

ABSTRACTS OF PAPERS

Comparison of the anti-sterility and anti-muscular dystrophy potencies of alpha-tocopherol. Marianne Goettsch (introduced by W. M. Sperry), and A. M. Pappenheimer (by invitation), College of Physicians and Surgeons, New York.

Alpha-tocopherol has been reported to prevent resorption gestations in rats and mice; testicular degeneration in rats; nutritional muscular dystrophy in rats, guinea pigs, rabbits, dogs, ducks and mice; cerebellar degeneration in chicks; and spinal cord lesions in rats. The minimum amounts of alpha-tocopherol required by animals on vitamin E low diets are being investigated.

Anti-sterility potency. Single doses (0.5-50.0 mg.) of alpha-tocopherol were fed to rats at the beginning of the first gestation. Observations were made upon number of first, second and third litters born, number of young per litter, number born alive, number surviving 10 days of lactation and number protected against muscular dystrophy at the end of lactation. The requirement of mice was similarly determined.

Anti-muscular dystrophy potency. Suckling rats of females on E low diets were given single doses (0.3-3.0 mg.) of alpha-tocopherol during the period of lactation and the minimum dose for prevention of the disease determined.

Guinea pigs were cured of moderately severe nutritional muscular dystrophy, as determined by microscopic examination of muscle at biopsy, by single doses (25 mg.) of alpha-tocopherol. The lesions disappeared within 7 days and did not reappear for 3 to 4 months.

The alpha-tocopherol was administered orally or parenterally, in the form of natural alpha-tocopherol, syn-dl-alpha-tocopherol, or syn-dl-alpha-tocopherol acetate.

Dark adaptation of children in relation to dietary levels of vitamin A. Lydia J. Roberts, Helen Oldham (by invitation), Kathryn MacLennan (by invitation) and F. W. Schlutz, The University of Chicago.

Three groups of children from different socio-economic levels were tested and dietary studies were made on two of the groups. Fifty matched pairs of children were selected from the group whose subjects had the lowest vitamin A intake. One of each pair was given a vitamin A supplement while the other served as a control. Both control and experimental subjects were retested after 2 and 9 weeks of supplementation.

Analysis of the results show that:

1. The mean rod thresholds of the three groups of children known to have had widely different vitamin A intakes were almost identical.
2. Very few children in any group had subnormal adaptation as measured by this test.
3. There was no correlation between adaptometer readings and daily vitamin A intakes although a number of children were receiving less than 1000 I.U. per day in their diets.

4. A slight but significant improvement was found in the mean rod plateaus of the fifty children receiving supplementation when compared with those of their partners. Actual improvement was found in only eleven experimental as against six control subjects. The effect of the supplementation was most pronounced in the fourteen individuals whose original readings were subnormal.

These findings indicate either that the adaptometer does not measure the first signs of a vitamin A deficiency or that such a deficiency is uncommon among children in this area.

Significance of lead in foods. L. G. Lederer (by invitation) and F. C. Bing, Northwestern University School of Medicine, Chicago.

Lead is a widely distributed toxic metal that is found in minute amounts in almost every food if sufficiently sensitive methods for its detection are used. When the lead content of foods is higher than 1 p.p.m., it is our opinion that there is need for further study to determine if contamination is involved. The amount of lead in ordinary foods is such that it would be difficult for an infant to receive less than from 0.25 to 0.33 mg. of this element daily. These amounts are great enough to warrant taking all possible action to avoid contamination of foods with lead, especially of products which are fed to children. Milk, because of its high calcium content, tends to prevent the absorption of lead. Fat in the diet has no demonstrable effect.

Zinc retention in childhood. A. Stern (by invitation), Margaret Nalder (by invitation), and Ieie G. Macy, Children's Fund of Michigan.

The polarographic method permits the easy and accurate determination of zinc in ash solutions of food, urine and feces. It was employed in the study of the physiological role of zinc in growth.

The average zinc content was found to be: for Irish potato, 0.077 mg./gm. dry weight; for mixed whole cow's milk, 2.89 mg./liter and in the daily composite, containing twenty-two individual foods, 15.6 mg. The average daily excretion in urine and feces of children amounted to 0.5 mg. (range 0.4 to 0.6 mg.) and 10.4 mg. (range 7 to 12 mg.) respectively. From 2.6 to 4.2 and 44.6 to 78.8% of the ingested zinc was excreted in the urine and feces, respectively.

The average daily zinc retention for eight children, 8 to 12 years of age, was observed. During 55 consecutive days for each child (eleven 5-day balances) totaling 440 experimental days the average daily zinc intake varied from 15.2 to 16.3 mg. (0.4 to 0.6 mg./kg. body weight) with an average retention of 4.8 mg. (0.11 mg./kg. body weight). The amount of zinc retained ranged from 17.0 to 52.3% of the zinc ingested, while the apparent absorption was 2.12 to 55.4%. The relation of zinc to iron, copper, manganese and nickel metabolism will be discussed.

The comparative effect of iron, protein, ascorbic acid and the vitamin B complex on hemoglobin formation in humans. Ruth M. Leverton (introduced by Helen S. Mitchell), and Alice G. Marsh, University of Nebraska, Lincoln.

