

# NUTRITIONAL STATUS OF AIRCRAFT WORKERS IN SOUTHERN CALIFORNIA

## V. A CONSPECTUS OF THE SURVEY AND ITS FIELD<sup>1</sup>

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**T**HIS is the concluding paper on the Study of the Nutritional Status of Aircraft Workers in Southern California. It is a summary of the whole Study and discusses the results in the context of related studies and their objectives.

The immediate impetus to the undertaking of the Study came from the call for maximum production in the war effort. In the years preceding the National Emergency and the War the general public had become increasingly interested in nutrition, especially in the question of the value of vitamin supplements. A few employers were convinced that production was improved by improving the nutrition of their workers. In most cases this opinion was an interpretation of the results of tests, without controls, of supplementing the diets of workers with vitamin concentrates. There were no adequate studies of the nutritional status of the workers before and after a vitamin supplement was used, nor of precisely what was gained by its use.

In most industrial groups in the United States there is probably relatively little severe or acute nutritional deficiency. At the time of the declaration of the National Emergency in 1941 the effects of improving the diet of such a population on health, working ca-

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capacity, and psychological state had not been demonstrated by adequately controlled studies. Such studies were desirable for purposes of war production, and also because of their bearing on a lively question before the War and since, epitomized as "optimal" versus "necessary" nutrition.

Accordingly the Committee on the Nutrition of Industrial Workers of the Food and Nutrition Board of the National Research Council recommended:

that adequately controlled studies be conducted in war or defense industries to determine the facts concerning the influence of diet and nutrition on health, working capacity, incidence of accidents, absenteeism, and the psychological state. (1)

A study among workers at the Lockheed Aircraft Corporation, Burbank, California, was undertaken to meet this need. The Study began in November 1941 and ended in March 1943. Detailed accounts of the methods used and the results obtained are given in preceding reports (2, 3, 4, 5).

#### THE SUBJECTS OF THE STUDY

The Study began with 1,173 men who had volunteered to cooperate. They were divided at random into two groups; one received a vitamin supplement, the other a placebo.<sup>4</sup> Together the two groups comprised about 2 per cent of the total number of employes. The number of subjects who remained in the Study to the end was reduced to about half the initial number by terminations and transfers (4).

The subjects were largely young men, approximately 70 per cent of them being under 30 years of age at the beginning of the Study. The age distributions of those in the Placebo and Vitamin groups were very similar. Also, the duration of employment was

<sup>4</sup>The content of the supplement was as follows: vitamin A (from fish liver oil) 50,000 I.U.; vitamin D (from fish liver oil) 800 I.U.; thiamin, 10 mgs.; riboflavin, 10 mgs.; niacinamide, 100 mgs.; ascorbic acid, 250 mgs.; and calcium (Ca CO<sub>3</sub>), 500 mgs. For details on method of distribution, *see* earlier paper (4).

alike for the two groups. The average duration of employment for those who remained in the Study nine to twelve months was 12.6 and 14.1 months for the Placebo and Vitamin subjects, respectively. Initially, all subjects were on the swing shift; that is, they worked from 4:00 P.M. to 12:30 A.M., but slightly over one-fifth of them were transferred to other shifts during the Study year.

For the purpose of appraising the psychotherapeutic effect, toward the end of the Study year a second control group was formed of men who did not participate actively in the Study and did not know of their inclusion in it. From Company records, this group was matched with respect to age, duration of employment, and type of work with the direct production workers on the swing shift who had remained in the Study and on the swing shift to the end. This group was designated the Control group.

The subjects worked in many departments of the plant; often members of all three groups worked side by side. The three groups were, therefore, subject equally to the same environmental influences in the plant, and the different kinds of work done were represented equally in each group.

#### CRITERIA USED FOR THE APPRAISAL OF INDUSTRIAL PERFORMANCE

Data were obtained from official Company records on absenteeism, classified as Unauthorized, Illness, and Authorized; on terminations, classified as Military and Nonmilitary; and on work performance (from Merit Review scores).

#### METHODS FOR THE APPRAISAL OF NUTRITIONAL AND PHYSICAL STATUS

The diagnostic problem was the recognition of mild, or moderately advanced, chronic, nutritional deficiency disease. We anticipated that there would be few or no cases of severe deficiency disease. Accordingly the examination technique was designed to

detect both mild and severe forms of these diseases. As there were no methods of proved reliability for the diagnosis of mild nutritional deficiency states, one of the purposes of the Study was to test, by therapeutic trial, the validity of claims made in this connection for certain methods and signs.

The following is a general summary of the procedure adopted. At the beginning all the subjects were given a physical examination, certain hematological and chemical analyses of the blood were made, and diet and medical histories were taken. Toward the end of the Study year all the subjects remaining in the Study were reexamined, their blood analyzed, and their diet and medical histories taken again.

In the initial examination, the procedure consisted of:

1. Medical history.
2. Diet history.
3. Physical examination with special reference to evidence of nutritional disease.
4. Biomicroscopic examination of the conjunctiva for evidence of vitamin A deficiency, and of the cornea for evidence of riboflavin deficiency.
5. Examination of the blood for syphilis, hemoglobin, red cell volume, red cell count, serum albumin, and plasma ascorbic acid.

The final examination consisted of the above with the following changes: a more detailed record of skin conditions, especially of follicular hyperkeratosis of even the slightest degree; quantitative determination of thresholds of vibratory sensibility at different frequencies; a more quantitative record of corneal vascularity; biomicroscopic examination of the tongue; routine urinalysis. The serum protein determination was omitted.

#### DIET HISTORIES

The diet histories obtained at the beginning and at the end of the Study showed that the diets of our subjects had remained

essentially unchanged (2, 4). The analysis of the diet histories of the initial examination (2), therefore, will serve for the diets of our subjects throughout the Study.<sup>5</sup> The quality of a diet may be appraised by a comparison with recommended standards of the consumption of protective food groups or of intake of specific nutritive essentials.

When the reported consumption of each of five food groups was compared with amounts recommended in the dietary pattern prepared by the Food and Nutrition Board of the National Research Council, the findings were:

(a) Percentages of diets for which the number of times used or amounts per week were equal to or slightly below that recommended:

	<i>Per Cent</i>
Green or yellow vegetables, 6 times or more	21
Citrus fruits or tomatoes, 7 times or more	36
Milk, 10 or more glasses	51
Eggs, 4 or more	59
Lean meat, fish, etc., 5 or more times	95

(b) Percentages of diets which were definitely below the recommended use per week:

	<i>Per Cent</i>
Green or yellow vegetables, 3 times or less—43 per cent	56
Less than 7 vegetables, with 5 or less green or yellow— 13 per cent	
Citrus fruits or tomatoes, 4 times or less	49
Milk, 5 glasses or less	33
Eggs, 1 or none	23
Lean meat, etc., 2 or less times	1

When amounts of all five foods in an individual diet are considered: 2 per cent of the diets included amounts of each of the five foods as described in (a) above; 11 per cent had smaller amounts for one or more foods but none as low as described in

<sup>5</sup> There was a little improvement in foods containing ascorbic acid. This improvement was not great and did not change the diet picture significantly (4).

