Abstracts of Current Literature

CHARLES R. SHUMAN, M.D., EDITOR

MARGARET W. BATES, D.S.C., Pittsburgh
RALPH E. BERNSTEIN, M.D., Johannesburg, South Africa
ELIAS COHEN, PH.D., Buffalo
A. B. EISENSTEIN, M.D., St. Louis
JAMES B. HAMMOND, M.D., Indianapolis
GUILL HOLLIFIELD, M.D., Charlottesville
M. K. HORKWITZ, PH.D., Elgin
F. F. HUTTON, M.B., D.S., PH.D., Aberdeen, Scotland
B. M. KAGAN, M.D., Los Angeles
S. M. LEVENSEN, M.D., Washington
JOHN F. MUELLER, M.D., Cincinnati
MORTON J. OPPENHEIMER, M.D., Philadelphia
FRANK E. RICE, PH.D., Chicago
JAMES H. SHAW, PH.D., Boston
MARTIN SILBERBERG, M.D., St. Louis
JANCIE M. SMITH, PH.D., Urbana
GREGG WALKER, M.B., Oakland
JOHN C. WATERLOW, M.D., Kingston, Jamaica

RECENT CONCEPTS IN OBESITY

The accumulation of body fat is the consequence of a caloric intake exceeding caloric expenditure. While it is easy to measure caloric intake the determination of caloric needs has not been precisely appraised for the daily activities of most persons. Nearer types of instrumentation now available should permit the accumulation of much significant data in this area. With a complete knowledge of caloric requirements for all types of activity an appropriate rating can be made for daily caloric balance.


This is an entertaining dissertation which most people connected with practical problems of nutrition could read with profit.

"There is no evidence that man is immune from the laws of thermodynamics. In every conceivable way it has been proved that the accumulation of excessive fat follows the intake of excessive calories." The causes of the excessive intake are examined, in particular those which affected the satiety center in the hypothalamus—Joliffe's "aperture," genetics, hormones, drugs, exercise and social and psychologic factors. The author has shown that glucose seems to act as a stimulant to appetite. It is argued that obesity is not usually due to a metabolic defect and that the person who can "eat as much as I like" without becoming fat is a fallacy.

The two most common factors in overeating are a low physical activity and a temptation to eat too much, particularly of sweet foods. The chief aim of treatment should be to increase activity and to give a diet which is satisfying but lower in calories. In practice this means restriction of carbohydrates. According to the author, methyl cellulose may be a useful adjunct to depress appetite while new dietary habits are acquired.

F. E. HUTTON


Brief histories and laboratory tests of endocrine function on five very obese women are presented in this paper. None showed any evidence of endocrine disease but one had a history of encaphalitics. The author uses these rather ordinary case reports as a point of departure for a discussion of the mechanisms by which obesity develops. The discussion is heavily loaded with information from various studies of experimental obesity in animals, but form an incomplete review of the subject.

G. HOLLIFIELD


One hundred consecutive patients, obese by the usual standards, were studied. Eighty-two of these were considered to be obese because of overeating. In the majority, motivation and cooperation were easily established. There were additional cases in which obesity was said to be unassociated with overeating and were mostly complicated cases of endocrine or metabolic disease.

The "social diet" is based on a moderate reduction in the quantities of all foods. No more than one slice of bread at any one meal is to be eaten. "Portions of
everything are to be reduced by about one-quarter.” Accordingly to the author, almost every determined patient will lose weight on this regimen.

Under the conditions of clinical management as described in the paper, five of the eighteen “non-overeating” patients had a satisfactory weight loss, and sixty-three of the eighty-two other patients also responded. Best results were in those in whom motivation was said to be strongest.

This clinical experience is interesting. Unfortunately, the personality of the physician and the circumstances of the therapeutic management are such that results cannot or need not necessarily be transposed to other situations.

S. O. Waife


A fair number of people can accept rigid calorie restriction over short intervals of time but not for prolonged periods. There would seem to be a psychological advantage in allowing “rest periods.” This study was undertaken to determine whether there may be also a physiologic advantage.

It had been observed that once long periods of weight reduction human subjects begin to lose nitrogen, calcium and phosphorus. Then, when changed from a reducing to a maintenance diet, they reach a state of equilibrium or retention with regard to all three nutrients.

Ten overweight young women were used in this study, divided into two groups of five each. One group was subjected to stepwise weight reduction, the other was kept on maintenance diets. The feeding period was sixteen weeks. Determined at intervals were nitrogen, calcium and phosphorus balances, measurements of fat pads soft-tissue x-rays, and skinfolds, as well as changes in body weights. Some comparisons were made with data obtained by the authors in earlier published experiments on subjects in whom straight uninterrupted reduction methods were employed.

All five subjects on restricted calorie intakes showed calcium deficits by the eighth week. Some of the subjects lost nitrogen and to a lesser extent phosphorus. Control subjects on maintenance diets showed no nutrient losses.

