NUTRITIONAL STATUS OF AIRCRAFT WORKERS IN SOUTHERN CALIFORNIA[1]

II. CLINICAL AND LABORATORY FINDINGS

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MOST workers in the United States are not obtaining adequate diets. Stiebeling and Phipard (1) examined the diets of families of employed (nonrelief) workers in four great geographical regions—North Atlantic, East North Central, East South Central, and Pacific—in the years 1934-1937. In the Pacific region on the average, 14 per cent of the family diets were "good," 46 per cent were "fair," and 40 per cent were "poor." In the three other regions the percentage of "poor" diets was even higher.

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This survey is under the direction of one of us (H. B.). We were assisted in the organization of the examination procedure by Miss D. G. Wiehl and Dr. H. D. Kruse of the Milbank Memorial Fund. The forms on which the data were collected were drawn up by Miss Wiehl. We are indebted to Miss Wiehl also for the tabulation of a part of the data reported here, and for her thorough and valuable criticism of the manuscript of this paper. Dr. Kruse instructed us in the use of the biomicroscope; his method of recording the biomicroscopic examinations was employed.

The physical examination and medical history procedures were worked out by Dr. Robert Goodhart and Dr. Elmer Alpert. Dr. E. D. Kremers participated in the physical examinations.

All the examinations including the laboratory determinations were carried out at the plant of the Lockheed Aircraft Corporation at Burbank, California.

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The basis for their classification of "good," "fair," and "poor" diets is given in Table 1.

The standards for vitamins B_1 and B_2, used by Stiebeling and Phipard, are lower than the allowances recommended by the Committee on Food and Nutrition of the National Research Council (2). If the latter standards had been used, the "good" diets in the Stiebeling and Phipard survey would have been much less than 26 per cent and the "poor" diets much greater than 50 per cent.

The Committee on Nutrition in Industry of the National Research Council has pointed to the abundance of other evidence from which the same conclusion must be drawn—that the diets of our workers are not as good as they should or can be (3).

One study may be cited (4), that in Pasadena between May and August, 1938, which was in the same region as the present survey. It was found that the intake of calories and protein was adequate in all families of employed workers; but the intake of calcium and

Table 1. Comparison of the basis of classification of diets used by Stiebeling and Phipard and daily allowances recommended by the Committee on Food and Nutrition of the National Research Council.

Nutrient	Standards for "Good" and "Poor" Diets[1] Used by Stiebeling and Phipard[2]		Daily Allowances[1] Recommended by Committee on Food and Nutrition, National Research Council (2)
	Quantities in Uncooked Food		
	"Good"	"Poor"	
Protein, Gm.	67	45	70
Calcium, Mg.	680	450	800
Iron, Mg.	15	10	12
Vitamin A, I.U.	6,000	3,000	5,000
Vitamin B_1, Mcg.[3]	1,500	750	1,800
Vitamin B_2, Mcg.[4]	1,800	900	2,700
Vitamin C, Mg.	75	37	75

[1] For a moderately active man weighing 70 kg.
[2] Diets that were better in every respect than the specifications for "poor" diets, but poorer in one or more specific nutrients than the specifications for "good," were classed as "fair."
[3] 1 I.U. taken as equal to 3 mcg.
[4] 1 Sherman Unit taken as equal to 3 mcg.

vitamins A and B was inadequate in more than one-third of the families studied. There is one important dietary difference between the 1938 group and the present one. In 1938 even the poorest families obtained 70 mg. or more of vitamin C per "consumption unit"; in 74 per cent of the families leafy vegetables contributed more vitamin C than citrus fruits. In the present survey over 40 per cent obtained unsatisfactory amounts of vitamin C (5). It is unlikely that the difference in vitamin C intake between 1938 and 1940-1941 can be ascribed to the difference in season of the two surveys—May through August in 1938 as against November through February in the present survey, because citrus fruit and fresh leafy vegetables are readily available throughout the year in this region.