(b) above; and 87 per cent of the diets had amounts as low as described in (b) above for one or more food groups. The latter group of 87 per cent included: 32 per cent of diets low in one food group, 36 per cent low in two food groups, 16 per cent low in three food groups, and 3 per cent low in four food groups.

One-third of the group reported having eaten less than seven servings of vegetables (other than Irish potatoes) of any type, including tomatoes, during a week. Twenty-four per cent had eaten green or yellow vegetables less than three times within the week.

Nearly one-half of the men reported no servings of tomatoes or tomato juice during an entire week, and about 30 per cent had had one serving. Although tomatoes are a moderately good source of vitamin A, they are generally more important as a substitute for citrus fruits to furnish vitamin C. The consumption of citrus fruits was also low and surprisingly so in a California group. About 23 per cent had had none during an entire week, and 17 per cent had had only one or two servings. Only 36 per cent reported seven or more servings of citrus fruit or tomatoes during the week. The blood ascorbic acid levels (3, 5) were in accord with this feature of the diet histories.

The consumption of milk was better. Eleven per cent had had a quart or more per day, and 37 per cent two or more glasses daily. Another 24 per cent averaged one but less than two glasses daily, only 37 per cent had less than one glass per day. Eleven per cent drank no milk and used none on cereals in an entire week.

Eggs were not eaten regularly. Thirty-six per cent averaged one or more a day, 46 per cent less than one a day, and 18 per cent had none.

Only 5 per cent had meat less than five times a week, and four-fifths had meat seven or more times. Liver and other glandular products were reported by 22 per cent, 15 per cent had had one serving during the week; and 5 per cent two servings.

One-third of the men ate no whole wheat, rye, or "dark" bread during a week.

Judged by recommended dietary patterns, the diet of the group considered as a whole was low in yellow or green vegetables, citrus fruits or tomatoes, somewhat better in milk and possibly eggs, and adequate in meat.

This diet would be expected to be low in vitamin A, thiamin, riboflavin, ascorbic acid, and calcium. This was borne out by quantitative estimates (made from tables) of each of the following specific nutrients in two-day diets: protein, iron, calcium, vitamin A, thiamin, riboflavin, niacin, and vitamin C.

The percentages of all diets furnishing less than two-thirds of the Recommended Daily Allowance of specific nutrients were: ascorbic acid, 46.0; riboflavin, 43.2; calcium, 24.8; thiamin, 14.0; vitamin A, 14.8; niacin, 7.2; iron, 4.0; and protein, 0.8.<sup>6</sup>

Many men were eating low-calorie diets. 8.8 per cent were estimated as getting less than 1,800 calories daily, 17.6 per cent 1,800-2,199 calories, and 20 per cent 2,200-2,599 calories. Stated in other terms, only about one-fourth the men reported eating amounts of food which furnished 180 per cent or more of their estimated basal requirement, an amount adequate for men doing eight hours a day of moderately active work. For another 36 per cent of the men, the caloric intake was from 140 to 179 per cent of their basal requirement. Nearly 40 per cent reported diets which would furnish less than 140 per cent of their basal needs; and 5 per cent reported eating less than their basal needs.

As the quantity of food eaten was reported from memory, no doubt some of the men ate more than they reported, it is unlikely that any men ate less than their basal needs. But making considerable allowance for omission of some food items or under-

<sup>6</sup> These figures are based on the original values of the Recommended Daily Allowances. The only figures which would be significantly changed by using the Modified Allowances would be those for thiamin and riboflavin. They would be reduced to 8 and 22 per cent respectively.

estimates of quantity, the evidence is strong that many men were eating quite low-calorie diets. Other studies have reported dieters which provided less energy than is usually recommended (10, 11, 12).

Estimates of caloric requirements now in use were made at a time when diets generally were inferior to those today, less fresh fruit and green or yellow vegetables were eaten and less milk was drunk, more physical work was done, the caloric intake was higher. The basal metabolic rate is influenced by the habitual caloric and protein intake (13). There is a need of redetermination of energy requirements.

The diets of most of our subjects could have been raised to the standards of "good" or "excellent" without any radical change in pattern. An increase in citrus fruits or tomatoes, and green vegetables, and a moderate increase in milk consumption—an additional glass a day for about one-fourth and an additional two glasses a day for one-third—would have been sufficient for this purpose. A small, but significant, proportion of the men ate a very restricted diet, and too little of it; they needed a generally increased consumption as well as better food choices.

It is a commentary on the difficulty of mass nutritional education of adults that the quality of the diets did not improve during the year of the Study, although there had been during this year intensive national and local nutrition campaigns which stressed the food groups of which most of our subjects ate too little. There was some improvement in the major deficiency, in the consumption of foods containing ascorbic acid.

Although most of the diets needed improvement, very few were so poor as to evoke clinical signs of severe nutritional deficiency disease. If they had been it is unlikely that the men could have held their places in the aircraft industry at the time the Study began, which was before December 1941.

Our Study group was, therefore, well suited for the therapeutic



test of methods and signs proposed for the diagnosis of mild, chronic nutritional deficiency states. The provision of a supplement containing large doses of a number of vitamins five days a week for nine to twelve months, it would seem, was a fair therapeutic test.

## RESULTS OBTAINED

I. *Industrial Morale and Work Performance* (4). At the beginning of the Study the Placebo and Vitamin groups were closely similar with respect to rates of absenteeism and of turnover (Non-military terminations) and in Merit Review scores.<sup>7</sup> Furthermore, for the first six months of the Study, absenteeism rates for the two groups did not differ significantly for any of the three classes of absences, that is, absences due to Illness, Authorized and Unauthorized absences.

In the last six months, the total absenteeism rate of the Placebo group was\* 4.79 days per 100 working days, and of the Vitamin group, 3.90 days. The difference is statistically significant and represents a reduction in absenteeism of 18.6 per cent. For each class of absences, the Placebo rate was higher, but the absolute difference between the groups was greatest for Unauthorized absences, and this difference accounted for 45 per cent of the total difference. The absenteeism rate for Authorized absences for the Vitamin group was one-third less than for the Placebo group, that for Unauthorized absences was 23 per cent lower, and that for Illness absences was only 9.5 per cent lower than for the Placebo group. The absenteeism rates due to Illness, 2.19 and 1.98 days per 100 days for the Placebo and Vitamin groups, respectively, were not significantly different; rates for both Authorized and

<sup>7</sup> Merit Reviews were made, by contract between the Company and the Union, of every employe by his immediate superior every six months. The review score given was an important factor in the decision whether or not an employe was given a raise in pay and how much. The scores used in the Study were from reviews made routinely; the reviewers had no knowledge, in most cases, of which men were participating in the Study, and, of course, were completely unaware that the subjects were divided into Placebo, Vitamin, and nonparticipating Control groups.

Unauthorized absences were very significantly lower for the Vitamin group.

Nonmilitary terminations in the last eight months of the Study were 13.5 and 8.4 per 100 employes in the Placebo and Vitamin groups. This difference is of borderline significance, the chances of its occurrence as the result of random influences being between 5 and 6 in 100.