As measured by nutrient deficits, there appeared to be no physiologic advantage in the stepwise reducing regimen over straight reduction. From a psychological standpoint the majority of subjects preferred stepwise reduction to an uninterrupted regimen. It was not possible to evaluate objectively a relation between emotional stability and nutrient losses, although the authors had the impression that those who showed the greatest tendency toward instability were the ones who were losing calcium.

Frank E. Rice


The remarkable findings reported by Kekwick and Pawan in 1953 and 1956, to the effect that during short periods on isocaloric submaintenance diets weight loss was greater on a high-fat than a high carbohydrate diet, have been widely applied. These authors consider the previous conclusions unjustifyable in view of the short periods of observation, and report here the effects on weight loss in obese subjects on 800 and 1,000 calorie diets of high fat, high-carbohydrate and mixed composition. The diets were continued for twenty-four-day periods and the general slope of weight loss is convincingly shown to be unaltered by the composition of the diet. When the diets were changed the slope changed temporarily, falling more steeply when a high-carbohydrate diet was substituted for a high-fat diet. These temporary effects lasted not more than ten days and were probably due to differences of hydration.

F. E. Hytten


A comparison was made of the results of both individualized and group dietary instruction for weight reduction among outpatients at the Mayo Clinic. Patients receiving reduction-diet instruction in a class lose nearly as much weight as do those receiving individual instruction, and the difference is not significant. The authors recommend that either method may be used, and from the point of view of efficiency and time, class instruction may be preferable.

S. O. Waife


The author attempted to evaluate hypnosis as a means of diet control and reorientation of eating habits. An attempt was made to determine whether or not ideas relating to the control of diet could be more deeply implanted in the hypnotic state than under normal circumstances. Forty-two women were selected on the basis of the ability to enter a sufficiently deep trance state and who were in good physical health except for obesity. At the onset the term hypnosis was not used and substitution phrases such as “relaxation and suggestion,” “subconsciously suggestion” were employed. After several inductions of a deep trance, the suggestions offered would last for several days. Training by hypnotic suggestion was most satisfactory when sessions were held approximately twice weekly for the first two weeks and then once weekly for longer periods of time.

Best results were obtained when suggestions were channeled along such lines as fortification of the desire for weight loss, explanation of caloric bounds, development of proper eating habits including elimination of
between-meal feedings and suggestions as to hunger sensations. The six-months average weight loss for the entire group was about 27 pounds, and patients varied from 9 to 58 pounds in the amount lost. No anorectic or metabolic stimulating drugs were used.

S. O. WAIFE


Seventy-one medical students, average age twenty-four years, participated in a double-blind test in which phenmetrazine (Preludin®) and dextroamphetamine were used. Only five were grossly obese. The students were placed on a reduced caloric intake and were asked to record their own weights, symptoms and degree of diet-following.

Fourteen students did not complete the course. Forty-five students received phenmetrazine for 281-patient weeks. The average weight loss was 3.32 pounds per week. Twelve students received dextroamphetamine for a total of 92-patient weeks and had an average weight loss of 2.5 pounds per week. According to the author, phenmetrazine was more effective in a short-term reducing program.

Side effects were rather frequent, including insomnia, nervousness, palpitations and headache. However it was not necessary to stop treatment because of the reactions.

S. O. WAIFE


A comparative study of the anorexigenic properties of two drugs, phenylpropanolamine and dextroamphetamine, was performed on eighty-one obese but mentally-deficient subjects. These patients were selected to obviate as much as possible the psychologic factors that may influence weight reduction in a "mentally alert population." Food intake was not restricted and the caloric consumption was at least 3,000 calories per day. The study was conducted on a "blind" procedure in that none of the personnel associated with the project were aware of the nature or identity of the drugs administered. The subjects were divided into four groups and each was given one of four preparations three times a day, one hour before meals, for six weeks. At the end of the study it was disclosed that one group received 25 mg. of phenylpropanolamine, the other 50 mg. A third group received 5 mg. of dextroamphetamine, and a fourth group received a placebo.

The results failed to demonstrate a significant reduction in weight in the groups receiving phenylpropanolamine three times a day and in those receiving a placebo. A statistically significant reduction of weight, however, was found in the group receiving 5 mg. of dextroamphetamine three times a day. It should be pointed out that the mean value of weight loss was only 4.6 pounds over a six-week period on dextroamphetamine. There was wide variation in the response of this drug, in that several patients lost 10 pounds, two actually gained weight. The authors conclude that although phenylpropanolamine is chemically related to dextroamphetamine, it does not possess significant anorexigenic properties.

It should be noted that in this study different drugs are compared in different populations. On the other hand, this would probably not alter the outcome of a study of this type.