The influence of daily supplements of iron, iron and ascorbic acid, certain vitamin B factors and protein on hemoglobin formation was determined in eighty college women. The subjects were matched according to their initial hemoglobin

value and then distributed equally into four groups. Group 1 received 120 mg. of iron from ferrous sulfate; group 2, 120 mg. iron plus 150 mg. ascorbic acid; group 3, 2 mg. thiamine plus 2 mg. riboflavin plus 25 mg. nicotinic acid; and group 4, 28 gm. protein from dry milk, cheese and peanuts.

At the end of 6 weeks the average rise in hemoglobin was 1.0, 1.2, 1.0 and 0.7 gm. per milliliter of blood for groups 1, 2, 3 and 4 respectively. For a second 6 weeks groups 1 and 2 were given only ascorbic acid, group 3 was given only thiamine and group 4, egg yolk. Values in all groups dropped but not as low as they had been at the beginning of the study.

These data, together with supplementary studies of iron absorption and excretion, emphasize the importance and value of dietary factors other than iron in overcoming the simple hypochromic anemia prevalent among women.

The influence of prenatal diet on the mother and child. J. H. Ebbs (by invitation), W. A. Scott (by invitation), and F. F. Tisdall, University of Toronto and Hospital for Sick Children, Toronto.

Studies have been made on the influence of good and poor prenatal diets on the health and obstetrical course of 400 women and their offspring. Each diet record was analyzed in order to determine as closely as possible the amount of the individual food components received by the mothers. Studies of the blood phosphatase, vitamin C and haemoglobin were made at intervals on both the mother and the child. Clinical observations and the laboratory investigations indicate that the prenatal diet has a striking influence on the health of the mother during pregnancy, labor and convalescence. The diet during pregnancy also markedly affects the health of the child during the first few months of life. The relation of the diet to the development of dental caries was also studied.

The influence of diet on the composition of weight gains in pre-school children.

Jean E. Hawks (introduced by Marie Dye), and Gladys Everson (by invitation), Michigan State College, East Lansing.

On equi-calorie diets, pre-school children gained weight faster when they had 4 rather than 3 gm. of protein per kilogram. Milk, meat and whole egg as protein additions to the diet produced muscle, fat and bone growth because retentions of nitrogen and calcium as well as phosphorus, sodium, potassium and chlorine were increased. Egg white and gelatin as protein additions produced only muscle and fat growth because there was an increase in nitrogen storage, but no increase in calcium. At the same time magnesium and potassium retentions were lower, causing decreased minerals in the tissue. Thus milk, meat and whole egg may have produced a better type of weight gain than egg white and gelatin.

Additional calories from fat, starch or sugar produced tremendous weight gains which represented protein and fat tissue. The fat supplement caused no added calcium retention, therefore no increased bone growth. Carbohydrate supplements produced more nitrogen retention than fat and some calcium retention indicating protein, bone and fat growth. All high calorie diets reduced sodium, potassium and chlorine retentions. Thus calories added to a diet containing 3 gm. of protein per kilogram may be an economical way of producing muscle and fat growth, but, since the mineral content of the tissue is low, the weight gain may be less satisfactory than that produced by milk, meat and whole egg.

Prewar diet in Belgium; the influence of restriction of imports on the health of the population. L. Brouha (introduced by D. B. Dill), Harvard University, Cambridge.

The National Council for Nutrition in Belgium made a survey of the food problem during the period preceding the invasion. This nation-wide inquiry showed: (1) Average calories intake was around 2725 per day. (2) Proteins were sufficient, but animal proteins at the lowest limit. (3) Fats were at the lowest limit and butter was extremely low. (4) Carbohydrates were in excess. The diet was ill-balanced, the proportions being protein 1, fat 0.95, carbohydrate 5. Calcium and vitamin B were at the limit of danger. Vitamins A and D were low. The situation was already serious for the children. As a result of the war, suppression of importations, reduction of cattle and poultry, the actual diet is as follows:

1. Average calories: 900 to 1400. The deficit varies from 25 to 75%.
2. Proteins: 30 gm. Deficit from 25 to 85%.
3. Fats: 12 gm. Deficit from 30 to 90%.
4. Calcium: deficit increasing to 90%, between 3 to 18 years of age.
5. Vitamins are very low, for butter, milk, eggs, cheese, citrous fruits have practically disappeared. Milk is available only for children under 4 years.

It is beyond doubt that such an insufficient and unbalanced diet will have an ill effect upon the health of the population, mainly upon the health of children and adolescents.

What are the foodstuffs which would be most helpful in case some could be sent?

What is the diet that the population should have after the war is over in order to counteract the ill effects of partial starvation?

The alimentary interconversion of thiamine and cocarboxylase. E. S. Nasset and J. F. Waldo (by invitation), University of Rochester.

About half of a 74 micromol dose of thiamine or cocarboxylase is recoverable from a duodenostomy in the dog. When thiamine is fed, about 11% of the recovered portion is phosphorylated. Conversely, when cocarboxylase is fed, 55 to 78% is recovered as thiamine. The absorption and interconversion of these forms of the vitamin in the operated dogs occur rapidly in the upper portion of the digestive tract, including the stomach and the duodenum. Experiments done in vitro with various digestive juices in an attempt to localize the enzymatic processes concerned have been only partly successful. It has not been possible to demonstrate phosphorylation of thiamine in vitro with juices from the stomach, pancreas, duodenum or jejunum. Mixture of juices and a mucosa extract also were inactive. The hydrolysis of cocarboxylase to thiamine is readily effected by duodenal or jejunal juice.