In the Merit Review, each employe was scored by his immediate superior on six characteristics; namely, quality of work, quantity of work, adaptability, knowledge of his job, dependability, and attitude. The scores given for each characteristic range from 1 to 8. The Merit Review ratings made for the Company in the last few months of the Study were higher, on the average, for every characteristic for the Vitamin group than for the Placebo group, although the difference had been very small and not consistent at the beginning of the Study for the same employes. The average Merit Review scores at the end of the Study were 6.22 and 6.38 for the Placebo and Vitamin subjects. This difference of 0.18 is very small but is very significant statistically.

Taken together, these findings of less absenteeism from causes other than Illness, lower turnover rates, and higher Merit Review ratings for the Vitamin group seem to indicate that superior industrial morale was the major factor underlying the superiority in all three respects of the Vitamin group in the later months of the Study year.

Two of the three types of evidence which indicated a therapeutic effect of the vitamin supplement on industrial morale are drawn from objective data depicting behavior, *i.e.*, absenteeism and turnover. The third piece of evidence, the Merit Review scores, while not objective, may not be discounted entirely. Those who made the scores received explicit and detailed instructions to ensure a uniform standard of grading. The score given was a serious matter to both management and the worker as it directly

affected wages. All three pieces of evidence are remarkably in accord.

Comparisons of the nonparticipating Control group with the Placebo group indicated a positive psychotherapeutic effect on Unauthorized absences, which was short-lived and became ineffective after the first six months, and a positive effect on Illness absences which persisted throughout the Study year. There was no psychotherapeutic effect on Merit Review scores, the ratings being almost identical for the Placebo and nonparticipating Control groups.

As the same psychotherapeutic influences operated equally in the Placebo and Vitamin groups, it was, therefore, cancelled out in comparisons made between them. The only known difference in the factors operating on the two groups was the possible therapeutic effect of the vitamin supplement. On the evidence, there appears no reasonable alternative but to ascribe the greater improvement in morale in the Vitamin group to this therapeutic effect.

The consistency of the trend toward superior performance in the Vitamin group as the Study year progressed is the most persuasive feature of the evidence for crediting benefit to the therapeutic effect of the vitamin supplement. This consistency runs through all the causes given for absence, the data on turnover, and all six individual items in the Merit Review scores; it is seen in the comparison of the total populations of the Placebo and Vitamin groups and in the comparisons of subgroups matched for working shift.<sup>8</sup>

The rates of absenteeism and of turnover of both the Vitamin

<sup>8</sup> Data were collected on the number of visits to the first aid stations, as a measure of accident rate, and on tardiness. These data were so inconsistent internally, as to cast doubt on their reliability, and to warrant their exclusion. Inspection of the manner in which these reports were made and the reasons for which men visited the first aid stations found additional evidence that the recorded reports on tardiness and visits to the first aid stations were neither fairly nor consistently representative of events. The inclusion of these data would not have invalidated the more reliable data, nor have affected the specific or general conclusions deductible from the latter.

and Placebo groups were lower throughout the Study year than in the aircraft industry as a whole in southern California (4), indicating that the industrial morale of the Study group as a whole was superior to the average in the industry. In addition, as the subjects were volunteers for the Study, they may be presumed to be men who were consciously desirous of improving their health, with initiative (they acted on an opportunity to do something about it), and of a cooperative frame of mind. These traits are not present in all workers, and in those who possess them, they make for better industrial morale. The initial superiority to the average of the Study group in industrial morale obviously reduced the degree of improvement in this respect which the vitamin supplement or any practicable welfare measure could achieve.

There is, in addition, a general consideration to be taken into account in appraising the effects of any single welfare measure, namely, the multiplicity of factors which affect absenteeism, turnover, and work performance. Even among those which are known, some of the most important factors are beyond the control or even influence of either employer or employe. Those responsible for personnel relations in industry therefore do not demand a very great improvement from any single ameliorating factor, even from those as persuasive and direct as pay increases, introduction of rest periods, and improved eating facilities. What is hoped for is a worthwhile over-all result from the accumulated small effects of many factors in a welfare program.

Only a small effect can be expected from a factor operating as indirectly as the giving of vitamins, as was done in this Study, to a relatively superior group, neither severely malnourished nor undernourished, especially as, for the great majority, the work was not heavy and there were no hazards such as high temperature, very high or low humidity, or exposure to toxic chemicals.

Furthermore, this Study was conducted during the first year that the United States was in the War, and awareness of the

need for aircraft production no doubt was a strong incentive to many workers to stay on their jobs unless illness of a relatively serious nature prevented them from working. Under such conditions, any improvement in the work performance of young men which may result from taking vitamins is likely to be small. It should be borne in mind when appraising the effect of the vitamin supplement on absenteeism, turnover, and Merit ratings that, in order to obtain a measurable effect, any benefits must have been converted into spontaneous action on the part of some members of the group and that this action must have differed to a measurable extent from that of persons not receiving the vitamins.

As the vitamin supplement apparently had a beneficial effect on a group such as the above, and at a time when other incentives tended to obscure or minimize so indirect an aid as the giving of a vitamin supplement, one may reasonably expect similar or larger benefits in the general industrial population, especially where the work is strenuous and the vitamin B complex and C requirements are accordingly greater, and where the prevailing diet is less adequate than it was in our Study group.

Reduction in absenteeism and turnover and improvement in general work performance are important in themselves, whatever the explanation of the mechanism by which they were effected by the vitamin supplement. But elucidation of the mechanism is important. As stated above, all the evidence is in accord that the benefits noted were manifestations of improved industrial morale. From this point on we can only speculate. It seems a reasonable guess that improved industrial morale was associated with an improved feeling of general well-being. This claim is often made by users and advocates of vitamin supplements. It has been discredited because the evidence is not objective and the "experiments" were not adequately controlled. The following studies bear indirectly on this question.

It is well known that pathological mental symptoms occur in severe thiamin deficiency, in pellagra, and other conditions associated with severe vitamin B complex deficiency, and it is established that these symptoms are often relieved by adequate, specific therapy. The question is whether such symptoms exist in attenuated and modified form when the diet is not so deficient as to produce severe acute deficiency diseases, and extending it further, whether a vitamin supplement to a "normal" diet may effect psychological improvement above the "normal."

The Medical Survey of Nutrition in Newfoundland (6) estimated that the most serious dietary inadequacies were of calcium, and vitamins A, B<sub>1</sub>, and B<sub>2</sub>; the average available supply of these nutrients was 415 mg., 1,443 I.U., 0.90 mg. and 1.03 mg. respectively. These levels are above those at which clinical signs of severe deficiency disease commonly occur; cases of the severe acute deficiency diseases were not reported, although signs of less severe deficiency were very prevalent. The Survey characterized the people living on this diet as slow in mental reactions and lacking in initiative. The children were apathetic and subdued; they played little indoors or out. The subjects of all ages seemed older than their years.

In a placebo-controlled study of the effect of a poly-vitamin supplement on British school children, the teachers reported that a higher proportion of those who received the vitamins had improved behavior, the report from the parents was similar, but in both the teachers' and parents' records there was a high proportion of children who had apparently been improved by the control pellets (7).