S. O. WAIFE


A double-blind study was planned to compare the efficacy of a capsule containing p-amphetamine and amobarbital with a combination of this capsule and liothyronine (L-triiodothyronine) in the management of obesity among fifty-seven outpatients. The group averaged forty-three years of age and an average weight of 193 pounds. A 1,000-calorie diet was prescribed for all patients (75 gm. protein, 100 gm. carbohydrate, 40 gm. fat). Half the patients received the amphetamine-amobarbital capsule first, the other half received this combination plus liothyronine. After eight weeks the dosage schedules were reversed. Patients were seen at two-week intervals.

The two therapeutic regimens produced equal weight changes for the first eight weeks. More weight was lost by the group that received the amphetamine-amobarbital preparation first and then the addition of liothyronine. At the dosage level used, no effect on the blood pressure, pulse rate or serum cholesterol level was noted. There were no symptoms of “hypermetabolism.”

Experiments on weight loss among clinic patients is one of the most difficult of human experiments. All results, unfortunately, must be considered with caution.

S. O. WAIFE


Twenty-one children, who all weighed over the ninetieth percentile of weight for age, took part in an investigation. For two weeks they were given no treatment and gained from 1/2 to 5 pounds. For the next four weeks they were given at random either phenmetrazine (Preludin®) tablets or dummy (placebo) tablets and for the next four weeks the opposite to their first tablets. There was no dietary restriction.

On the drug, eighteen of the children lost between 1/4 and 8 pounds, two remained stationary and one gained 4 pounds. On the dummy tablets all the children gained more than on phenmetrazine; seventeen
Abstracts

Gained from 1 to 5 pounds, two remained stationary and two lost from 1 to 1½ pounds.

There were no untoward effects except in one child who became ill-tempered while on this regimen, but four weeks, in a condition such as obesity, is hardly a fair trial of possible ill-effects. F. E. HYTTEN

Rapid losses of body water may promote a prompt reduction in body weight. The psychological effect of this change may be used to advantage early in the course of weight reduction programs by employing oral diuretic agents.


A significant part of the initial weight loss incurred when obese patients go on a reducing diet has been ascribed to loss of body fluids. In this paper a quantitative assessment of the initial water loss and subsequent retention by seven patients is described. Each patient was studied for six weeks on a strictly controlled and rigorous reducing regimen. Under the conditions of the experiment the following observations were made.

Changes in water intake appear to be unrelated to the rate of loss of water, and the fluctuation in the urinary output is explained by an inconstant proportion of changes in body water. The loss of fluids by evaporation was quite variable from patient to patient.

Losses and gains of body water were not associated with changes in fluid intake. They could only be partly explained by variations in output. The electrolyte changes indicate that during initial dehydration there were losses of both intracellular and extracellular water. In subsequent periods, water retention was associated with increases of extracellular water despite probable continuing losses of intracellular water. S. O. WAIFE


An estimation of body water and electrolytes was made in seven obese patients who were losing weight. The average composition of the tissue lost was found to contain 14.5 per cent total water (4.4 per cent extracellular and 10.1 per cent intracellular) and 2.7 mEq. of potassium per kg. S. O. WAIFE

In obesity, the metabolizing tissues may be more efficient in the oxidation of fatty acids due to the conditioning of cellular enzymatic mechanisms for these substrates. The obese patient is less likely to utilize carbohydrate efficiently because of this enzymatic setting for fat combustion. The converse is true for non-obese patients who utilize carbohydrate more efficiently than fat.


It is well known that ketosis does not develop readily in obese persons. Two possible explanations for this were investigated: (1) that ketone bodies are utilized or excreted faster in obese subjects than non-obese subjects; (2) that ketone bodies do not form so rapidly in obese subjects.

The first possibility was tested by intravenous injections of 30 or 60 mg. per kg. body weight of sodium, β-hydroxybutyrate. Blood levels fell rather more steeply after this injection in obese subjects but the difference was thought to be negligible. Less than 1 per cent of the injected "ketone" was excreted in the urine of either group. The first possible explanation was therefore untenable. To test the second possibility an attempt to produce ketosis was made by feeding obese and non-obese subjects a diet providing 1,000 calories daily of which 90 per cent was supplied as fat. All the obese subjects were able to take the diet for as long as required; the non-obese subjects rapidly became ketogenic and seven of eight had to abandon the diet by the fifth day because of symptoms. Progressively lower fasting blood sugar levels developed in the non-obese subjects who were in negative nitrogen balance averaging -8.6 gm. daily. The obese subjects maintained their blood sugar levels and were almost in nitrogen balance.

It is calculated that in neither group was there sufficient carbohydrate available either from the diet or from carbohydrate sources to supply even the minimal requirements of the brain and that this suggests the ability, particularly in obese subjects, to produce carbohydrate from fat. F. E. HYTTEN


Determination of dilution of administered labeled acetate by endogenously produced acetate in two types of obese mice, goldthioglucone obese mice (regulatory obesity) and obese hyperglycemic mice (metabolic obesity), shows that this dilution is of the same order for obese and non-obese mice when fed "ad libitum." When fasted, dilution is again of the same order for goldthioglucone obese mice and normal control animals, but is twice as great for obese hyperglycemic mice. These data in conjunction with results obtained on incorporation of C14 into fatty acids and cholesterol show that the increased synthesis of these lipids is related solely to the hyperphagia in the case of the goldthioglucone obese mice. By contrast, the obese hyperglycemic mice show rates of fatty acid and cholesterol synthesis which are three times the control levels even when fasted. These results justify the previously drawn distinction between "regulatory" and "metabolic" obesities.