The inadequate diets of our defense workers affect their health and productivity (3). The studies of Williams, *et al.*, (6) have shown that a thiamin intake as low as that of many of our workers may be responsible for such common symptoms as undue fatigue, soreness of muscles, backache, loss of interest in work, and depressed mental states.

A few employers in this country are already convinced that the productive capacity of their workers can be improved by improving their nutrition. In most cases, they have supplemented the diets of their workers with vitamin concentrates. It does not appear, however, that these measures have been supplemented by, on the one hand, an adequate study of the nutritional state of their workers, before and after the vitamin supplements were used, nor, on the other hand, have they attempted to ascertain precisely what has been gained by the use of the vitamin supplements.

It is of the highest importance for public health nutrition where measures such as these are taken that the results be carefully recorded and interpreted critically. In spite of all the experimental work which has been done, the influence of diet on human health (in cases where severe or acute nutritional deficiency disease is not present), on working capacity, on the incidence of accidents, and

on the psychological state needs to be demonstrated by rigorously controlled studies. There appears to be little reason to doubt that improvement in the nutrition of workers will improve their health and productivity; but the particular respects in which these benefits will manifest themselves remain to be demonstrated.

The Committee on Nutrition in Industry recommended "that adequately controlled studies be conducted in selected war or defense industries to determine the facts concerning the influence of diet and nutrition on health, working capacity, incidents of accidents, absenteeism, and the psychological state." (3)

A study among workers at the Lockheed Aircraft Corporation, Burbank, California was undertaken to meet this need. The initial examinations began in November, 1941, and ended in February, 1942.

The subjects of this survey are all white, male volunteers who came for examination on their own time (*i.e.*, without pay) between the hours of 9:00 A.M. and 2:00 P.M. Most of the subjects are plant workers on the swing shift—from 4:00 P.M. to 12:30 A.M., with one-half hour for lunch between 8:00 and 8:30 P.M. This shift was selected for the survey deliberately because it is the swing shift which has the most accidents, the most absenteeism, and the most complaints.

There were 1,173 men examined, coming from all the major departments of the plant and including some office workers and foremen. In a few cases, one or more parts of the examination had to be omitted because of lack of time. In some of the tables, data from thirty-two additional male subjects are included, whose work is supervisory or executive.

The subjects are receiving certain nutritional supplements. This will be continued for at least one year, after which all the subjects remaining in the survey will be reexamined. The nature of these supplements and their effects on health and work performance will be described in a later paper.

Scope of the Examination

A. Medical history.

B. Physical examination with special reference to evidence of nutritional disease.

C. Biomicroscopic examination of the conjunctiva and cornea.

D. Examination of the blood for syphilis, hemoglobin, cell volume, red cell count, serum albumin, and plasma ascorbic acid.

E. Diet history.

A previous paper contains an analysis of the diet histories obtained (5). A summary of the pertinent facts in the medical histories and the findings in the physical, instrumental, and blood examinations are presented here.

Some comment is called for on the methods chosen for the diagnosis of nutritional deficiency. The signs of severe malnutrition, *i.e.*, of xerophthalmia, beri-beri, cheilosis, pellagra, scurvy, anemia, and undernutrition of calories or protein, are now well established, and easily recognized by the above tests.[4]

We could not expect to find, except in very few cases, acute or severe nutritional deficiency states in a group such as that participating in this survey. The subjects are young men; they were selected, in part by a pre-employment medical examination. They live in a section of the country where the quality of the diet is, on the whole, superior to that in any other part of the country (1). It was clearly necessary, therefore, to pay special attention to the recognition of mild but chronic nutritional deficiency disease. The diseases we had specially in mind here were deficiency of vitamins A, B_1, B_2, niacin, and of C.