Simonson *et al* (8) carried out a placebo-controlled study on the effect of a vitamin supplement on flicker fusion by "normal, healthy" adults. The daily vitamin supplement contained 6.0 mg. B<sub>1</sub>, 8.0 mg. B<sub>2</sub>, 80 mg. niacinamide, 0.24-0.32 mg. B<sub>6</sub>, and 80-120 Jukes-Lepkovsky units of filtrate factors. Twelve subjects re-

ceived the vitamin supplement and eleven the placebo. Flicker fusion was improved in eight of the twelve vitamin subjects and in one of the eleven controls. One of the vitamin subjects could not maintain his improvement when the vitamin content of the supplement was halved. The subjects with improved flicker-fusion reported improvement in mental alertness and in the feeling of general well-being.

Simonson *et al* measured on the same subjects the effect of the vitamin supplement on working capacity and endurance in five different forms of physical work. No effect was found, which was the result found by Keys and Henschel (9). Keys and Henschel drew the general conclusion that a vitamin B complex supplement to a good diet was an ineffective aid against fatigue or for the performance of muscular work. Simonson *et al* commented on this conclusion:

Working capacity and endurance depend on different functions in different types of work. Only one type was investigated by Keys and Henschel. . . . Functions of the central nervous system, which appear to be influenced by vitamin B complex, were not investigated.

The findings of Frankau (65) (*see* below) support Simonson's criticism of the drawing of final conclusions in this field from the results of one type of test.

There is a suggestive relationship between our findings that the vitamin supplement appeared to have improved industrial morale and the findings of Simonson *et al* that their vitamin B complex supplement appeared to have improved the function of the central nervous system, and that with this improvement there was a concomitant improvement in the feelings of mental alertness and of general well-being.

The experiment of Simonson *et al* resembled our Study in the type of subject, the quality of the diet, and the supplement used. They differed in, among other conditions, that our Study was carried on for a longer time; we employed no test of central nerv-

ous system function nor of resistance to fatigue; Simonson *et al* measured a physiological function while industrial morale is a psychological function.

Simonson's experiment is the first placebo-controlled study, as far as we are aware, in the important border region of physiological-psychological phenomena, in which a positive result was obtained by objective measurements on healthy adults in the relatively short period of a few months, by enrichment of a diet which was better than the minimum "necessary" for the prevention of deficiency disease. If the results are confirmed, they will indicate a fruitful direction for future investigation.

2. *Evidences of Vitamin A Deficiency* (5). Evidences of vitamin A deficiency were sought in (a) conjunctival opacity, thickening, and elevations, and in (b) the frequency of follicular hyperkeratosis. The reasons for this choice are discussed in previous reports (3, 5).

A biomicroscopic examination of the conjunctiva was made at both the initial and final examinations; the observers and rating criteria were the same on both occasions. The Study afforded, therefore, a therapeutic test of the conclusions of Kruse that conjunctival opacity, thickening, and elevations in adults are reversible signs of mild, chronic vitamin A deficiency.

At the first examination all the subjects had some degree of conjunctival opacity or thickening; 80 per cent had one or more elevated spots on the conjunctiva, most of them in the horizontal meridian near the cornea. At the end of the Study year there was no difference between the Placebo and Vitamin groups in the number of conjunctival elevations. In subjects of both groups there were differences between the findings recorded at their initial and final examinations, but these differences were slight, on the whole, and the frequency of increases and decreases was practically the same in both groups.

The results of the therapeutic test on conjunctival opacity and



thickening (other than spots) were evaluated by numerical rating of the condition observed at the beginning and again at the end of the Study in fourteen small subdivisions of the bulbar conjunctiva of each eye. The changes in rating at the two examinations were not consistent in any one individual for all parts of the conjunctiva in subjects in either group, and there was some improvement in subjects in both groups. On the basis of an arbitrary amount of improvement representing fairly extensive thinning of the conjunctiva, 23 per cent of the Vitamin subjects and 13 per cent of the Placebo subjects showed this maximum change and the difference is very significant statistically. The average ratings of the Vitamin and of the Placebo groups as a whole showed slightly less opacity and thickening at the end of the Study year in the Vitamin than in the Placebo group.

A fair summary of the therapeutic test is that administration of 50,000 I.U. of vitamin A five days a week for nine to twelve months did not produce in most of the recipients a large or unmistakable improvement, there appears to have been a small positive effect in some subjects. The result in the group as a whole was not definitely positive, but it may be considered as suggestive.

It is possible, and our Study affords no information on the question, that a more prolonged period of therapy or larger doses than were given in this Study may effect more complete reversal of conjunctival thickening and opacity than we observed. Another related question on which our Study provides no data is whether or not any level of vitamin A intake maintained all through life will prevent or retard the development of conjunctival opacity and thickening. The question resolves itself into whether or not the pre-xerotic condition described by Pillat and others (5) which has been proved to be associated with vitamin A deficiency and which responds to vitamin A therapy is etiologically related to the similar appearing, very frequent, conjunctival condition in a population such as ours. Is the latter condition

the result of a more chronic, milder vitamin A deficiency requiring more prolonged and massive therapy to reverse it than the former?

A high prevalence of mild follicular hyperkeratosis was found at the second examination, less in the Vitamin than in the Placebo group; rates were 68 and 83 per cent, respectively. A severe form of this condition has been proved to be associated with a vitamin A deficiency in man and in the rat. The condition is reversible, *i.e.*, it disappears nearly completely with adequate vitamin A therapy (5). In our cases it was milder than in the cases described by Frazier and Hu and others. Its frequency, severity, and the extent of skin involved were less at the final examination in the Vitamin than in the Placebo group.

At the first examination only the severe form of follicular hyperkeratosis was noted (very few such cases were found), while on the second examination even the mildest degree was recorded. The data of the two examinations, therefore, are not comparable, and it is not permissible to conclude that the less frequent and milder follicular hyperkeratosis found in the Vitamin than in the Placebo group at the second examination represented a therapeutic effect of the vitamin supplement.

There is reason to believe, however, that this difference between the two groups may have been a therapeutic result. At the beginning of the Study the two groups were practically the same in every respect in which they were compared. If one assumes that they were probably the same at that time with respect to follicular hyperkeratosis, then the difference in the two groups at the end of the Study in favor of the Vitamin group would represent a therapeutic effect of the vitamin supplement. But a firm conclusion cannot be drawn so long as it rests on such an assumption, it must be classified only as a suggestion which warrants an adequately controlled therapeutic trial.

There is another reason for caution. The prevalence of mild

follicular hyperkeratosis at the end of the Study year was quite high in the Vitamin as well as in the Placebo group. Would more prolonged therapy clear these cases, or, are there both reversible and irreversible forms of mild follicular hyperkeratosis? If there are, is their etiology the same, or is it different? The Study leaves these questions open.

3. *Evidences of Thiamin Deficiency* (5). The first examination found a considerable number of our subjects with conditions frequently associated with proved thiamin deficiency. A relatively small number had absent ankle and knee jerks. Calf muscle tenderness and plantar dysesthesia were found in 15 per cent of subjects, and impaired vibratory sensibility in over 25 per cent. Other studies have reported similar findings.

The Study provided a therapeutic test of whether these neurologic changes can be reversed in a year by a supplement containing large doses of thiamin and other vitamins.