The method of Melnick and Field was used in the determination of thiamine. Cocarboxylase was converted to thiamine with the aid of Taka-Diastase.

Studies of the excretion of thiamine and its degradation products in humans.

H. Pollack, M. Ellenberg (by invitation), and H. Dolger (by invitation), Mt. Sinai Hospital, New York.

There are two components in human urine which stimulate the rate of glucose fermentation by yeast. One has definitely been isolated and identified as thiamine.

The other, not oxidizable in alkaline ferricyanide and not inactivated by bisulphite saturation, has been identified by inference as a pyrimidine. Schultz, Atkins and Fry have shown that the pyrimidines possess the same fermentation-stimulating activity as thiamine, mole for mole. Since the pyrimidine nucleus is an integral part of the thiamine molecule, it is important to determine the relationship of urinary pyrimidine to thiamine metabolism.

Evidence is presented to show: (a) Complete deprivation of dietary thiamine for a period of 10 days changed the urinary thiamine to pyrimidine ratio from approximately 9:1 to 1:9. (b) During this 10-day deprivation period the absolute amount of pyrimidine excretion remained at approximately the same level; while the free thiamine disappeared almost completely. (c) The 1 mg. "load test" before and after a 10-day deprivation period was not altered significantly. (d) The parenteral administration of 100 mg. of thiamine daily produced a tremendous increase in urinary pyrimidine excretion. (e) The deprivation of thiamine for 10 days did not give rise to any evidence of vitamin B₁ deficiency, either subjectively, or objectively as measured by electrocardiogram, blood sugar, cholesterol, total protein, hemoglobin, red blood count, blood pressure and pulse rate.

We wish to express our thanks to Dr. C. N. Frey and his associates. This work was supported in part by the Williams-Waterman Fund.

Further observations on induced thiamine deficiency in man; thiamine requirement of man. R. D. Williams (introduced by R. Wilder), and H. L. Mason (by invitation), The Mayo Foundation, Rochester, Minnesota.

Twelve healthy adult women were maintained for a period of 5 months on a rigidly controlled basal diet containing 400 to 450 μ g. of thiamine. Factors of the vitamin B complex other than thiamine were supplied in the form of autoclaved brewers' yeast. This report will describe the mental state, the cardiovascular, gastrointestinal, metabolic and hematologic disorders observed during this period of moderate restriction of intake of thiamine and will compare them with observations made during a previous study,¹ already reported, in which subjects received a diet containing less than 150 μ g. of thiamine.

Six of these subjects, maintained continuously on the controlled basal diet, were selected for the study of thiamine requirement of man. They were divided into two groups: Group 1 received thiamine chloride in an amount and for a period of time sufficient to replenish depleted stores of this vitamin; group 2 received only the basal diet. Thereafter, both groups of subjects received identical supplements of thiamine chloride in gradually increasing amounts. The mental and physical states of the subjects were correlated with the various levels of intake of thiamine and with the excretion of this vitamin in the urine.

¹ Williams, R. D., H. L. Mason, R. M. Wilder and B. F. Smith. Observations on induced thiamine (vitamin B₁) deficiency in man. *Archives of Internal Med.*, vol. 66, p. 785, October, 1940.

Fat metabolism in rat acrodynia. F. W. Quackenbush (by invitation), F. Kummerow (by invitation), and H. Steenbock, University of Wisconsin, Madison.

Ethyl linolate was found to cure completely an acrodynia which had been produced in rats on a diet free from unsaturated fatty acids. Pantothenic acid

had no effect, pyridoxine alleviated the symptoms somewhat and a supplement of the two was more effective than either alone. Rice bran extract (Vitab) was still more effective but when fed for long periods did not prevent a remission with the appearance of scaly feet and tails. Further supplementation with either linoleic or arachidonic acid effected a cure; linolenic acid was not curative. Linoleic acid and arachidonic acid also promoted normal reproduction and satisfactory raising of the young.

Analyses of the total body fats revealed: (a) a reduction in the fat content and an increase in the iodine value with the production of dermatitis; (b) an increase in the fat content and a decrease in the iodine value after feeding linoleic acid; (c) a slight increase in the fat content but no decrease in iodine value after feeding pyridoxine; (d) a marked increase in fat content and a decrease in iodine value after feeding rice bran extract or pyridoxine and pantothenic acid.

The fatty acids from acrodynic rats or from rats which had been cured with rice bran extract were non-curative.

Fatty livers were not encountered.

Nicotinic acid and coenzyme levels in animal tissues. W. J. Dann and P. Handler (by invitation), Duke University Medical School, Durham, N. C.

Nicotinic acid in tissues has been measured by a new procedure (Proc. Am. Soc. Biol. Chem., vol. 35, p. li, 1941) and parallel V-factor (coenzymes I and II) estimations by the method of Kohn have been made. Results in two species are reported.