Authors
NUTRITIVE VALUE OF MILK

Milk is the oldest food known to man; it receives no less than forty-four references in the Old Testament. Both human and cow's milk supply basic caloric and protein requirements in infant feeding, and the latter provides an excellent nutritional source for adults. Interesting data concerning hypogenesis in a lactating patient indicates that in addition to forming fats de novo, the mammary gland may secrete fats resembling those found in human depot fat.


A twenty-three year old white woman was admitted to the hospital on the fifth postpartum day; she remained under metabolic ward conditions for seven weeks on a liquid formula. The breast milk output was determined by weighing the baby immediately before and after each nursing. At the end of a dietary period, milk was collected and sampled.

Lactation was established by the ninth postpartum day, and the daily milk production averaged 723 gm. It was found that the fatty acid composition of human breast milk could be radically altered without affecting the volume or the fat output in the milk. During energy equilibrium, milk fat closely resembled dietary fat. However, when insufficient calories were fed, the milk fat approached the composition of human depot fat. These findings indicate that dietary fatty acids are readily transported into milk fat, but that when the depot fat has to be used for energy, the fatty acid excretion in the milk parallels that of its source. When excess calories (nonfat) were fed, the milk showed a striking increase in lauric and myristic acids and a marked decline of all polyunsaturates. synthesis of fatty acids in the breast appears to be promoted when excess calories are fed, and the accumulation of C20 and C24 acids in the milk suggest that mammary fatty acid synthesis differs in several important respects from extramammary depots.

S. O. Waife

The following investigation demonstrates that the fat content of milk can be lowered by manipulation of rations. This will not be a popular study among dairymen.


The principal objective of this study was to develop rations that would consistently effect a decrease in the fat content of milk. Other workers had shown that the fat content of milk can be depressed by feeding low roughage rations, and that this depressive effect is associated with lowered production of acetate in the rumen and increased production of propionate. Four breeds of cows were used. Various concentrate mixtures were prepared from bread, potato meal, cooked polished rice, corn meal and other cereals, brewers grains, bran, dry skim milk, and varying proportions of alfalfa hay. White bread was used in some feeding studies because of earlier field observations implicating bread in connection with low-fat milk. Rumen fluid was obtained for analysis at intervals about five hours after feeding. Four diets were tested: (1) high protein concentrate plus 4 pounds alfalfa hay daily; (2) white bread, with molasses plus 6 to 7 pounds of hay; (3) low protein concentrate plus 4 pounds hay; (4) low protein plus 12 pounds of alfalfa.

Diet 2 causes a significant reduction in the per cent of fat in the milk as compared with the other three diets, among which no differences were apparent. During the feeding period total milk production decreased in all groups; group 3 showed the greatest reduction, group 1, the least. Analyses of rumen samples showed highest acetic acid in group 4, lowest in group 2; in propionic acid, highest in group 2. The reduction in rumen acetate seems to be implicated in lowering the percentage of fat in the milk. (It is noted that acetate has been demonstrated to be a precursor of the lower fatty acids.) Milk solids, nonfat, remain relatively constant regardless of diet.

Frank E. Rice

Vegetable oils substituted for butterfat in the diet of calves produces a number of undesirable effects.


Previous studies have established that highly unsaturated vegetable oils adversely affect growth and physical conditions when used as substitutes for butterfat in the diet of dairy calves. In the present experiments, filled milks were prepared by homogenizing the various test fats at a 3.5 per cent level into pasteurized skim milk, which in some cases had been fortified with nonfat milk solids. Minerals and vitamins were added as required. Observations were made on 150 calves.

When corn oil-filled milks were fed, there resulted marked diarrhea, various symptoms of unthriftiness including susceptibility to infections, muscular involvement and early death. These observations were in marked contrast to the results from feeding whole milk, or filled milks compounded from hydrogenated corn oil, hydrogenated cottonseed oil, lard, or blends of hydrogenated cottonseed oil and soybean oil, or a butter oil-filled milk. The presence of 0.1 to 0.15 per cent butterfat in the fortified skim milk ration was sufficient to produce normal growth and physical conditions in calves from fourteen days up to ninety days of age. (Note that during the first fourteen days of life the calves had been receiving colostrum and whole milk.) The daily
Abstracts


This is a review of the literature from January 1956 to January 1958, mainly on milk fat, milk protein, vitamins and milk in infant nutrition and includes 266 references.