The results of the test were negative.<sup>9</sup> All of the data, including measurement of thresholds of sensibility to different frequencies of vibration were consistent in showing no significant differences between the Vitamin and Placebo groups at the end of the Study year.

Impaired vibratory sensibility and paresthesias evoked by vibratory stimulation were significantly more frequent in the older than in the younger age groups. As these signs of impaired neurologic function occur in an otherwise healthy population, they appear to warrant classification as "pre-senile" changes.

<sup>9</sup> For conditions which occur infrequently in the population, the difference between two rates must be relatively larger in order to be statistically significant than in the case of conditions which are fairly prevalent. For example, one or both ankle jerks were absent in 10.0 per cent and 8.1 per cent of the Placebo and Vitamin subjects, respectively, and although the latter rate is 19 per cent lower than the former, a difference of this amount may be expected to occur from chance in 40 to 50 out of 100 trials for groups of about 260 persons. The rate for the Vitamin group must be less than 5.0 per cent, or a reduction of 50 per cent as compared with the Placebo rate, in order to show a statistically significant difference. On the other hand, the prevalence of follicular hyperkeratosis was 68 per cent among Vitamin subjects compared with 83 per cent among Placebo subjects, or 18 per cent less frequent, and the difference would be expected to occur from chance less than once in 1,000 times.

Yet it is anomalous that the same signs disappear with adequate therapy in proved cases of thiamin deficiency and not in a group of "normal" subjects. To classify these signs in the latter group as "pre-senile," *i.e.*, as signs of an irreversible condition, when they are demonstrably not so in a group whose reparative processes might be expected to be less effective, seems premature.

There are a number of possible explanations of the anomaly: we might have found a different result if the vitamins had been given parenterally instead of orally, or if our supplement had included other members of the vitamin B complex and such therapeutically allied substances as are contained in liver extracts, or a mild deficiency of long duration may lead to greater irreparable damage than a severe deficiency of short duration.

The high incidence of neuropathology in "normal" young people calls for thorough study. And judgment on its etiology, cure, and prevention may well be suspended at present.

4. *Evidence of Riboflavin Deficiency: Corneal Vascularity* (5). Since the publication by Kruse *et al* that vascularization of the cornea is an early and specific sign of riboflavin deficiency, it has been the subject of much investigation and discussion (5).

As practically all our subjects had some degree of corneal vascularity at the first examination, and over 40 per cent had "streamer" type vessels extending beyond the limbus into the cornea, the group was well suited for a therapeutic test of corneal vascularity as a reversible sign of riboflavin deficiency.

The results of this test, as in most other studies of the question, were negative.

5. *Evidence of Vitamin B Complex Deficiency* (5). The evidence sought was in the face and skin—seborrheic and pellagrous dermatitis and angular stomatitis; in the lips—cheilosis; and in the tongue—abnormal coloration, hypertrophy or atrophy, and abnormalities of the papillae (by biomicroscopic examination).

Most of these are signs of severe deficiency states; few cases with

signs of severe deficiency were found either at the first or second examination. This was to be expected in subjects such as ours. On the second examination, when milder degrees of the above abnormalities were noted, 17.2 and 7.3 per cent of the Placebo and Vitamin subjects, respectively, were found with two or more signs on the tongue associated with niacin or vitamin B complex deficiency.<sup>10</sup> The conditions found are presumably referable to chronic, mild deficiency states. Our findings suggest a possible therapeutic effect of the vitamin supplement, they afford no proof as there were no comparable data from the initial examination. The situation is the same as in the prevalence of follicular hyperkeratosis. The findings in both instances are in accord with those of other studies which were adequately controlled.

6. *Results of Laboratory Tests (5)*. On the first examination many subjects had low plasma ascorbic acid levels, in 32 per cent they were below 0.40 mg. per cent and in 10.7 per cent below 0.20 mg. per cent. As the vitamin supplement supplied 250 mg. ascorbic acid daily the Vitamin group levels at the second examination were high; nearly all were above 0.90 mg. per cent. The Placebo group levels were a little higher than at the first examination, in only 17.7 per cent were they below 0.40 mg. per cent and in 2.6 per cent below 0.20 mg. per cent.

We were not in a position to obtain any evidence of the effect of the ascorbic acid supplement on gum conditions which have been interpreted by some workers as prescorbutic signs, *i.e.*, as indicating mild to moderate, acute or chronic vitamin C deficiency.

The hematological picture was not improved by the vitamin supplement, even in the cases of anemia, most of which was mild. There were no cases of severe anemia.

<sup>10</sup> A lower prevalence of seborrhea and sebaceous plugs on the nasolabial folds (a condition attributed to riboflavin deficiency) in the Vitamin group than in the Placebo group was suggestive of a possible therapeutic effect, but the difference in rates, 8.4 and 12.0 per cent, respectively, was not statistically significant. A difference as great as this may be expected to occur as a result of random sampling once in five to six times, *see* footnote 9.

There were no notable findings in the routine urinalyses of either the Placebo or Vitamin groups.

7. *Effects of the Vitamin Supplement and of the Placebo on Symptoms.* In the medical histories of the first examination about 80 per cent of the subjects reported having had one or more colds recently; more than half had symptoms of eye discomfort, or of gastro-intestinal malfunction; and between 10 and 25 per cent reported cramps, burning, or pins and needles in the feet, and of being easily irritated. When the data of the second medical history were compared with those of the first no evidence was found of any consistent beneficial effect of the vitamin supplement on the incidence or severity of upper respiratory infections, including colds, nor of improvement in symptoms. Nor was consistent evidence found of a beneficial psychotherapeutic effect.

The reports in the two medical histories were often inconsistent with the replies when the subjects were asked, "Did you get any benefit from the pills?" and when the answer was "yes," "what benefit?" Over 70 per cent of the subjects in the Placebo as well as in the Vitamin group reported a number of symptomatic benefits which they ascribed to the tablets and capsules they had been taking. The benefits they most frequently reported in answer to these questions were fewer or less severe colds, improved appetite, a feeling of better general well-being, and improvement in eye symptoms. There were slightly more such reports from the Vitamin than from the Placebo subjects.

#### INTERPRETATION OF THE CLINICAL RESULTS

In an appraisal of the clinical value of vitamin supplements such as were used in this Study, and based on our results, certain characteristics of our subjects should be taken into account. Over 70 per cent were under 30 years of age at the beginning of the Study. They had passed preemployment medical and psychological aptitude examinations, and their health and their psycho-

logical aptitude were important points in their selection for employment. The factor of selection was real because, at the time these men sought employment, the labor supply exceeded the demand.

No acute or severe nutritional deficiency diseases were found at the beginning nor at the end of the Study. This was to be expected in a group so selected, which was relatively well paid, on steady employment, and living in a section of the country where the quality of the diet was, on the whole, superior to that in any other part of the country (16). Consequently there was no opportunity for dietary improvement, by vitamin supplements or other means, to effect dramatic improvement in health, which undoubtedly would have occurred had there been a relatively high prevalence of severe or acute nutritional deficiency diseases.