Mean figures for twelve albino rats follow: Coenzyme content, expressed as micrograms coenzyme I equivalent to 1 gm. fresh tissue, were liver 396 ± 33 ; kidney 650 ± 20 ; muscle 466 ± 9 . Nicotinic acid content, micrograms per gram, liver 175 ± 3.7 ; kidney 132 ± 3.6 ; muscle 86 ± 0.9 . All the nicotinic acid of muscle and probably all in kidney was present in coenzyme, but more than half the nicotinic acid in liver was not so combined. Direct nicotinic acid determinations on tissues of rats on a diet low in this factor gave rigid proof that the rat can synthesize this compound.

For ten normal dogs tissue contents of coenzyme were: liver 438 ± 46 ; kidney 504 ± 18 ; muscle 310 ± 12 . Nicotinic acid contents were: liver 153 ± 12 ; kidney 95 ± 3.4 ; muscle 71 ± 1.9 . All the nicotinic acid of kidney is combined in coenzyme but this is not the case in liver and muscle. In blacktongue the liver content decreases to 42% of normal and that of muscle to 72%; kidney content is unchanged. The liver nicotinic acid not bound in coenzyme is scarcely decreased at all.

The sources of the wide discrepancies between the results of different workers will be discussed briefly.

Factors affecting the increase in blood plasma ascorbic acid after oral ingestion of vitamin C. E. Neige Todhunter, State College of Washington, Pullman.

In mass studies of vitamin-C nutrition it is not always possible to obtain fasting blood samples. This study was undertaken primarily to ascertain how rapidly and to what extent ascorbic acid with breakfast would cause a rise in plasma ascorbic acid above the fasting level; also to study the effect of different

food sources of the vitamin in raising the plasma level, and to gain some further knowledge of the metabolism of vitamin C. Ascorbic acid was determined by Farmer and Abt micromethod and by a photoelectric colorimeter method. Blood samples were taken at 7:50 A.M., 8:30 and each succeeding $\frac{1}{2}$ hour till noon. At 8:00 A.M. 50 mg. ascorbic acid, either crystalline, or in a test food was taken with a standard breakfast. Data for each subject (college women) were collected for 3 days for each test food, and good agreement was obtained. All subjects showed fair agreement in time of attaining the peak of the absorption curve. The amount of increase in plasma level was influenced by the initial level, and the hour of maximum increase depended on the source of the vitamin, that from strawberries and cauliflower being later than from orange juice, whole orange or crystalline ascorbic acid. Within 3 to 4 hours after the meal, blood values returned to the fasting level. Iron salts, in either ferrous or ferric form, did not appear to delay absorption, nor did a high fat intake. Increased intakes of 100, 200 and 400 mg. of crystalline ascorbic acid gave corresponding increases in the peak of the plasma absorption curve.

The influence of certain organic compounds on perosis. T. H. Jukes, University of California, Davis.

Perosis was produced in chicks by a diet of glucose, washed casein, gelatin (or creatine), yeast, gum arabic, salt mixture, soy bean oil, and fish oil. Perosis was prevented and the growth rate was doubled by the addition of choline. However, if manganese was omitted from the salt mixture, choline did not prevent perosis. Manganese and choline are thus both necessary for the prevention of perosis in chicks as well as in turkeys.

A number of choline derivatives, supplied by Dr. A. D. Welch, were studied for their effects on perosis and growth. The triethyl homologue of choline was neither anti-perotic nor growth-promoting, while the monomethyl-diethyl homologue prevented perosis but did not promote growth. Betaine was completely ineffective, but betaine aldehyde had weak anti-perotic and growth-promoting effects similar to those observed on insufficient levels of choline. This may indicate a partial conversion of betaine aldehyde to choline in vivo. Furthermore, the failure of monomethyl-diethyl choline to promote growth while preventing perosis (a result also obtained with turkeys) may indicate that the growth-promoting and anti-perotic properties of choline reside in different parts of the molecule.

If gelatin (or creatine) was omitted, perosis was not produced by the basal diet. This contrasts chicks with turkeys, which develop perosis even when gelatin (or creatine) is omitted from a similar diet.

Isolation of lanthionine from various proteins. D. B. Jones and M. J. Horn (by invitation), Bureau of Agricultural Chemistry and Engineering, United States Department of Agriculture, Washington, D. C.

Recently there was described by the authors the isolation from acid hydrolysates of sodium carbonate-treated wool of a new thio ether diamino acid, lanthionine, $\text{HOOC.CH}(\text{NH}_2).\text{CH}_2.\text{S.CH}_2.\text{CH}(\text{NH}_2).\text{COOH}$. By following the same procedure as was used with wool, we have now found that this amino acid can be isolated not only from other keratins, such as hair and feathers, but also from lactalbumin.

Lanthionine has also been isolated from the hydrolysis products of wool that had been treated with dilute sodium sulfide solution in the same manner as with sodium carbonate. Apparently the reagents used cause a splitting of the disulfide bonds of cystine resulting in structural changes of the protein so that on subsequent hydrolysis a thio ether amino acid is formed. It appears probable that the formation of lanthionine under these conditions may well be a property common to all proteins containing cystine. It is possible that the cystine of dietary proteins may be converted into lanthionine in the intestinal tract, which at times is distinctly alkaline in reaction. That a thio ether amino acid may play an important part in the sulfur metabolism of animals has already been assumed in connection with the possible intermediary relationship of cystine and methionine. Feeding experiments are in progress in order to see whether lanthionine can replace cystine or methionine in the diet.