For the detection of vitamin A deficiency, the advisability of measuring dark adaptation was, of course, considered. The arguments against our using it were as follows: In two individuals having initially the same moderately high dark adaptation time, in one

[4] In man the signs of deficiency of such vitamins as B_6, pantothenic acid, inositol, and of choline had not yet been established.

the time is shortened after taking large doses of vitamin A, in the other, it is not. Except, therefore, when the dark adaptation time is very high, it is not possible to state, in regard to any one subject, whether or not a moderately high dark adaptation time will be reduced by vitamin A therapy, *i.e.*, whether the subject is vitamin A deficient or not. If we had used this test, we could have carried out only two determinations on each subject, one at the beginning of the survey, the other a year later. We would have obtained, therefore, only a statistical value for the group as a whole, and the interpretation of this statistical value rests on a comparison with groups who have been receiving vitamin A. Obviously this is unsatisfactory for an evaluation of nutritional status at any one time.

Furthermore, a definitely high dark adaptation time, *i.e.*, beyond the range of normal physiological variation, occurs only where the vitamin A deficiency is very marked; this deficiency may be of very short duration. Administration of vitamin A, in many cases for a short time, can reduce the dark adaptation time to the normal for that subject (7). In this survey, we were interested as much in the habitual diet and corresponding nutritional state as in recent dietary history and its consequences.

Accurate measurement of dark adaptation takes a good deal of time and repeated determinations are necessary. The men in this survey were examined in their own time, in the interval between arising and going to work. There were many tests and none could be used which took a great deal of time, or which required repetition as part of the initial examination.

Measurement of dark adaptation was therefore excluded.

Measurement of blood vitamin A was excluded because it, also, reflects only recent dietary history. The main reason for its rejection was, however, that we had not sufficient personnel to carry out this laborious and time consuming assay as quickly as would have been necessary on 1,200 subjects.

We chose to rely, therefore, mainly on biomicroscopic examina-

tion of the conjunctiva (8), supplementing this method by the findings on physical examinations. The reliability of the biomicroscopic method has been challenged (9, 10). This point is discussed below (page 127). We hope, after the reexamination of the subjects who will have received a large vitamin A supplement for a year or more, to be able to evaluate the reliability of the biomicroscopic method for the detection of vitamin A deficiency.

The same general considerations and limitations of personnel and time, which excluded blood vitamin A determinations, also excluded determination of the pyruvate tolerance test for thiamin deficiency. We have had to rely exclusively, therefore, on the findings on physical examination for evidence of thiamin deficiency, whether acute or chronic. In the course of our examinations, it was found that a large percentage of the men were unable to detect in their toes the vibration of a C-256 tuning fork. This may afford a quick test of degeneration of the nervous system possibly attributable to chronic thiamin deficiency, if the re-examination discloses any improvement in this respect.

Evidence of riboflavin deficiency fell into three categories. One category consisted of seborrheic changes in the face, fissuring at angles of the mouth, eyes, and lips, and magenta coloration of the tongue. These changes are rapidly reversible with adequate riboflavin therapy and may, therefore, be taken to indicate acute riboflavin deficiency (11).

The second category consisted of certain symptoms of ocular discomfort which are relieved by riboflavin therapy. These are described and discussed below (page 132).

A third category of evidence was obtained from biomicroscopy of the cornea. In riboflavin deficiency the cornea undergoes a characteristic vascularization; this has been described in rats (12) and in man (13). This corneal vascularity disappears with riboflavin therapy; but more slowly than the fissuring of the mouth and eyes.

As evidences of niacin deficiency we have used the well-known signs in the skin, mouth, and tongue (14).

The characteristic signs of vitamin C deficiency in the skin and gums, visible by gross examination occur only after months of nearly complete deprivation (15). Kruse has described changes in the gums, visible by biomicroscope, which he attributes to chronic vitamin C deficiency of a milder grade than complete deprivation (16). As in the case of the signs of chronic niacin deficiency in the tongue described by Kruse, these recent observations of his on vitamin C deficiency were not available at the time of our examinations. Here also we hope it may be possible to make biomicroscopic observations of the gums in the re-examinations.