A preponderance of evidence suggests that there is no significant difference between the nutritional values of raw, pasteurized and sterilized milk, although one investigator reported greater weight gains in feeding raw milk to rats. In infant nutrition, the authors draw the following conclusions from their review of the extensive literature: "In general, recent work would seem to support the previous conclusions that a number of artificial milks are, for all practical purposes, in no way nutritionally inferior to human milk..." "...the conflicting results being attributable largely to the different techniques employed, some methods not necessarily measuring nutritive value and others being susceptible to factors entirely unrelated to the diets fed." Special attention is given to the literature on the effect of sterilization by heat, and by radiation, on the biological value of milk proteins and on the availability of the lysine.

Publications are reviewed wherein milk fat has been compared with other fats from the points of view of digestibility, absorption rate, growth action, degree of saturation of the fatty acids, blood cholesterol levels related to diet and such. The authors find it difficult to speculate on the significance of some of the findings. A dietary interrelationship between milk fat and milk carbohydrate (lactose) has been demonstrated to be more favorable than when corn oil and lactose are fed together. *Frank E. Rice*

An optimum level of dietary fat for the production of enzymes by lactating women has been demonstrated. This may be related to the caloric requirements for synthesis of these protein factors.


Sixty lactating women in normal health living in and around Baroda, India, and in about the same lactation period (three to four months), were the subjects of this study. Milk samples were collected uniformly at about 3 p.m. Dietary fat intake averaged 60.54 gm. per day as compared with groups receiving 37.43 and 18.36 gm. per day. The milk produced was significantly higher in fat, and in lipase, esterase and alkaline phosphatase activity. Milk produced by mothers' with a fat intake averaging 88.98 gm. per day was no higher in fat content, nor was the lipase, esterase or alkaline phosphatase activity significantly higher. Acid phosphatase declined steadily with increasing fat intake. *It*


The continued feeding of corn oil-filled milk to calves resulted in lowered blood plasma levels in both tocopherol and vitamin A. Lowered blood tocopherol levels also were observed when feeding hard-filled milk, or a ration containing butter oil which had been prepared from oxidized butter. Plasma tocopherol levels could be raised by supplementing the corn oil and lard diets with tocopherol. Storage of corn oil-filled milks caused rapid reduction in tocopherol content; in one sample 42 per cent was lost in seven days. The feeding of such samples to young calves had a detrimental effect, possibly due to the presence of peroxides formed during storage. *Frank E. Rice*


"Filled milks" prepared by homogenizing various fats at the 3.5 per cent level into skim milk were fed to calves. Corn oil-filled milks induced severe diarrhea, which was not reduced by dietary supplementation with tocopherol. Dry matter digestibility coefficients for the corn oil-filled milks were lowest of all. There were no significant differences between the others, hydrogenated corn oil, butter oil or lard.

Feces of animals fed skim milk with no more than 0.1 per cent fat contained 5.3 per cent fat on the dry matter basis. This figure, assumed to be metabolic fecal fat, was deducted from the total fat excretion in calculating fat digestibility. Fat digestibility data show that butter oil is superior to that of the other fats.

Studies of fecal fats showed about the same partition between neutral fat, soaps and free fatty acids, whether the animals were on a fat-free diet or one containing butter oil. The partition pattern on feeding any of the other fats was significantly different. The fecal fat from the fat-free and butter oil diets analyzed higher in neutral fat and lower in soaps than when any of the other filled milks were fed. *Frank E. Rice*

Growth rate of animals on a filled milk prepared from fortified skim milk and the mixture of hydrogenated cottonseed oil and soybean oil was unusually high, even greater than the growth rate of the animals on whole milk or fortified skim milk. Supplementation of the corn oil diets with high levels of tocopherol prevented the development of muscular involvement but did not improve weight gains. It is concluded that "the inclusion of corn oil in the diet depresses growth in some manner." *Frank E. Rice*
was observed that neither dietary protein nor milk protein affected the activities of these enzymes.

Frank E. Rice

The importance of trace elements in human nutrition is now widely appreciated. Further studies of these factors, as they exist in milk, as one of the most widely used foods are essential.


At least two factors have tended to turn attention to trace elements in recent years: (1) discovery of the importance they play in metabolism as constituents of body pigments, enzymes and hormones, important especially to the young of all species; and (2) constant refinement of methods of analysis. This is a critical review, with 194 references, of our present knowledge with respect to aluminum, arsenic, barium, boron, bromine, manganese, molybdenum, nickel, radium, rubidium, selenium, silicon, silver, strontium, tin, titanium, vanadium and zinc.

Data on human milk are reported, and the milk of other species, as well as the cow. Figures are given on variations between colostrum and milk, and on the effect of supplementing the feeds with salts of the trace elements.

