and Negro were observed.

In all subjects, regardless of race or age, the major

fatty acid in the CEFA fraction was linoleic acid minus 43.0 to minus 52.8 per cent. Oleic acid ran 20.8 to 25.1 per cent; arachidonic acid 5.3 to 7.1 per cent. In children, linoleic acid was higher and oleic acid lower than in older subjects; there was no significant change in arachidonic acid with age. Negro and white subjects of the same age did not show significant differences in the CEFA spectrum. Total blood cholesterol was higher in the older subjects of both races. The authors suggest a correlation between the increase in serum cholesterol, the reduction of the linoleic acid content of the CEFA fraction, and the known susceptibility of the human race to atherosclerosis with increasing age.

FRANK E. RICE

**Carcinogens in the Human Environment.** W. C. Hueper. *Arch. Path.* 71: 237, 1961.

This comprehensive paper deals with environmental carcinogens. The data concerning the carcinogenicity of food stuffs and their derivatives will be of interest to the clinical nutritionist. Thermic and oxidation products of oils and fats seem to be particularly harmful. Lard, vegetable fats, salad dressings, margarine emulsifiers, polymerized and oxydized fatty acid emulsifiers and contaminants of heated fats and of natural and bleached oil may induce cancers especially of the lungs, the alimentary canal and the bladder. Consumers of such products and employees of plants using or producing such material are particularly endangered. Contact with these injurious agents is probably being made by inhalation or ingestion.

M. SILBERBERG

**The Pathogenesis of Osteoporosis.** B. E. C. Nordin. *Lancet*, 1: 1011, 1961.

There is a lot of detailed information in this lecture which will repay reading in the original.

Evidence is assembled which suggests that primary osteoporosis could be due to long continued negative calcium balance. The mineral removed from the bone under these conditions is followed at once by the removal of matrix, thus reducing bone mass without reducing the mineral content of the residual bone.

It is further argued that osteitis fibrosa is only a more severe degree of osteoporosis; the essential feature of bone resorption is common to both.

At contrast is drawn between osteoporosis and osteomalacia in which there is a low calcium content of bone. In osteomalacia, the low mineral content is due not to removal but to a failure of mineral deposition in young osteoid, leaving large uncalcified osteoid seams. For reasons not yet understood uncalcified osteoid is left intact in the bone whereas decalcified osteoid is rapidly removed.

F. E. HYTEN

**Treatment of Nutritional Megaloblastic Anaemia.** P. W. G. Tasker. *Tr. Roy. Soc. Trop. Med. & Hyg.*, 54: 171, 1960.

Results in the treatment of nutritional and pregnancy megaloblastic anemia with folic acid and vitamin B<sub>12</sub>



indicate that the use of folic acid gave more consistent results than did vitamin B<sub>12</sub>. With vitamin B<sub>11</sub> alone, half failed to respond at all. When long-term results of treatment were compared, there was no apparent superiority from a combination of folic acid plus vitamin B<sub>12</sub> over the use of folic acid alone.

S. O. WAIFE

**Distribution of Fluoride in Teeth from Areas with Different Levels of Fluoride in the Water Supply.** S. H. Yoon, F. Brudevold, D. E. Gardner and F. A. Smith. *J. Dent. Res.*, 39: 845, 1960

The distribution of fluoride was studied in various areas of teeth of subjects of different ages from several geographical areas where water supplies contained from 0.1 to 5.2 p.p.m. fluoride. The concentration of fluoride in the enamel was greatest on the outer surfaces of the teeth in subjects from all areas and decreased rapidly until the low values were reached in the mid-enamel. Fluoride levels increased in all portions of the enamel with increased water concentrations of fluoride to maintain a gradient from outer surface to inner enamel. Surface enamel fluorides increased with age but no relationship to age was noted in the deeper layers. Higher fluoride concentrations were always found in the layers of dentin adjacent to the pulp and on the root surface than in the inner dentin. Age again was related to increased fluoride concentrations in the pulpal layers of dentin and in the root surface. Greater increases percentagewise were noted in the dentin than in the enamel as a result of higher water fluoride concentrations. The average fluoride concentration was invariably greater in the dentin than in the enamel; however, the average dentin value was lower than the fluoride concentration in the surface layers of enamel.

J. H. SHAW

**Intravascular Effect of Heparin on Plasma Non-esterified Fatty Acid and Triglyceride During Alimentary Lipemia.** M. A. Rizack. *Proc. Soc. Exper. Biol. & Med.*, 104: 111, 1960.