The test of mild vitamin C deficiency we relied on was the plasma ascorbic acid concentration. This test suffers from the same limitation as the blood vitamin A, in that it reflects only recent dietary history. However, because it was possible to determine the plasma ascorbic acid in all the subjects examined, this was done. The utility of the test and the interpretation of the findings in large scale surveys are discussed below (page 136).

There is a great need today in the field of human nutrition of reliable, convenient tests of mild, but chronic, nutritional deficiency states. None of the tests proposed has yet found general acceptance. In the present survey we expect to be able, by re-examination, to observe on several hundred subjects the effect of nutritional supplementation for one year or more. One of the hoped for by-products of this survey is a verdict on the reliability and usefulness of some of the diagnostic tests for mild, but chronic, nutritional deficiency which have been proposed.

Dietary habits and the quality of the prevailing diet vary in different regions of the United States. They also vary with age. The economic factor, and whether a man is married and obtains most of his meals at home, or is single and eats mostly in restaurants or a boarding house often affect nutritional status. The information

summarized below under "residence," "age distribution," and "marital status" furnish some of this background information which may be useful in interpreting the observational data on nutritional status.

Residence. Of 1,177 employes the duration of whose residence in California at the time of their examination was recorded, 69 per cent had resided in California for more than a year. Of the remaining 31 per cent, the great majority came from the western states, Arizona, Iowa, Minnesota, and Nebraska supplying the largest number of these; only a few came from the East.

Age Distribution of 1,173 *Employes.* (Excludes 32 of unknown age and includes the executive and office personnel.)

	Per Cent
Under 20 Years	7.5
20-24 Years	38.2
25-29 Years	27.3
30-34 Years	14.7
35-39 Years	6.2
Over 40 Years	6.1

It was characteristic of the aircraft industry at the end of 1941 that most of the workers were young men. The above figures show that 73 per cent of the men examined were under 30. One year later more older men and many women were employed.

Marital Status. 44.6 per cent of 1,174 men whose marital status was recorded were single, 54.0 per cent were married, and 1.4 per cent were separated or divorced. Of the total number married, 43 per cent had no children, 30 per cent had one child, 17 per cent two children, and 10 per cent more than two children.

At the time they were examined approximately 68 per cent of the men were responsible for the support of not more than one other person besides themselves.

Incidence of Syphilis. Kahn and Kolmer tests for syphilis were done on nearly every subject. Of 1,205 men examined there were

two positive (both tests positive) and two questionable cases (one test positive, the other negative in each case).

The Company in its pre-employment examination has found positive serology for syphilis in 0.4 per cent of applicants. No man was rejected for employment solely because he bore evidence

Table 2. Ranges of height and weight found among 936 employes in the Lockheed Aircraft Corporation.

Height				Weight			
Height (Inches)	Number of Subjects	Per Cent of Total Number	Cumulative Percentage	Weight (Pounds)	Number of Subjects	Per Cent of Total Number	Cumulative Percentage
TOTAL	936	99.8			936	99.9	
62 Less Than 63	1	0.1	0.1	100–109	3	0.3	0.3
63 Less Than 64	7	0.7	0.8	110–119	7	0.7	1.0
64 Less Than 65	17	1.8	2.6	120–129	55	5.9	6.9
65 Less Than 66	30	3.2	5.8	130–139	107	11.4	18.3
66 Less Than 67	71	7.6	13.4	140–149	169	18.1	36.4
67 Less Than 68	99	10.6	24.0	150–159	194	20.7	57.1
68 Less Than 69	129	13.8	37.8	160–169	138	14.7	71.8
69 Less Than 70	152	16.2	54.0	170–179	118	12.6	84.4
70 Less Than 71	145	15.5	69.5	180–189	63	6.7	91.1
71 Less Than 72	107	11.4	80.9	190–199	39	4.2	95.3
72 Less Than 73	89	9.5	90.4	200–209	23	2.5	97.8
73 Less Than 74	49	5.2	95.6	210–219	7	0.7	98.5
74 Less Than 75	23	2.5	98.1	220–229	4	0.4	98.9
75 Less Than 76	7	0.7	98.8	230–And Over	9	1.0	99.9
76 Less Than 77	5	0.5	99.3				
77 Less Than 78	4	0.4	99.7				
78 Less Than 79	1	0.1	99.8				