These characteristics of our subjects are doubtless responsible, in part, for the slightness of the improvement of clinical signs in the recipients of the vitamin supplement. One of the objectives of the Study was to ascertain in precisely such a population as the subjects of the Study the degree, if any, of mild, chronic nutritional deficiency. The proof of the existence of such states and their diagnosis are two aspects of the same question. This was, and still is, an unsettled question, and the slight, inconclusive, though suggestive results obtained in the Study may aggravate the controversy. It seems worthwhile, therefore, to place in juxtaposition interpretations of the clinical results of the Study from the two opposed points of view, and to indicate the qualifications necessary to a fair summary of the findings and their implications.

The interpretation from one point of view is that the vitamin supplement contained therapeutic, *i.e.*, large doses, of vitamin A, thiamin, riboflavin, niacin, and ascorbic acid. It was administered for a long period, *i.e.*, five days a week for nine to twelve months, long enough to expect a definite therapeutic response if the conditions taken as indicative of nutritional deficiency be really such.

The Vitamin group was not better than the Placebo group at the end of the period of therapy with respect to elevated conjunctival spots, corneal vascularity, and neurological abnormalities, including vibratory sensibility; and was only slightly so with respect to conjunctival thickening, follicular hyperkeratosis and tongue conditions. Of the three positive results, only that on conjunctival thickening may be taken as established by the comparison of strictly comparable data obtained at the beginning and at the end of the Study, the other two positive results are admitted to be only suggestive. More important than the slight positive results, established or suggested, is the persistence of most of the alleged signs of nutritional deficiency in the Vitamin subjects to the end of the Study year. These, accordingly, must be considered either irreversible or not the result of nutritional deficiency. They may not be construed as evidence of currently existing deficiency. As they do not appear to affect the subjects, the burden of proof is on those who would ascribe to these conditions any morbidity significance. Such proof, adequately confirmed, has not yet been presented.

The foregoing summary and interpretation take no account of the improved industrial morale in the Vitamin group; on this point the evidence is conclusive. The improved morale manifested itself in measurable, objective behavior. It was superimposed on a psychotherapeutic effect and, on the evidence, must be taken as a therapeutic effect of the vitamin supplement. Hence there must have been an organic basis of nutritional deficiency or of suboptimal nutritional status, whether detectable by present clinical or instrumental methods or not. It is well known that chronic disease requires long treatment, and it is not excluded that a longer period of therapy than in this Study may have cleared up many more, if not most, of the abnormal conditions observed on the conjunctiva, skin, and tongue.

The interpretation from the other point of view is that all the



positive results found in the Study, on industrial morale, conjunctival, skin, and tongue conditions fit consistently into a general interpretation that in the great majority of the subjects the signs observed were manifestations of mild, but prolonged, previous deficiency. The therapeutic response in such conditions is very slow. Even symptomatic improvement in terms of feeling better, which in acute deficiencies comes quickly with appropriate therapy, was sufficient to affect the behavior of our subjects only after a number of months, which is evidence of the chronicity of their condition. The concept of chronic and acute deficiency states as formulated by Kruse (39) is consistent with the finding of marked improvement or cure of physical signs in only a small percentage of cases, even for those signs for which positive results were obtained. In vitamin A deficiency, follicular hyperkeratosis is a later sign than conjunctival changes; every person in the Study exhibited the latter condition and not all the former. The follicular hyperkeratosis showed a somewhat better response or quicker response than the eye lesions. Conjunctival spots did not disappear, but as these are areas of greater elevation than the surrounding tissue they will continue to be so until repair of tissue is nearly complete. In the case of tongue changes nearly every person had furrows or fissures, a moderately advanced chronic state, and this sign did not respond to therapy. Redness and hypertrophied papillae frequently are associated with a subacute process and therefore the therapeutic response was more rapid and more definite. More prolonged therapy would have enlarged the demonstrable improvement.

Against this interpretation it must be pointed out that in the three therapeutic tests from which firm conclusions could be drawn (in which the data of the examinations at the beginning and at the end of the Study are strictly comparable), *i.e.*, conjunctival and corneal conditions and vibratory sensibility, there was only slight improvement in conjunctival thickening, much less

than might have been expected from the observations of Kruse, and no improvement was found in conjunctival elevations, corneal vascularity, and impaired vibratory sensibility.

The failure of conjunctival spots to respond is inconsistent with the "theory"; these are a later lesion<sup>11</sup> in xerosis than opacity; reports on healing in cases of Bitot's spots indicate that the first stage in repair is fragmentation of the spots (which is in accord with Kruse's conception that the sign last to appear is the first to disappear in therapy). Yet no change in the spots was observed. No firm conclusions may be drawn from the other positive results, *i.e.*, on follicular hyperkeratosis and tongue conditions, because the data on the first and second examinations are not comparable, and as has been emphasized, they may be taken only as suggestive. The definitely negative results on corneal vascularity and vibratory sensibility remain unaccounted for.<sup>12</sup>

The crucial point is whether or not a more prolonged period of therapy would have enlarged the demonstrable improvement. The expectation that this would be the case is based on the work of Kruse. It needs confirmation. Our results are suggestive, they are far from proof, and they emphasize the need for very long time studies on humans and on animals in which similar chronic deficiency lesions have been produced before conclusions may be drawn.

#### TESTS PROPOSED FOR THE DIAGNOSIS OF MILD NUTRITIONAL DEFICIENCY

We shall exclude entirely from the following discussion the diagnosis of severe nutritional deficiency, and confine it to those

<sup>11</sup> In a private communication, Kruse expresses disagreement with the view that spots appear late in the development of xerosis conjunctivae. Instead, the area of the spot is the site of early change and the one most severely affected; in chronic deficiency, the lesion progresses and opacity usually develops over an increasing area of the conjunctiva. Under therapy, healing occurs in the reverse order. In this connection, it should be mentioned that in this Study elevated "spots" were noted in cases showing all different degrees and extent of translucency and opacity.

<sup>12</sup> See discussion above in the section "Evidences of Thiamin Deficiency."

cases where the diet and medical history may indicate the possibility of a mild, chronic deficiency.<sup>13</sup>

There are, in general, two different circumstances in which diagnostic tests are needed. One is in the treatment of an individual patient in a physician's office or hospital where even a tentative diagnosis is useful as a guide to therapeutic trial. The therapeutic trial is of an abnormal condition which has been proved to be remediable by the therapy to be used, *i.e.*, the abnormal condition is reversible.

The results obtained in our Study indicate that mild forms of follicular hyperkeratosis, and possibly acne, appear to offer some promise of a positive response to massive doses of vitamin A continued for a number of months. In a small per cent of cases there may also be some lessening of conjunctival opacity and thickening. In the majority of cases, vitamin A therapy will not affect these conjunctival conditions within a period of a year or less.

Abnormal coloration of the tongue, hypertrophy or edema of the tongue, and abnormalities of the lingual papillae (observed with the biomicroscope) appear to offer some promise of a favorable response to vitamin B complex therapy.

The following conditions, according to our experience, will not respond to one year's therapy by the vitamins tested in the Study: localized elevations of the conjunctiva, absent reflexes, paresthesias and dysesthesias, impaired vibratory sensibility, corneal vascularity, mild anemia, ocular and gastrointestinal discomfort.