Previous studies which claim to show reduction of the plasma triglyceride concentration after heparin injection may be invalid because appreciably lipolysis continues *in vitro* even at 0 to 4°C. The addition of paraoxon (p-nitro-diethyl-phenyl-phosphate) to blood inhibits lipoprotein lipase activity. Experiments in which injections of heparin were given to normal subjects and blood was immediately mixed with paraoxon showed a much smaller rise of plasma nonesterified fatty acids than when the same blood was chilled and centrifuged at 0 to 4°C. A significant fall of plasma triglyceride five hours after feeding cream was seen after a heparin injection in plasma separated at 0 to 4°C., but not in plasma separated from blood which was mixed immediately with paraoxon.

G. WALKER

**Food and Indigestion. An Investigation of Possible Relationships.** P. H. Friedlander. *Brit. M. J.*, 2: 1454, 1959.

Many people with no abnormality of the alimentary tract find that certain foods are "indigestible." Little is known about the mechanism of this phenomenon and in this investigation seventy patients with dyspepsia but no x-ray abnormality were studied. "Indigestible" food was mixed with barium in a test meal, the gall-bladder was visualized and in some, gastric acidity was studied. In fact only four subjects had symptoms with the test meal and in two this was due to gastroesophageal reflux. Other subjects had symptoms with a control meal of food which was not considered "indigestible."

It is concluded that the composition of food plays little part in producing dyspepsia.

F. E. HYTTEN

**Fiber and Pectin in the Diet and Serum Cholesterol Concentration in Man.** A. Keys, F. Grande and J. T. Anderson. *Proc. Soc. Exper. Biol. & Med.*, 106: 555, 1961.

Middle-aged men, maintained under controlled conditions, were tested for the effect on serum cholesterol levels of dietary cellulose (fiber) and of pectin fed at levels of 15 gm. per day. There was no tendency for serum cholesterol to fall when the diet was high in fiber. There was a small but statistically significant decline when pectin was added to the diet, a fall of about 5 per cent of the level without the pectin supplement. The pectin effect was apparent in three weeks.

"The largest usual source of pectin in human diets is probably in apples but 15 gm. daily, as used here, would be obtained from this source only by a most enthusiastic apple eater."

FRANK E. RICE

**Some Cases of Gout in Reptiles.** E. C. Appleby and W. G. Siller. *J. Path. & Bact.*, 80: 427, 1960.

In mammals, gouty deposits similar to those observed in man have so far been recorded only in a dog, and occasionally in fowl and reptiles. The salt deposits occur in two types: (1) periarticularly and (2) in the viscera. In the latter type, frequent in fowl, urates are laid down on the serous membranes. Occasionally, a combination of both types are seen. Nine cases of gout in reptiles are reported (lizard, alligator and tortoise). In eight, urates were deposited in the joint capsule, and in three cases visceral involvement was evident. The kidneys of these animals showed tophi in the tubules or interstitial tissue with minimal cell reaction including multinucleated foreign body giant cells. The center of these tophi contained periodic acid-Schiff positive material. No evidence could be established that kidney disease preceded the development of gout. However, a positive correlation was noted between the intensity of the urate deposits and the severity of renal disease. The observations seem important because these animals may serve as tool for experimental studies of gout.

M. SILBERBERG

**Retentions of Nitrogen and Minerals by Babies One Week Old.** J. E. Slater. *Brit. J. Nutrition*, 15: 83, 1961.



Infant feeding formulas prepared from cow's milk, as usually fed, are of about the same caloric content as average human milk. The infant, however, receives more nitrogen and minerals from formula feeding. The purpose of this study was to determine how the newborn baby deals with the greater uptakes of these elements than may be presumed to be intended by "Nature."

Thirteen babies in the study were fully breast fed; nine received from birth a cow's milk formula prepared from dry whole milk and lactose, with added vitamin D. In one experiment, ten breast-fed babies were given 120 mg. phosphorus as a 1:4 mixture of  $\text{KH}_2\text{PO}_4$  and  $\text{Na}_2\text{HPO}_4$ . Metabolic balance studies were made for three complete days, the sixth, seventh and eighth days of life. Caloric intakes were about the same for the bottle-fed and breast-fed babies, 96 and 97 cal. per kg. per day.