RELATION OF WEIGHT TO HEIGHT
(Deviation of weight from the standard (17) for height and age)

Per Cent	Per Cent of Total Number of Men
20 or More Above Standard	7.4
10 to 20 Above Standard	13.4
5 to 10 Above Standard	11.7
Less Than 5 Above or Below Standard	33.6
5 to 10 Below Standard	15.8
10 to 20 Below Standard	15.1
20 or More Below Standard	3.0

of syphilis. The low incidence of positive serology for syphilis in the group of men in the survey is not, therefore, because they were explicitly selected in this respect.

Height and Weight. The subjects were weighed in their shoes with coats or sweaters off. Table 2 summarizes the ranges of height and weight found.

Graded on the basis of standard height-weight charts (17), 33.6 per cent were in the range of ± 5 per cent of the standard weight for their height and age. 20.8 per cent weighed 10 per cent or more above the standard and 18.1 per cent weighed 10 per cent or more below the standard.

The height-weight relation of the men, as a group, is normal; 77 per cent were between 67 and 72 inches (inclusive) tall, and the weights observed fell mainly (77 per cent) between 130 to 179 pounds. The standard weight of adult men 67 to 72 inches tall is given as 146 to 168 pounds. The correspondence between the "observed" and "standard" ranges of weights is good.

The same good correspondence exists between "observed" and "standard" weights at the maximum of the distribution curves of heights and weights. There were more men, 31.7 per cent, in the height range of 69 to 70 inches (inclusive) than in any other 2-inch range. The "standard" weight for this height is 157 pounds. The observed weight range containing the largest number of men, 20.7 per cent, is 150 to 159 pounds (inclusive), which brackets the "standard" weight of 157 pounds.

Evidences of Vitamin A Deficiency Observed

We have presented above our reasons for employing biomicroscopy of the conjunctiva rather than any other instrumental or laboratory method of diagnosing vitamin A deficiency.

There are several clinical signs, visible on gross inspection, which, it is believed, are indicative of vitamin A deficiency. One of these signs is follicular hyperkeratosis (18, 19, 20).

The difficulty in interpreting the significance of follicular hyperkeratosis is that on careful inspection it is observed, in varying degrees, in practically every adult person. In some there are only a few hyperkeratotic follicles; in others a large area of the skin is involved. All permutations of pigmentation, elevation, induration, infection, location, and duration are found.

Follicular hyperkeratosis is not specifically pathognomonic of vitamin A deficiency. It occurs in severe vitamin C deficiency, it can be caused by trauma.

Even granting that follicular hyperkeratosis is commonly the result of vitamin A deficiency, there are, for us, several pressing, unanswered questions. One is, are some of the hyperkeratotic changes reversible and some irreversible? An observation which prompts this question is that the incidence of this condition often appears to bear no relation to dietary history, present or past. An answer to this objection may be that the vitamin A requirement is much higher than is the general opinion. Against this explanation is the observation that even when hyperkeratotic follicles have been seen to diminish in size and number with massive vitamin A therapy, after several years of such therapy the skin has not become completely free of hyperkeratotic follicles.

Is it safe to conclude that only a few hyperkeratotic follicles do not indicate vitamin A deficiency, that only when a large area of the skin is involved is a positive diagnosis permissible? If so, where is one to draw the line? Another question: Is the area of involvement of pathognomonic significance?

We were gradually impressed with these questions, unfortunately, only after our examinations began. Having begun by recording as positive only extensive and marked follicular hyperkeratosis we were constrained to continue to do so in all cases. Seventeen persons, or 1.47 per cent of the 1,153 men receiving the physical examination, were recorded as having follicular hyperkeratosis. It is possible that in our re-examination it may be useful

to employ a more refined and extensive classification of this condition.