References to the iron content of milk outnumber those pertaining to any other element. While iron is present normally in the cow's milk as drawn (average 0.45 p.p.m.), more is found in milk which has passed through a processing plant. At best cow's milk must be considered a poor dietary source of iron. Human milk generally is found to run only a little higher (average 0.8 p.p.m.). More zine has been found in milk than any of the other trace elements. Human milk averages 4.4 p.p.m., normal cow's milk 3.7 p.p.m. Milk that has been in contact with galvanized surfaces may run very high in zinc. Cobalt is present in the milk of ruminants when it is in the ration. Microbiological conversion to vitamin B12 takes place in the digestive canal of these animals. Copper is normally in cow's milk, the average being 0.13 p.p.m. Human milk averages 0.5 p.p.m. In commercial processing, the milk picks up additional copper from plant equipment and containers. Cow's milk averages 0.15 p.p.m. of fluorine. The amount in the milk can be raised significantly by giving the cow large doses of fluorine either in feed or drinking water. This has been suggested as a means of bringing this important element into the diet of those in whom it would do the most good and more readily than through the water supply. Iodine in cow's milk averages 0.04 p.p.m., somewhat more in milk produced in coastal areas than in central areas.

Manganese is present normally in cow's milk, average 0.03 p.p.m. One investigator reports 100 to 150 p.p.m. of manganese in the ash of human milk. Molybdenum is normally in milk as well as blood, bile and eggs. The element has been found to be associated with the enzyme, xanthine oxidase.

The authors conclude that the values reported in the literature of trace elements other than those recorded herein, are too scanty and variable to justify averaging. Except for copper and iron, the effect of feeding supplements of each specific element increases the amount of that element in the milk. Response to feeding the other elements varies from slight to very marked. Colostrum of all species contains more of any trace element than is found in the "normal" milk.

Differences of opinion prevail as to the form in which the trace elements exist in milk. It is generally agreed that they are linked in organic complexes, perhaps "chelated." There is evidence that iron and copper are protein-bound and that the protein-metal complexes are adsorbed on the surface of the fatglobules.

Frank E. Rice


Earlier studies have occasionally indicated that copper and iron naturally occurring in milk is predominantly a part of the protein that surrounds the fat globules, i.e., in the cream of the milk, whereas copper and iron that have their origin from direct addition, may be expected to be found in the skim milk fraction. The present investigators undertook to obtain evidence on these points using modern radioactive-tracer techniques. Radioactive copper and iron were (1) infused into the jugular vein of cattle ("natural" copper and iron in the milk results from this treatment) and (2) added to the warm milk immediately after being drawn. The milk was then centrifuged; both the skim milk and cream were further fractionated.

Natural copper favored the fat phase of the milk. From 10 to 35 per cent was found to be associated with the washed fat globules. The membrane surrounding the fat globules contained fifty times as much natural copper per 1 per cent of protein as in the casein and whey proteins. Natural iron also was highly concentrated at the fat globule surface. On the other hand, of the added copper only 2 to 3 per cent appeared in the fat globule membrane, and none of the added iron.

The findings have some significance in comparing the nutritional value of whole milk and skim milk, the former having the advantage in retaining more of the copper and iron found naturally in milk.

Frank E. Rice

GLUCOSE, FAT AND THE LIVER

The release of glucose from hepatic stores of glycogen in response to hypoglycemia is one of the important mechanisms in the maintenance of normal blood glucose levels. Experimental preparations have indicated the probability of an increased secretion of glucagon and/or epinephrine in promoting glycogenolysis under these conditions. However, the continued intraportal infusion of insulin,
either endogenous or exogenous, appears to inhibit glucose-
6-phosphatase activity resulting in a reduced rate of glu-
cose release creating hypoglycemic unresponsiveness until insulin effect is terminated.


Catheters were placed in the hepatic and portal veins of normal dogs and were maintained for varying periods of time.  With these animals in an unanesthe-
tized state, and recovered from the acute effects of the catheter implanta-
tions, infusions of small amounts of insulin were made slowly into the portal vein and the hepatic output of glucose was determined.  It was
concluded that, under the experimental conditions, insu-
lin did not significantly depress the hepatic output of glucose but that it did inhibit the hepatic response to hypoglycemia.  The hepatic glucose output during the infusion was similar to control values, but there was a marked rise in glucose output following the cessation of the infusion.  


The immediate and direct effect of intravenously or intra-arterially administered insulin upon hepatic blood flow was studied in unanesthetized dogs whose hepatic vessels had been previously catheterized.  Comparison was made between two dose levels, 0.1 or 0.2 unit/kg, and 1 unit/kg, the latter being infused over a thirty-
minute period.  At the 0.1 or 0.2 unit/kg range, there was no immediate statistically significant increase in flow.  Sporadic increases in flow occurred in about half
the animals during the recovery phase of the hypogly-
cemia (twenty to forty-five minutes after the admin-
istration of insulin).  At the 1 unit/kg level, insulin produced a definite increase in hepatic blood flow which reached its maximum at fifteen minutes.  These
changes in flow were interpreted as secondary effects to the insulin induced hypoglycemia.  