Nutrition in carcinogenesis. C. P. Rhoads (introduced by W. T. Salter), and C. J. Kensler (by invitation), The Memorial Hospital, New York.

Experimental evidence has been obtained that hepatic cancer in three different strains of rats can be produced regularly by the administration of dimethyl amino azobenzol to rats taking a diet of brown rice and carrots. Supplement of this diet with yeast or liver extract in adequate amounts prevents completely the development of the cancer. The protective factor is none of the constituents of the vitamin B complex so far described. Certain evidence as to its nature will be presented.

The effect of feeding the carcinogen to animals taking the deficient diet is an inhibition of the activity of at least two enzyme systems, co-carboxylase and cozymase, thus producing a conditioned or secondary deficiency disease. The metabolic breakdown products of the carcinogen have been isolated from the excreta of the treated animals and their structure established. One of these products is profoundly inhibitory to both co-carboxylase and cozymase systems *in vitro*. Acetylation of this compound, which occurs *in vitro*, removes all toxicity.

The development of the mutation which characterizes the malignant tissue is marked by the presence of an oxidizing enzyme system which is no longer susceptible to the inhibitory effect of the toxic metabolic product of the carcinogen. The oxidation of the normal liver from which the cancer is derived is extremely susceptible to inhibition by this compound. This is the first demonstration that cancer tissue induced by a known chemical possesses an oxidative system which is immune to that chemical or its metabolic product.

Progressive iodination of serum albumin. W. T. Salter and Jytte Muus (by invitation), Thorndike Memorial Laboratory, Boston City Hospital.

When horse serum albumin is iodinated in alkaline solution, it assumes such marked thyroïdal activity that it becomes a useful hormone with which to treat human myxedema. When the iodine is added to the protein in stages, at first no thyroïdal activity is encountered—up to about 6% iodine content. This stage corresponds to iodination of the tyrosine in the protein. Thereafter thyroïdal activity steadily increases as more iodine is added up to about 11%. This iodine moiety is greater than can be accounted for by the histidine present. In the course

of this latter treatment a thyroxine-like fraction is developed, which separates on hydrolysis. Thus simple alkaline iodination of a circulating protein molecule transforms one or more of its constituent amino-acids into thyroid hormone.

This finding is of special interest because the circulating "hormonal" iodine of blood plasma is found to be prominent in the albumin fraction. This circulating albuminous iodine also consists of a thyroxine-like and a non-thyroxine fraction.

ABSTRACTS OF PAPERS READ BY TITLE

Vitamin A metabolism of college students. Jane C. Ebbs (by invitation and Esther L. Batchelder, Rhode Island Agricultural Experiment Station, Kingston.

Dark adaptation records of 223 healthy college students (approximately one-fifth of the college enrollment) have been measured and analyzed statistically. The instrument used for the tests was the "rhodometer" previously reported. A bell-shaped distribution curve has been attained (skewness of 0.3315) for the minimum brightness perceived at the end of a 15-minute test. The mean, median, and mode were $\log 5.28 \pm .045$, $\log 5.34$ and $\log 5.40$ micro-microlamberts, respectively.

Several studies have been made of the response to massive doses of vitamin A. The first observations were of the dark adaptation 24 hours after administration of the test dose. One subject who had shown a gradual decrease in dark adapting ability which eventually fell below that of any of the subjects tested in the campus survey was tested each hour for 6 hours after administration of 91,000 I.U. as halibut liver oil. After 1 hour no apparent change in dark adaptation was observed; after 2, 3, 4 and 5 hours progressive increase was observed, reaching $\log 5.35$ micro-microlamberts (the median value of the campus survey) after 5 hours. This value was maintained in tests given 24 hours following taking of the massive dose. It was maintained for several days on an intake of 91,000 I.U., but no further increase was observed.

Prophylactic requirement for alpha-tocopherol in male and female rats. Gladys A. Emerson (by invitation), and H. M. Evans (by invitation), University of California, Berkeley.

Alpha-tocopherol acetate was administered at three levels six times weekly to rats held on an E-low ration; the levels were 0.1, 0.25 and 0.75 mg.

E-low animals of both sexes showed the typical plateauing in weight characteristic of vitamin E deficiency. Growth of all tocopherol-fed rats exceeded that of natural-food-fed rats.

Twenty-five hundredths milligram α -tocopherol was sufficient for normal reproduction in the male, while 0.1 mg. was inadequate as evidenced by the fact that half the copulations with normal females were sterile.

The number and weight of young born to the females in each tocopherol group were the same. A striking difference in the young appeared in the lactation period. The offspring of 0.1 mg. mothers exhibited the dystrophy typical of vitamin E deficiency; half were dead by the thirtieth day and most of the survivors exhibited some degree of paralysis.

The young of the mothers receiving 0.25 mg. showed the same incidence but a less severe dystrophy, all affected animals having recovered by the thirtieth day.