Another sign, easily visible on gross examination, which is attributed to vitamin A deficiency, is localized elevation of the conjunctiva, usually in the equatorial region and near the limbus (8). Among 1,172 cases, there were 552, or 47.1 per cent, with such localized elevations. There were in addition, 34 cases, or 2.9 per cent, with one or more pterygia. The total number with conjunctiva elevations visible by gross inspection was 586, or 50.0 per cent.

Kruse has described other conjunctival changes, visible by gross inspection, which he has attributed to vitamin A deficiency. These are absence of the milky blue color, pigmentation, and thickening. The two last named conditions are more easily seen with the biomicroscope and hence they were not recorded with any precision in the gross inspection.

As stated above, we have relied mainly on biomicroscopy of the conjunctiva for the diagnosis of vitamin A deficiency. One observes, in different cases and often in the same individual, varying degrees of opacity, thickening, and localized elevation.

Kruse has described the reversal of these changes when massive doses of vitamin A have been administered for an adequate length of time, which may be many months.

The above criteria and conclusions of Kruse have been challenged (9, 10). The issue needs to be clarified. Following Kruse, one must conclude that an individual who throughout his life has always ingested and absorbed an adequate[5] amount of vitamin A would, barring injuries, have a perfectly transparent conjunctiva. Through the biomicroscope the conjunctiva would offer no translucency or opacity to obstruct vision of the fine capillary network

[5] It is understood that the amount of vitamin A which is "adequate" may vary, *e.g.*, during a prolonged infection the need may be much greater than a good maintenance level. Habitual exposure to bright light may call for a larger amount. Imperfect absorption through the intestine, or liver disease, may necessitate the ingestion of increased amounts of vitamin A in order that an adequate amount be physiologically available.

in the sclera. When the vitamin A ingested has been inadequate for a sufficient length of time to cause thickening, opacity, or elevation of the conjunctiva, these conditions will not be cleared up by an adequate maintenance level. A mild, but prolonged suboptimal intake, will also lead to degenerative changes in the conjunctiva. Nutrition surveys have shown that the intake of vitamin A is commonly below a good maintenance level and rarely is the intake sufficient to provide against contingencies calling for a greatly increased vitamin A requirement.

It is well known that curative doses of many therapeutic agents (vitamins included) are necessarily much larger than the preventive or maintenance doses. No correlation need exist, therefore, between the presence or absence of pathognomonic conjunctival changes and the amount of vitamin A in the diet at any one time. Even though the diet may at present contain a normal maintenance amount of vitamin A, the conjunctival changes may reasonably be expected to disappear only when massive doses of vitamin A are taken for months.

Nor need there be any correlation between the condition of the conjunctiva and dark adaptation. Subnormal dark adaptation is a sign of severe vitamin A deficiency. In many subjects improvement in dark adaptation occurs in a very short time, sometimes in a few hours following the administration of a single large dose of vitamin A. This was observed by Pett and Le Page (7), and we have confirmed this observation.

This is to be expected from the physiology of vitamin A in the retina. This substance undergoes there a rapid metabolism, its combination with protein is continually being formed and broken, it is also continually being destroyed. And its rate of replenishment is obviously dependent on the amount of vitamin A in the blood stream. It is analogous, in this respect, to liver glycogen.

What is observed in the conjunctiva, on the other hand, is the end result of complex structural changes. These changes are macro-

scopic, whereas those in the retina concerned in dark adaptation are of molecular dimensions.

The conjunctival changes are the result of degenerative processes induced by long-standing vitamin A deficiency. It is reasonable to expect that massive doses are required for long periods to repair the gross structural damage of long standing, even if mild, vitamin A deficiency.

It seems to us therefore, that it is not necessarily a discrepancy that dark adaptation can be returned to normal by vitamin A therapy without any detectable change in the conjunctiva.

Table 3 contains a summary of conjunctival conditions pertinent to vitamin A deficiency observed both by gross inspection and with the biomicroscope. Graded according to severity of vitamin A deficiency, conjunctival spots represent the most severe condition, opacity without elevated spots next, and translucency which still permits the scleral vessels to be seen, the least severe deficiency.