The bottle-fed babies ingested more nitrogen than the breast-fed babies, and retained 127 mg. per kg. per day more. The concentration of urea in the blood of the bottle-fed babies was higher. Urea excretion also was greater. But this could account for only a small proportion of the additional uptake of nitrogen. There was no difference between the groups in excretion of creatinine and uric acid nitrogen.

Breast milk samples were widely variable in potassium content, but it was estimated that babies so fed received about half as much potassium as those on the cow's milk formula. Retention of potassium from formula feedings was much greater.

With respect to calcium, bottle-fed babies ingested four times as much as breast-fed and retained five times as much. In some measure this is accounted for by the fact that the former received supplementary vitamin D and those that were breast fed did not. Urinary excretion of calcium was unexpectedly less in bottle-fed babies than in those breast fed. With magnesium also there was more ingested and less excreted in urine in the bottle-fed group. Intake of phosphorus was five times as high in formula-fed babies as in those fed breast milk and retention was three times greater in the former. Serum phosphorus was higher in bottle-fed babies but not enough higher to account for the extra phosphorus retained.

The negligible urinary excretion of phosphorus of breast-fed babies, and the fact that supplemental feeding of phosphate reduced the urinary excretion of calcium and magnesium would indicate that the small amount of phosphorus in human milk limits the retention of these minerals.

The author calculates the increases in weights of skeleton, skeleton muscle and skin of an average infant from birth to six months of age, and the increases in nitrogen, calcium, magnesium and phosphorus, normally contained in such tissues. From this it is concluded that retentions from average human milk of these elements could hardly be sufficient for normal tissue production.

"It is suggested that the chemical maturation of the soft tissues and of the skeleton of babies receiving

cow's milk preparations proceeds faster than that of the tissues of breast-fed babies."

FRANK E. RICE

**Tocopherol Deficiency in Adults with Chronic Pancreatitis.** H. Braunstein. *Gastroenterology*, 40: 224, 1961.

The authors searched for histologic evidence of tocopherol deficiency in autopsy material from malnourished subjects. The lesion demonstrated by others to be associated with tocopherol deficiency is ceroid pigmentation of smooth muscle. The ceroid is a lipofuscin presumably containing unsaturated lipid and was satisfactorily demonstrated by a Nile blue sulfate stain. The lesions were found chiefly in the smooth muscle of the alimentary tract in 61 per cent of thirty-six patients with chronic pancreatitis, 27 per cent of fifteen subjects with nutritional cirrhosis, eleven per cent of nineteen subjects with simple malnutrition, and in 23 per cent of thirteen subjects with biliary cirrhosis. All three subjects with biliary cirrhosis demonstrating ceroid pigmentation had associated pancreatitis.

The authors conclude from an analysis of the clinical records of the patient material correlated with the pathology that the ceroid pigmentation was probably a stigma of fat malabsorption with resultant tocopherol deficiency. It was their impression that the widespread and massive infiltration of smooth muscle fibers with ceroid pigmentation might be expected to interfere with the function of smooth muscle. They suggest that a controlled clinical trial of tocopherol in patients with chronic pancreatitis is indicated to determine whether improvement in intestinal function can be accomplished.

It is unfortunate that clinical studies of fat absorption had not been carried out during life on their patient material to permit correlation with the finding of ceroid pigmentation. Also, a primary impairment of intestinal motor function has not been described in patients with pancreatic steatorrhea.

J. B. HAMMOND

**Cholesterol Content of Human Liver after Feeding of Corn Oil and Hydrogenated Coconut Oil.** I. D. Frantz and J. B. Carey. *Proc. Soc. Exper. Biol. & Med.*, 106: 800, 1961.

Among the hypotheses that have been advanced to explain the reduction of serum cholesterol by dietary unsaturated fats are (1) increasing excretion of the products of cholesterol catabolism, (2) increased excretion of bile acids, (3) decreased synthesis of cholesterol, or (4) a shift of cholesterol from serum to tissues. The objective of this research was to test the last named.

Twelve healthy men with high serum cholesterol levels were divided into two groups, one of which was



given 1 ounce corn oil before each meal, the other 1 ounce of hydrogenated coconut oil. At the beginning and end of one month, cholesterol was determined in serum and in samples of liver taken by punch biopsy. Serum cholesterol fell an average of 25 per cent in the group receiving corn oil; also to a significant extent there was a drop in liver cholesterol concentrations. Changes resulting from coconut oil feeding were inconsistent.