No dystrophy occurred in the young of mothers receiving 0.75 mg. and it is notable that their average weight at 30 days (92 gm.) was 9 gm. higher than in the offspring of mothers on the natural food diet.

A second litter series gave almost identical results.

The influence of sex on iron assimilation in the rat. S. W. Kletzien, New York State Institute for the Study of Malignant Disease, Buffalo.

Various published reports on the influence of sex on iron assimilation convey the impression that the female organism more efficiently assimilates iron than the male. Our data based on iron analyses of the total blood, liver, spleen, and carcass do not bear out this impression. We have found, as have others, that the female responds more quickly with a higher concentration of hemoglobin and exhibits evidence of greater liver iron stores than the male, but presumably these result from the lesser requirements for growth in contrast to those of the male. The male animal puts out a larger volume of blood of a lower hemoglobin content and builds into its soft tissues more iron on the other hand, thereby off-setting any apparent gains in the female and actually exceeding them in total iron assimilated.

Carrying our studies further we have found that ovariectomy increases iron assimilation as does castration; such procedures nullify any previous differences in the pattern of iron distribution and bring about comparable responses in both sexes. Pregnant females as compared with virgin litter mate controls and males reveal however an increased capacity to assimilate iron on similar iron, copper, and basal diet intakes. This in itself is however not sufficient to maintain pre-pregnancy stores of iron. The iron assimilation of the pregnant female thus simulates that of the rapidly growing male.

Calcium balances of young women on their customary or self-chosen diets. Hughina McKay (by invitation), M. B. Patton (by invitation), Margaret A. Ohlson (by invitation), Martha S. Pittman, Ruth M. Leverton (by invitation), and G. Stearns, Agricultural Experiment Stations of Iowa, Kansas, Nebraska and Ohio.

Calcium balance studies of 109 college women, following their customary mode of living, eating their customary diets, and presumably in good health, showed a mean daily intake and balance of 0.9538 and 0.0307 gm. respectively. Corresponding figures for another young woman studied for forty-five 5-day periods were 1.2389 and 0.0711.

Thirty-six of the large group were studied for two or more periods. The variability of the "repeat" group was similar to that of the one individual.

Average daily intakes for the 110 women ranged from 0.322 to 2.323 gm. One-third of the women having intakes less than 0.699 were in positive balance, as compared to two-thirds of the women having intakes greater than 0.699.

There was a trend toward more efficient utilization of calcium by women from 17 to 20 years of age than by older women.

Treatment of the data by linear regression indicates that, in 95% of the predictions for a population of which the group of 109 is representative, positive calcium balances will occur on intakes ranging from 0.758 to 0.895 gm. daily.

The relation of pantothenic acid and succinic acid to the growth of certain micro-organisms. L. Rane (by invitation), and Y. Subbarow (by invitation), Massachusetts Department of Health and the Harvard Medical School, Boston.

Micro-organisms have been used as biological reagents to isolate pantothenic acid. Strains of group A hemolytic streptococcus and types of pneumococcus require the whole conjugated compound for growth. The β -alanine fraction is an essential growth factor for certain strains of the diphtheria bacillus while the acid portion is necessary for some strains of group D hemolytic streptococcus.

Fractionation of a highly purified liver extract yielded a crystalline compound, the activity of which in promoting the growth of a strain of group D hemolytic streptococcus was comparable to that of hydrolyzed and non-hydrolyzed pantothenic acid. The compound was identified as succinic acid. Synthetic succinic acid was similarly active when large inocula of organisms were used to seed the test media. Light inocula capable of inducing growth with the natural compound failed to show any activity with the synthetic. This variation indicated the possibility of a slight contamination of the natural compound by pantothenic acid or a component of pantothenic acid. The addition of pantothenic acid in completely inactive concentrations to synthetic succinic acid produced full growth of even small inocula.

Further discussion will be made of the possible nutritional significance of combinations of compounds in sub-optimum proportions.

Studies on the specificity of inositol. D. W. Woolley (by invitation), The Rockefeller Institute for Medical Research, New York.

Since it has been shown that inositol cures alopecia in mice fed on a purified diet, it was of interest to determine if other related substances possessed similar activity. In order to compare the responses of widely-separated species and to improve the quantitative aspects of the technique, a species of yeast was also tested for its behavior towards the compounds. For the yeast inositol was active; phytin, sodium phytate, inositol hexaacetate, soybean cephalin, quercitol, d-inositol, d-inositol monomethyl ether, l-inositol and l-inositol monomethyl ether were less than one-tenth as active as inositol. Mytilitol (methyl inositol) was active. The chief difference found between the responses of yeast and mice was the ability of mice to respond to esters of inositol. Thus phytin, inositol hexaacetate and soybean cephalin were active in mice.

Pantothenic acid has also been found to influence alopecia in mice. Hair may be lost in the absence of inositol or of pantothenic acid. In alopecia which results from lack of inositol, eventual spontaneous cure (either partial or complete) may occur.

Nutritional status of college women; factors contributing to variability in basal metabolism. Charlotte M. Young (by invitation), Martha S. Pittman, Elva G. Donelson (by invitation), and Gladys M. Kinsman (by invitation), Kansas State College, University of Minnesota, Oklahoma Agricultural and Mechanical College and Iowa State College. (Approved for publication by the Advisory Committee of the Regional Project of the North Central States Relation to the Nutritional Status of College Women.)