Forty-seven per cent of our cases, as stated above, had conjunctival spots seen to be elevated by gross inspection. These spots were, of course, more conspicuous when viewed through the biomicro-

Table 3. Conjunctival conditions pertinent to vitamin A deficiency. Results of gross and biomicroscopic examination of the eyes of 1,172 employes of the Lockheed Aircraft Corporation.

Conjunctival Rating	Number of Cases	Per Cent of Total
Number Examined	1,172	100
Findings on Gross Examination		
Pterygium, 1 or More	34	2.9
Spot—1 or More Elevated Areas	552	47.1
Biomicroscopic Findings		
1 or More Elevated Areas Seen Only in the Biomicroscope But Not in the Gross	374	31.9
2 to 4 Zones Opaque But Not Elevated	158	13.5
1 Zone Opaque But Not Elevated	31	2.6
2 to 4 Zones Markedly Translucent	23	2.0

scope. Another 32 per cent had spots seen as elevated only through the biomicroscope. Judged by the above criteria 79 per cent of our subjects had evidence of severe conjunctival degeneration resulting from vitamin A deficiency which was not healed by subsequent diet or therapy. In only 2 per cent were the major portions of all four conjunctival regions sufficiently translucent for the network of fine scleral vessels to be seen through the biomicroscope.

According to the above criterion every subject carried unresolved degenerative changes resulting from vitamin A deficiency, most of them of a moderate to severe character.

It must be emphasized that the reference state in this criterion is perfection. It is possible that the deepening opacity and thickening described above may not be reversible on account of their long chronicity, even though the cause was originally vitamin A deficiency. The data obtained on the re-examination of these subjects may enable us to distinguish the reversible changes.

Evidences of Thiamin Deficiency

We found no cases of acute, severe polyneuropathy or other evidence of beri-beri in any of our subjects. This was to be expected in this group.

A priori, the only evidences of thiamin deficiency we were likely to encounter would be of a chronic character. This evidence was sought in the nervous system. Our findings are summarized in Table 4.

The above signs are, of course, not specifically pathognomonic of thiamin or other nutritional deficiency. On the other hand, plantar dysesthesia is a striking sign in the peripheral neuropathy of chronic alcoholics and it disappears with adequate thiamin therapy.

Loss of vibratory sensation in the toes to a C-256 tuning fork in men under 35 is pathological; *i.e.*, it is an abnormally early degeneration. About 26 per cent of our subjects showed evidence of this premature degeneration of the nervous system. The results of the

Finding on Physical Examination	Number of Cases	Per Cent of Total
Number of Cases	1,153	
Absence of Ankle and Knee Jerks	3	0.3
Absence of Ankle Jerk	21	1.8
Calf Muscle Tenderness	5	0.4
Plantar Dysesthesia	170	14.7
Loss of Vibratory Sensation in Toes to C-128 Tuning Fork	9	0.8
Number of Persons With One or More of Above Signs	195	16.9
Number Examined With C-256 Tuning Fork	996	
Loss of Vibratory Sensation in Toes to C-256 Tuning Fork	256	25.7

Table 4. Evidences of thiamin deficiency observed upon examination of 1,153 employes of the Lockheed Aircraft Corporation.

re-examination may indicate to what extent impaired vibration sensation in the toes can be repaired in young adults by large vitamin supplements taken for approximately a year.

Evidences of Riboflavin Deficiency

Sebrell and Butler have described (11) the signs of riboflavin deficiency on the face and tongue. They are fissures at the sides of the mouth, seborrheic (fine, scaly, greasy desquamation on a mildly erythematous base) changes at the angles of the nose and eyes and a characteristic magenta coloring of the tongue. Table 5 summarizes the incidence of the facial signs of riboflavin deficiency. The incidence of severe cheilosis, fissures at the angles of the mouth or of the lips, is seen to be quite low.