The authors conclude that it is unlikely that the fall in serum cholesterol produced by corn oil feeding in man is due to a shift of cholesterol from the blood to the liver.

FRANK E. RICE

**Post-prandial Lipemia in Health and in Ischemic Heart Disease. A Comparison of Three Indexes of Fat Absorption and Removal and Their Modification by Systemic Heparin Administration.** D. F. Brown, S. Heslin and J. T. Doyle. *New England J. Med.*, 264: 733, 1961.

Postprandial lipemia was determined in normal men and in men who had had a myocardial infarct one month to one year earlier, by feeding a fatty meal containing  $I^{131}$ -labeled triolein and then measuring (1) lipid-bound  $I^{131}$  of the plasma, (2) optical density of the plasma, and (3) plasma content of total esterified fatty acids. Fasting total esterified fatty acid levels were higher in patients with ischemic heart disease than in normal men. Differences for lipid-bound  $I^{131}$ , optical density and total esterified fatty acids were found between the two groups. Nine hours after ingestion of the fatty meal only 7 per cent of the patients with ischemic heart disease had levels of total esterified fatty acids below fasting values while 83 per cent of the healthy group had values which fell below this level. This was thought to be the most reliable method of distinguishing healthy persons from those with ischemic heart disease.

Heparin was given to a few subjects in each group and levels of lipid-bound  $I^{131}$  and total esterified fatty acids were determined before and after heparin administration. Little differences were found in the healthy persons before and after heparin administration and the results in the diseased group were variable. In two of the four patients treated, normal postprandial lipid curves were observed. In one patient there was a fall in total esterified fatty acid level and in one patient the abnormal rise in lipid level after ingestion of a fatty meal was not prevented by the administration of heparin.

The authors conclude that changes in plasma  $I^{131}$ -labeled triolein are a useful and valid index of post-prandial lipemia since it closely parallels changes in optical density and total esterified fatty acids. This method, however, lacks sensitivity and specificity which is needed in revealing preclinical heart disease. It does seem to be of greater value than the determination of fasting cholesterol and total esterified fatty acids levels of plasma.

M. W. BATES

**Diet Rich in Unsaturated Fat.** J. K. Lloyd and H. R. Jukes. *Lancet*, 1: 312, 1961.

The use of diets low in saturated fats is now established in some centers as an important part in the prevention of degenerative vascular disease.

In this paper an outline is given of diets in which most of the fat is unsaturated. Corn oil is the basis of the substitute; it is incorporated into a "milk," margarine, cheese spread and cooking oil all of which are commercially available, and the corresponding natural products are eliminated from the diet.

Hints on the use of the substitute products are given.

F. E. HYTTEN

**Diet of London Busmen. A Sample Study.** E. M. Bramwell. *Proc. Nutrition Soc.*, 20: 30, 1961.

Drivers of double-decker buses in London have a higher incidence of coronary heart disease than conductors, and often it develops at an earlier age. In general, they are also heavier and fatter. In this progress report, the two groups are compared with respect to food habits and meal patterns. Nutrient content of intakes of the two groups were similar. Calorie intakes also were similar, which is noteworthy in view of the higher energy expenditure by the conductors. In both groups about one-fifth of the calories was from protein foods such as meat, fish, eggs and cheese; about one-fourth from bread and butter (or margarine); 7 to 8 per cent from the milk used in tea and milk drinks. It was concluded that differences between the two groups in nutrient intake and food patterns are insignificant.

FRANK E. RICE

**Growth and Development of Children with Galactosemia.** G. N. Donnell, M. Collado and R. Koch. *J. Pediat.*, 58: 836, 1961.

Sixteen families with twenty-four children affected with galactosemia were studied at the Children's Hospital of Los Angeles over a twelve year period. Sixteen children are still living. Eight died in early infancy with findings strongly suggestive of galactosemia. One is in an institution for the mentally retarded and the remaining fifteen were the subjects of longitudinal observations. The physical growth patterns of all but three of the fifteen children are within normal limits. The intellectual abilities of the parents are normal, and all but one of the siblings were normal. By contrast, four of the children with galactosemia were mentally defective, and one was in a state hospital.

Late inauguration of dietary management was associated with a greater incidence and severity of mental handicaps. The authors suggest strict adherence to a galactose-free diet and that soya products be avoided until additional knowledge is available. It appeared from observations on three children, that their progress was not as good when they were being fed soya products. The reason for this was not clear. These same infants progressed better when they were fed Nutramigen.

B. M. KAGAN