The glycogen content of the isolated perfused liver taken from fed normal rats is remarkably stable for three to six hours (Am. J. Physiol., 195: 295, 1958) and thus affords an isolated system for studies of the effect of various agents on glycogen synthesis and glycogen-
ylysis.  The effects of glucagon and tolbutamide in this
system are described.  Glucagon given by continuous infusion (30 to 225 µg./hour) caused prompt glycogen-
ylysis, with blood glucose concentrations rising to
levels as high as 970 mg. per cent.  Hyperglycemia of
600 to 700 mg. per cent did not inhibit the glycogenolytic action of glucagon; however, at glucose levels of 800 to 1,000 mg. per cent glycogenolysis did not proceed to completion.  High concentrations of tolbuta-
amide, maintained before and during the administration of glucagon, failed to inhibit the glycogenolytic action of the latter agent.  


A comparative study of glucose utilization, insulin sensitivity and in vivo incorporation of acetate-C14 into liver fatty acids and cholesterol in male adult rats.  These animals were maintained for four weeks on three high carbohydrate diets (glucose, fructose or galactose), a high protein diet (casein), a high fat diet (lard) or Ralston Purina laboratory chow.  Glucose utilization was high in rats on the glucose diet and low in those on the fat diet.  Incorporation of C14 into liver fatty acids was very high in rats on the fructose diet, high in rats on the protein and glucose diets, low in rats on chow, and very low in rats on the fat diet.  Incorporation of C14 into liver cholesterol was relatively high in rats on chow and relatively low in those on the fat diet.  Glucose utilization in fasted states and in-
Abstracts

659
corporation of acetate into liver fatty acids in fed states were roughly parallel in rats on various diets, but no correlation could be noted between glucose utilization and acetate incorporation into liver fatty acids on the one hand and incorporation of acetate into liver cholesterol on the other.

AUTHORS


The acclimation of rats to low environmental temperatures was found to alter the hepatic metabolic response to fasting for one day at 0 to 2°C. Liver glycogen was stabilized, fatty infiltration of the liver did not occur and liver slices were better able to oxidize acetate-1-C14 and palmitate-1-C14 to C14O2. These results provide an excellent example of an acclimation process occurring at the molecular level.

AUTHORS


Choline deficiency in chronic alloxan-diabetic rats resulted in deterioration of the diabetic state. In alloxan-diabetic rats fed a choline-deficient diet the fatty infiltration of the liver was less than in nondiabetic rats on the same diet. Insulin administered to alloxan-diabetic and nondiabetic, choline-deficient rats further decreased the hepatic fat content and improved the diabetic state in the former. Administration of insulin during life caused a marked increase of fatty acid synthesis in liver slices from both choline-fed and choline-deficient, alloxan-diabetic rats. Substituting fructose for starch in the choline-deficient diet failed to increase the hepatic fat of the diabetic or the nondiabetic animals. The decrease in hepatic fat following the administration of insulin to choline-deficient, alloxan-diabetic rats is apparently due to an extrahepatic effect of insulin, for it occurs despite the increased synthesis of fat in the liver induced by insulin.

AUTHOR

Deposition of fat within the livers of obese subjects and of polyphagic experimental animals has been demonstrated. The well known lipotropic effects of choline and casein do not prevent lipid infiltration associated with obesity.


In young male Albino rats polyphagia and obesity were produced by electrocoagulation of the ventromedial nuclei of the hypothalamus with the aid of a stereotaxic instrument. In the first experimental group (rats weighing 117 to 148 gm.), the effect of dietary choline was studied in thirty-nine rats operated upon and fourteen rats not operated upon which were fed a semisynthetic diet supplemented with 0.05 or 0.5 per cent choline chloride, respectively, for about two months. In the second experimental group (rats weighing 155 to 275 gm.), the additional effect of increased amounts of casein was tested in forty-nine rats operated upon and ten not operated upon which were fed a stock diet or a diet containing 20 per cent casein, respectively, with a supplement of 0.5 per cent choline. Only the rats that were operated upon became polyphagic and about 50 per cent were obese.

At necropsy, hepatic lipid content (wet weight) and total lipid concentration of the carcasses were determined and the distribution of fat in the liver was studied with the light and the electron microscope. Obesity was associated with hypertrophy and fatty change of liver cells. The fat consistently accumulated in the perportal areas of the liver lobules in the form of droplets in cytoplasm and nuclei, while the cells retained their polygonal shape. The amount of fat sometimes was as much as 47 per cent of the wet weight of the liver. The microglobules of fat failed to coalesce or to be extruded to form fatty cysts as seen in choline-deficient rats. The liver cells of polyphagic rats were thus capable of storing large amounts of fat without cell injury as occurring in choline deficiency. The lobular distribution of fat differed also from that in choline deficiency inasmuch as in the polyphagic rats fat was deposited first in portal areas rather than pericentral, and cells about the central vein remained to some degree unaffected even in the presence of advanced fatty metamorphosis. Neither a high concentration of choline nor the supplement of casein decreased the fatty change or altered its pattern of deposition in the liver cells.