The other circumstance in which diagnostic tests of nutritional deficiencies are needed is in surveys of nutritional status. Ideally the tests used would enable distinction to be made between signs of current, *i.e.*, active deficiency states and those which may be designated as passive, *i.e.*, where the deficiency which precipitated the sign in question no longer exists. As many or all of these

<sup>13</sup> For the sake of clarity our conclusions are stated here with a minimum of qualification. The qualifications are discussed in preceding reports with the detailed presentation of the data.

signs do not affect the individual noticeably, knowledge of their long-time morbidity significance, whether they be active or passive, would be of great value. The available tests and knowledge fall far short of these ideal specifications.

Nevertheless enough work has been done for a useful beginning to be made. Our experience in the Study suggests the following specifications as a practical working basis. A *sine qua non* is confirmed evidence that the sign appears in nutritional deficiency states, or evidence that it responds favorably to therapeutic trial. Its usefulness, even when it satisfies these conditions, is in proportion to its specificity. Still another condition needs to be satisfied: when a sign of a specific deficiency is found in a population there should be a good correlation between it and the prevalence of the related dietary deficiency. On the other hand, a wide prevalence of the sign in a population where diet is not deficient in the nutrient in question need not, for the present at least, be held too strictly against the validity of that sign, because it is possible that the deficiency had occurred some time before and the subsequent diet did not contain enough of that nutrient to repair the tissue damage, for which therapeutic doses would be needed.

Of all the diagnostic signs employed in this Study, follicular hyperkeratosis most nearly meets the above requirements. Moulton (17) found follicular hyperkeratosis to occur in rats on a vitamin A intake several times that required for a normal growth rate. A relatively high prevalence has been found in surveys of populations in England (18), in Newfoundland (6), and in Tennessee (19); the allied condition of follicular conjunctivitis has been found in American school children (20).

No correlation was found between the prevalence of the dermatosis and plasma vitamin A levels by Youmans *et al* (19) and by Milam and Anderson (21). Nevertheless, Youmans *et al* expressed the opinion,

It is true that at best the dermatosis is not pathognomonic. It is

however a sign of considerable reliability and meaning when properly applied.

Our findings suggest that abnormalities of the tongue may be a useful sign of mild or moderate nutritional deficiency. There are stronger indications to this effect in the more adequate studies on this point of Kruse (22) and of Sevringhaus and Kyhos (23).

Abnormalities of the gums may prove so also (24, 25).

In different population groups, other deficiency signs which we did not study or test may be useful, *e.g.*, subnormal stature (26, 27), faulty bone structure (27), mild anemia because of protein or iron deficiency (28, 29). They need to be studied further in this connection.

The foregoing appear to be useful guides to the recognition of active mild or moderate nutritional deficiency states.

No other clinical signs have won any confidence among the consensus of investigators of populations living on diets whose quality was intermediate between that generally recommended and of those known to precipitate signs of severe deficiency (19, 21, 30-36). Though our findings are in accord with theirs we would not subscribe, at present, to the firm negative conclusions drawn by some workers.

In most of the studies reporting negative results, the tests employed were used with the expectation that they were of active deficiency states. When no correlation was found between the prevalence of the sign in question and the quality of the diets (usually the sign was found in many individuals whose diets were not considered deficient in the related nutrient), it was concluded or inferred that the sign had no nutritional morbidity significance, past, present or future; which is not warranted for reasons discussed above.

There is need for further investigation of pathological conditions which appear during a period of severe deficiency, are specifically associated with that deficiency, and are removed by thera-

peutic but not by normally adequate nutritional amounts of the deficient nutrient—but, if not treated adequately, do not respond, after a time, even to therapeutic doses. Subnormal size in rats has proved to be such a phenomenon (37). Aykroyd (38) observed in patients with beriberi that unless they were energetically treated, foot and wrist drop, localized impairment of tactile sense, and paralysis may become permanent.

Long period studies of mild chronic nutritional deficiencies would be even more important for American and European populations, as such deficiencies are probably by far the most frequent among them. According to Kruse, mild chronic deficiencies are analogous to acute deficiencies in the sense that the resulting pathological conditions require therapeutic doses for a long period for their correction, and this is his explanation of the common finding of stigmata of nutritional deficiency in subjects with amounts of the nutrient in question in their diet and blood which are considered adequate for maintenance of a normal nutritional state (39). It is possible also, as in acute deficiencies left too long without adequate treatment, that mild chronic deficiencies may lead eventually to irreversible changes.

Until more and definite information is obtained on the change from reversibility to irreversibility (relative or absolute) of pathological conditions associated with nutritional deficiency, surveys of populations where only mild nutritional deficiencies are possible or probable will be severely handicapped, and can provide information of only very limited usefulness either to the public health nutritionist or in the treatment of an individual case.

#### OPTIMAL VERSUS NECESSARY NUTRITION

The point of departure of this Study was the premise, widely held, that there is a difference between “necessary” and “optimal” nutrition. Among its other purposes, the Study was designed to test the validity, *i.e.*, the demonstrability of the distinction in man. The subjects of the Study were well suited for the purpose.

The word "versus" in the statement of the question (it is in the title of one of Sherman's papers) implies the controversial attitude which has prevailed much of the discussion of it in recent years. In the course of the controversy the implications of the fundamental experimental evidence which gave rise to the question have received little attention, and certain necessary distinctions have been overlooked.

The original and fundamental experiments are those of Sherman and his collaborators extending over the years 1921 to 1945 (40-52). The experimental animal was the rat. The findings may be summarized as follows: The work began with a diet consisting of whole milk and whole wheat which was adequate for a normal rate of growth, adult size and vitality, length of life, and the successful breeding of healthy offspring. Enrichment of that diet by calcium, vitamins A and B<sub>2</sub> (and other nutrients present in larger amounts in milk than in whole wheat), gave a superior rate of growth, greater average adult size and vigor, a longer duration of reproductive life, longer average life, a greatly improved breeding record both with regard to the number and health of the offspring, and superior ability of the offspring to withstand periods of nutritional deficiency. Sherman *et al* stated in 1939,

As yet, each of our modifications of an already adequate dietary which has increased the length of life has extended the period of adult capacity and vitality rather than the period of physiological old age.

An important consideration in the application of these findings to man was that these "modifications of an already adequate dietary" were well within the bounds of normal and adequate nutrition. It was found later that threefold increase of some nutrients (calcium, vitamins A and B<sub>2</sub>), which may be beyond "the bounds of normal and adequate nutrition," continued to produce beneficial results.

The basic diet in the above experiments appears to have been somewhat low in choline and possibly other factors. Using a different basic diet, Waterman and Ammerman (53) found that rats on increasing levels of thiamin, far above that required for normal growth, grew faster and attained greater adult size; and this effect persisted through successive generations maintained on high thiamin levels.

Spector *et al* (54) found that high levels of riboflavin permitted dogs to withstand loss of blood better than a "normal" riboflavin intake.

It is well known in the poultry industry that enrichment of a good diet of hens improves their egg-laying record and the hatchability score of their eggs.