At least four basal metabolism observations are reported on more than 400 college women from one university and three colleges. About half of the students were observed for 2 to 4 years. Thus both a longitudinal and a cross sectional study have been possible.

The purpose of the study was to record the basal metabolism of the college woman measured under her usual living conditions. Variability was considered a fundamental characteristic of basal metabolism. Certain factors contributing to variability have been segregated by statistical methods.

Standard deviations for inter- and intra-individual variabilities confirmed the work of Boothby and Berkson (*Am. J. Physiol.*, vol. 121, pp. 660-683). Data have been obtained to show that the method of selection of data is a variability factor of importance. The procedure of choice is (1) a careful control of the testing environment and (2) use of all data except that discarded at the time of the test for errors in technique or non-basal condition of the subject. Significantly more variable results were obtained on the first day of testing which suggests the use of one "practice day" for adaptation to the testing routine. Increased scholastic or extracurricular responsibilities were found to increase the variability of basal metabolism. Certain other factors are being investigated.

GROUP DISCUSSIONS

7:30 P.M.

A. Making nutrition function. Helen Mitchell, presiding.

Dr. Helen Mitchell, chairman, stated that the standards for specific nutrients had been set up in 1925 by the League of Nations and are now being revised. Dr. Lydia Roberts, member of the Committee on Food and Nutrition of the National Research Council, presented the tentative revision, pointed out the problems encountered in trying to establish values, stated the bases for selection of proposed standards, and how to meet them with a diet of natural foodstuffs. Dr. E. V. McCollum considered that the thiamine, riboflavin and ascorbic acid levels are too generous, the iron and vitamin D levels too low. Dr. R. M. Wilder defended the thiamine figures and Dr. W. H. Sebrell those for riboflavin. Doctor Wilder then gave the history of the enriched flour program, concluding that since food fortification is here to stay we should fortify the foods used in large amounts by the poorer classes. Dr. Muriel Brown explained the use of nutrition clinics in Tennessee as part of the defense program. They hope to teach the people to desire to improve

their food habits by means of a cooperative health program for the undernourished children in the community. Dr. Martha Koehne emphasized the need to inspire people with the desire to be better than they are, to give them the information to make them better and to help them to apply this information. Colonel Paul Howe discussed the feeding of the army, and methods used to secure for the men menus that are nutritionally adequate and to have the food properly prepared.

B. Trace elements in nutrition. C. A. Elvehjem, presiding.

The significance of trace elements in nutrition was summarized by seven different speakers and after each speaker there was considerable informal discussion. M. O. Schultze reviewed the recent work on iron and copper with emphasis on the forms of iron in the body and the action of copper in the production of these compounds. E. Hove discussed both zinc and boron and presented ample evidence for the essential nature of zinc, but stated that clear-cut evidence for the necessity of boron in animal nutrition was still not extensive. We were fortunate in having present in our group W. G. E. Eggleton of Lester Institute, Shanghai, China, and he discussed briefly his recent work on zinc. A very complete summary of all our knowledge regarding cobalt and manganese was given by J. M. Orten. The role of cobalt in both the prevention of anemia and the production of polycythemia stimulated considerable discussion. The so-called toxic trace elements, fluorine and selenium, were discussed by P. H. Phillips and A. L. Moxon. Phillips emphasized the importance of maintaining the fluorine content of all diets at a low level in spite of certain experimental results indicating that fluorine retards dental caries. Moxon described recent studies on methods of counteracting selenium poisoning. C. V. Moore gave an excellent summary of the clinical aspects of the trace elements, and showed the limitations of our knowledge regarding the importance of these elements in human nutrition. The final discussion centered around the variable results obtained with different species, especially in regard to studies on the availability of iron.

C. Nutritive significance of individual carbohydrates.

H. J. Deuel, Jr., presiding.

Phosphorylation and the comparative absorption of various sugars.

G. T. Cori. When the rate of phosphorylation is compared with the rate of absorption it is found that the two mechanisms do not proceed at a parallel rate. For instance galactose is the most rapidly absorbed of the sugars studied, followed in turn by glucose and fructose. On the other hand fructose is the best phosphate acceptor with galactose the poorest. Iodoacetic acid and phlorhidzin poisoning affect the organism in somewhat different ways. Phosphorylation is not abolished by adrenalectomy as the phosphorylation of some of the vitamins can occur under this condition.

The relative glycogenic and ketolytic action of the various sugars.

J. R. Murlin. The conclusion seems evident, even though the ketonuria is produced by such widely different experimental procedures as phlorhidzin poisoning, a high fat diet, fasting in humans, or feeding four carbon atom fatty acids to rats, that the individual carbohydrates vary in their ability to reduce an acetonuria. In general the results may be summarized in that galactose or fructose are markedly superior to glucose, with lactose and sucrose occupying intermediate positions. Galactose seems to form a glycogen more resistant to breakdown than that formed after glucose.

Respiratory metabolism.