The observations indicate that high caloric intake did not increase the choline requirements in young rats, and that progressive accumulation of perivascular lipid could be prevented by choline or casein supplements.

M. Silberberg

Protection against hepatic lipid infiltration and hemorrhagic renal changes induced by choline deficiency is provided by the administration of linoleic acid and by diethylstilbestrol. The effect of these substances upon choline metabolism requires further investigation.


Since choline is an essential part of biliary phospholipid, which has a definite effect on holding cholesterol in solution in bile, the incorporation of exogenous choline into liver and biliary phospholipid has been studied using choline-methyl-C14 and silicic acid column chromatography. Exogenous choline is demonstrated to be rapidly incorporated into liver lecithin, sphingomyelin and biliary lecithin. Indirect evidence is presented showing that bacterial degradation of choline in the intestine is not likely responsible for the urinary excretion of large amounts of trimethylamine after the oral
administration of choline. The choline portion of ingested lecithin is metabolized similar to free choline; ingested lecithin, which is absorbed as such from the intestine, will remain in general circulation for a considerable length of time.  

**AUTHORS**


Duplication of deoxyribonucleic acid (DNA) must occur in the cycle of cell division. In certain tissues there must exist some mechanism for the control of the mitotic rate. It, therefore, seemed possible that there might exist in tissues naturally occurring inhibitors of DNA biosynthesis which would be mitosis inhibitors. Rabbit bone marrow homogenates or cell suspensions were incubated with sodium formate-C\(^1\)\(4\), and the incorporation of the formate into RNA and DNA was measured. It was found under the conditions described that bone marrow homogenates actively incorporated formate into DNA, whereas liver homogenates did not. Further, when liver homogenates were added to the bone marrow system, there was marked inhibition of DNA biosynthesis. Some attempts were made to concentrate this liver factor. The material is alcohol-soluble. Further studies indicated that this inhibition is due to thymine biosynthesis inhibition.

This work has obvious fundamental importance, and it is hoped that further work along these lines will continue.  

**S. O. WAIFE**


This study indicates that patients with viral hepatitis and cirrhosis of the liver conjugate BSP (sulfobromophthalein) poorly and retain large amounts of the unconjugated dye. On the other hand, patients whose liver function is impaired as a result of methylenethione therapy or extrahepatic biliary obstruction conjugate the dye and accumulate large amounts in the serum. This accumulation may be noted before changes in the serum bilirubin, alkaline phosphatase and glutamic oxalacetic transaminase are evident. Thus, the measurement of the BSP conjugates may differentiate liver defects.  

**S. O. WAIFE**

**ITEMS OF GENERAL INTEREST**


It is well known that protein catabolism is increased, for example, after injury, but a quantitative measure of this destruction can only be made by the tedious expedient of nitrogen balance.

In this preliminary communication a simple measure is suggested. An injection of albumin labeled with radioactive iodine is given; when this breaks down the iodine is not recombined in the body with other albumin but is excreted (so long as the thyroid gland is saturated). The breakdown in plasma albumin closely parallels the breakdown of body protein generally so that the estimation of \(^1\)\(31\) excretion is a measure of the body’s protein catabolism. Three illustrative cases are given.  

**F. E. HYTTEN**


Isolated rabbit heart: were perfused with Krebs-Henseleit solution deficient in potassium, calcium or both. Ventricular monosomic action potentials registered with the suction electrode, electrocardiograms and intraventricular pressures, were recorded simultaneously for periods up to twenty minutes. Perfusion with potassium-deficient solutions resulted in a brief initial prolongation of the entire descending limb of the action potential and of the T wave, followed by progressive increase in slope of the initial portion and decrease in slope of the terminal portion of the action potential. During this time the T wave became shorter and a U wave-like deflection occupying the entire diastole developed. QRS showed progressive prolongation. Finally, A-V conduction disturbances, ectopic beats and ventricular fibrillation developed. The force of contraction increased slightly. Perfusion with calcium-deficient solutions decreased the slope of the initial portion while increasing the slope of the terminal portion of the action potential. This was accompanied by prolongation of the S-T segment and reversal in the direction of the T wave. The duration of the action potential reached a maximum after forty to eighty seconds of perfusion, while the force of contraction decreased progressively. Perfusion with solutions without potassium and calcium prolonged the initial as well as terminal portion of the action potential.

**Authors**


Some observations on the urinary output of B vitamins (pantothenic acid, vitamin PP, vitamin B\(_2\), folic acid, thiamine and vitamin B\(_6\)) in rats treated with tetracycline 30 mg./kg. for thirty-five days and 200 mg./kg. for twenty days are reported. The results show the great variability in the urinary output of B vitamins following the administration of the antibiotic. An increase of these factors was sometimes observed, which can reach the significance level: sometimes a decrease or even no variation at all was observed.

**Authors**