Rapid growth is not always correlated with postponement of senility and longevity (37, 51), with this modification the main conclusion may be taken as established that enrichment of a so-called "normal" diet of animals is beneficial to them and to their offspring. The enriching factors may be natural foods, food concentrates, or synthetic substances.

The beneficial effects observed in the adult animals were relatively small, in some instances they were not seen until the next or successive generations. A "one to one" correlation of differences between single pairs or of small groups of animals did not occur because of the variability of biological material, and, as a result, a statistical analysis of the differences in fairly large groups was required to demonstrate the significance of the differences.

In the application of these findings to human nutrition there is no reason to expect greater or more dramatic effects than are observed in experimental animals. In fact they may be expected to be smaller in view of man's longer life cycle, and his exposure to a variety of unfavorable conditions in his external environment, especially when the enrichment is begun in adult life.

It is this implication of the findings on animals which has com-



monly been overlooked by critics who appear unwilling to accept in experiments on human subjects a difference between experimental and control groups which, though small in an absolute sense, appears to be significant on statistical analysis.

Furthermore there is a need for more precise definition of the terms "normal" or "necessary" and "optimal" nutritional states. Sherman and others judged the "normal" or "necessary" level of nutrition for their experimental animals by arbitrary standards of growth, fertility and longevity; enrichment of diets so designated led to superior performance by these criteria. They made no histological studies to ascertain whether or not their animals, when fed the "necessary" or higher dietary levels, were entirely free of certain pathological changes which are now either proved or suggested to be the result of a nutritional deficiency. Thus, Moulton (17) showed that follicular hyperkeratosis occurs in the rat at levels of vitamin A intake several times that required for a "normal" growth rate. Should "normal" or "necessary" nutrition be defined as that in which there is not even minimal tissue pathology of nutritional deficiency origin? And is there an "optimal" nutritional state above such a level? It would be only confusing to attempt to provide answers to these questions by convention.

A more realistic position at the present time and a practical point of departure for future studies would appear to be that pathological tissue changes occur on diets which are sufficient to prevent the classical picture of gross severe deficiency disease. These lesser lesions require special methods for their detection. Sometimes their deleterious effects may be inferred (statistically) from the inferior performance of subjects on such a diet as compared with those on a superior diet. In other instances they appear to have no current deleterious effects, but long period, large scale studies of their possible effects on morbidity are needed before it would be safe to conclude that this is the case. At any rate it is certain that the benefits one may reasonably expect from the cure

of lesser lesions (some of which are considered by some as "normal") are not dramatic nor easily measured. Nevertheless over the whole life cycle or for a nation as a whole they may be profoundly important.

In investigations of the effects of different dietary levels above that required for the prevention of acute or severe deficiency disease it would appear, judging from the work on animals, that the most striking positive effects are likely to be found in children. No positive effects can be expected in adults in a few weeks or months, and the benefits in adults will consist in the arrest or improvement of changes associated with increasing age, *i.e.*, retardation of so-called senile changes.

In such investigations the levels of at least some of the specific nutritive essentials tested need to be carried far above even those of the Recommended Daily Allowances and for long periods, for years. Such studies would furnish data on levels of "optimal" nutrition and of therapy necessary to repair the effects of chronic deficiency. Only those studies on man in which high levels are administered for long periods afford valid comparisons with the experiments of Sherman and others on "optimal" nutrition in animals.

The relevant experiments on man to test the possible effects of dietary enrichment have, on the whole, yielded results which may be considered as positive when viewed from the context of the related animal experiments, and considered simply as the effects of improving a diet which was sufficient to prevent the appearance of a classical picture of severe nutritional deficiency disease, with the definition of the terms "necessary," "normal," and "optimal" left in abeyance. Thus Ebbs *et al* (56) found that pregnant women on "poor" diets which were enriched with a supplement of protective foods and food concentrates had fewer complications during pregnancy and at term, and healthier offspring, than those on un-supplemented "poor" diets. In a number of respects the record

on the supplemented "poor" diets was slightly better than that on "good" diets. Similar results have been obtained in other studies (57-58).

Colby *et al* found that an increased thiamin intake accelerated the mental and physical growth of infants (59). The differences were marked in the first months of life and grew smaller at the end of twelve months.

Beneficial effects of vitamin supplements were observed by Kohn *et al* (60), Harper *et al* (61), and Bransby *et al* (62) in school children and young adults in England during the war years. The three studies did not agree in all their findings, but they were in accord that "endurance" (measured differently in the different studies) was better in the vitamin than in the placebo groups.

Harrell (63) found in a placebo-controlled study that the rate of learning of children receiving 2.0 mg. thiamin daily was greater than those receiving 0.9 mg. daily.

We have referred to the experiments of Keys and his co-workers (9, 64) who found no benefits from increased thiamin or riboflavin intake in young adults performing severe muscular work, neither in the amount of work performed nor in recovery from fatigue. These experiments were relatively short, the longest not extending over a few months, and are, therefore, not pertinent, for reasons discussed above, to the question of whether the findings of Sherman and others on animals occur in man.

Also against them stand the findings of Egana *et al* (65) that some subjects on a vitamin B complex deficient diet supplemented with 36 gm. of yeast daily recovered better from exhausting physical work than in the subsequent period on an unsupplemented "normal" diet.

The findings of Frankau (66) in a series of carefully controlled experiments are in the same direction. The subjects were healthy adult males in the age group 18-32 (R.A.F. air-crew cadets) "in

excellent physical condition.” The tests chosen involved both physical effort and coordination; they were severe and called for the utmost cooperation from the subject, whose condition at the end of the test was just short of distress as evidenced by his breathing and pulse rate. The giving of 50-200 mg. niacinamide a few hours or daily for several days before the test, alone or with other vitamins, was followed in every one of six experiments by greater efficiency in the group receiving the vitamins than in the comparable placebo control group. The differences between vitamin and placebo groups were always small, but in every instance they were statistically significant.

Possibly the most promising experiment here is that of Simonson *et al* (8), summarized above. Their findings suggest that a greatly needed bridge may be found between neurophysiological and psychological phenomena. Such a bridge is needed, for example, to analyze the beneficial effect of the vitamin supplement on industrial morale observed in this Study (4).

None of the above studies on human subjects is without shortcomings as proof of benefits conferred by a level of nutritional quality above that designated as “necessary.” No studies yet carried out provide even rough estimates of “optimal” levels of one or more specific nutrients for the whole lifetime of men and women and their succeeding generations. Nevertheless, the few studies on man, taken together, suggest that the findings in experimental animals will be found to occur, in some degree, also in man. These experiments, of course, need to be confirmed before any, even tentative, conclusions may be drawn.

Measurement of function, especially of the central nervous system, in different age groups, and of ability to withstand and recover from physiological stress over fairly long periods appear promising. Improvement of function in the central nervous system can occur without demonstrable anatomical changes, and may accompany and thereby provide a measure of the feelings of

well-being. If a bridge can be found between psychological phenomena and measurable physiological functions which parallel the state of well-being, it will be valuable obviously in other studies of human behavior as well as greatly facilitate study of the effects of improved nutrition. The successful application in psychosomatic medicine of Cannon's findings on the physiological concomitants of emotional states is an indication that such a bridge may be found.

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