T. M. Carpenter. When heat production was used rather than surface area as a basis of sugar feeding, a better correlation was observed between different species. After fructose feeding a similarity is noted in the R.Q. of the canary, the goat, monkey, and man. The rat behaves differently. After galactose feeding man responds in a manner different from all other species studied. After ingestion of glucose the monkey and man behave similarly. The R.Q. of the canary increases very markedly. In the cat the R.Q. continues to rise for a long period.

Metabolism of hexitols.

Fred W. Ellis. In a comparison after feeding mannitol and sorbitol it was noted that sorbitol was well tolerated while mannitol was not. When fed in cocoa butter over a 2-3 day period sorbitol did cause a slight increase in liver glycogen while mannitol failed to elicit such a response.

Citric acid metabolism.

A. H. Smith. Citric acid is always produced in metabolic processes. In man from 0.20-1.00 gm. per day is eliminated. The origin of citric acid is as yet unknown, although the effects of various foods and regimes have been studied. Thus when bicarbonate is fed the citric acid output is increased. The ingestion of acid causes the opposite effect. Of the various foods carbohydrate causes the greatest output of citric acid, although there is a variation in the response to the individual sugars. Sucrose, starch, and dextrin are about twice as effective as glucose, fructose, and galactose.

D. Effect of heat upon the nutritive value of proteins.

Agnes Fay Morgan, presiding.

Various phases of the effect of heat upon proteins were discussed by Drs. D. Breese Jones, L. C. Norris, J. W. Hayward, Helen Parsons, Joseph Routh, H. A. Mattill, R. J. Block, and A. G. Hogan. Several others also participated in the discussion.

Among the many points brought out was the fact that moist heat greatly improves the digestibility and the biological value of many plant proteins. Dry

heat may also improve the biological value of soybean meal but temperature and exposure time are more important than the type of cooking. This is also true for fish meals. Other animal proteins, meat products, when heated, have a decreased biological value not due to destruction of lysine and histidine since the heated protein when hydrolyzed is comparable with the unheated hydrolyzed protein. Because the loss in the biological value of wheat, casein, edestin, and liver, caused by dry heat, can be restored by either hydrolysis or additional lysine, it was suggested that dehydration results in protection of the lysine against enzymatic reactions. The addition of valine and leucine to lactalbumin made appreciable improvement in the biological value lowered by heating. Dogs on diets containing heated casein at death showed fatty livers and reduced serum protein. Neither additional lysine and histidine nor an increased intake of the protein compensated for the heat injury. It was suggested that new methods of studying the molecular structure of protein must be sought to unravel the story of its biological value. The significance in human nutrition of the deleterious effects of heat upon most animal proteins was emphasized.

E. Heat regulation. L. H. Newburgh, presiding.

Dr. R. L. Day emphasized that the premature infant had a higher heat loss than the adult because of a much greater proportionate surface area and for other reasons. Diurnal variations in body temperature were absent in early infancy. He pointed out that body temperatures as low as 88°F. were compatible with apparently normal health in premature infants. Dr. H. G. Barbour was concerned with the mechanism of control of loss of heat. He showed that in a cold environment or when the internal temperature is rising at the beginning of a fever, heat is retained because vaporization of water is diminished. This diminution is brought about by concentration of the blood, the result of the passage of water out of the blood. It can be shown that there is a general increase in intra-cellular water content at this time. With an increase in environmental temperature there is a dilution of the blood before the increase in vaporization. The control of regulation of internal temperature appears to lie in the hypothalamus; cooling anteriorly, heating posteriorly. Dr. J. D. Hardy pointed out that there are two types of fever. One is due to a dramatic increase in heat production, and the other is due to a slight to moderate increase in heat production with an active suppression of heat loss. The first type occurs with exercise or a chill and may occur in health or disease, whereas the second type occurs in disease. Quantitative aspects were brought out by means of lantern slides. Dr. D. B. Dill spoke about acclimatization to high environmental temperatures. He pointed out that there was a large individual variation in capacity to adapt to high temperatures. A great variation occurs in individuals to sweat and also in the composition of sweat. When first exposed to such temperatures the sweat is concentrated, but later it becomes diluted. Dr. J. A. Greene described a method for measuring the per cent of heat lost by vaporization of water in the rat in the basal state and throughout the 24 hours. He also compared the per cents of heat dissipated by vaporization on the part of various mammals and noted that the albino rat lost 22%, the marmot 20%, the elephant 19%, the cow 26%, the rat 24% and the rabbit 25%.

F. Comparative nutritional requirements of various species.
C. M. McCay, presiding.

A brief introduction showing the interplay between insect and animal nutrition was given by the chairman. Dr. R. Wulzen reviewed briefly her many years of study of the nutrition of planaria. Dr. W. H. Peterson then talked about the recent advances in determining the vitamin requirements of bacteria. Dr. Marianne Goettsch reviewed the history of the discovery of vitamin E and its importance to many animal species in the prevention of muscular dystrophy, and Dr. K. Mason summarized recent knowledge of sterility in the male. Dr. F. C. Bing presented an interesting paper concerning the usefulness and limitations of the mouse for experiments in nutrition. From the floor, Dr. C. A. Mills presented data showing the higher requirement of mice for thiamine when kept in a warm room. The program was concluded with a comparison by Dr. I. McQuarrie of the diseases of children and adults observed in China with those of similar people in America.