Kruse, *et al* (13) have described in detail certain ocular signs and symptoms which respond to riboflavin therapy (5 to 15 mg. daily). The most conspicuous of these are photophobia, burning of the eyes, "eye strain," conjunctivitis, circumcorneal injection, keratitis (corneal vascularization), and corneal opacity. The photophobia and burning of the eyes cleared up within forty-eight hours. The

Finding on Physical Examination	Number of Cases	Per Cent of Total
Total Examined	1,153	
Seborrhea of Cheeks, Forehead, Face, Eyelids	38	3.3
Sebacious Plugs on Naso-labial Folds	62	5.4
Fissures of Lips	20	1.7
Fissures at Angles of Mouth	7	0.6
Number of Persons With One or More Signs	107	9.3

Table 5. Evidences of riboflavin deficiency observed upon examination of 1,153 employes of the Lockheed Aircraft Corporation.

keratitis (vascularization) also improved rapidly, but when the vascularization of the cornea was extensive, five to eighteen days elapsed before all the vessels emptied.

Among our subjects, 35 per cent complained of a burning, itchy, or gritty feeling in the eyes; 25 per cent complained of eye fatigue or eye-strain; 43 per cent stated that they were sensitive to light, that is, they were uncomfortable in bright light, and 23 per cent reported that light caused lachrymation.

The cornea was examined with the biomicroscope in every subject and the degree of corneal vascularization recorded (Table 6). Every case had some degree of corneal vascularization. "Streamer" type invasion, *i.e.*, active capillaries extending a considerable dis-

Table 6. Corneal vascularity noted on biomicroscopic examination of 1,171 employes of the Lockheed Aircraft Corporation.

Extent of Vascularization (Rating Based on Eye Showing Greater Vascularization.)	Number of Cases	Per Cent of Total
Total Examined	1,171	100
Streamer Type Arcades	478	42.5
3 Arcades or More, No Long Streamers	539	46.0
2 Arcades	99	8.4
1 Arcade	29	2.5
1 or 2 Arcades Without Circulating Blood	6	0.5

tance into the cornea were shown by 42.5 per cent. Another 46 per cent had three or more tiers of capillary arcades in the cornea. This was seen at the poles as well as in the equatorial regions.

No correlation was observed between such symptoms as photophobia and lachrymation and the degree of corneal vascularity. Furthermore, the diet histories showed that most of the men were getting moderate amounts of riboflavin as judged by the daily allowances recommended by the Committee on Food and Nutrition of the National Research Council. (Table 1.) This allowance, 2.7 mg. daily for a moderately active man weighing 70 kg., approximates the amount required for "saturation," *i.e.*, it is far from a minimum maintenance requirement to prevent cheilosis. On the basis of the older standard of riboflavin requirement, 1.8 mg. daily, the intake of more than half the men would have been considered satisfactory.

No correlation was found between ocular complaints, the incidence of cheilosis, and corneal vascularity. Yet by the criterion of corneal vascularity, every subject, regardless of age or economic status, must be considered as deficient in riboflavin.

Observations similar to those summarized above have been reported by Youmans *et al* (21). In a considerable number of subjects they noted mild but definite corneal vascularization not accompanied by ocular symptoms and in whom there was no correlation with dietary intake of riboflavin, other dietary factors or evidence of deficiency disease. Proceeding a step further, Youmans and Patton observed on re-examining their subjects an improvement or disappearance of vascularization in the winter or spring season compared with the fall, in spite of a lower intake of riboflavin in the former period. In the latter connection it should be noted that the observations, in the studies reported here in which practically every subject had some degree of corneal vascularity, were made in the winter season—November through February.

In the same connection Jolliffe and Goodhart (22) stated "evi-

dence is accumulating however that not all increased vascularity of the limbus and cornea is necessarily due to ariboflavinosis."

Similarly Sebrell (23) has warned "It should be noted that there is no proof that all vascularization of the cornea is due to riboflavin deficiency. Vascularization of the cornea is a non-specific symptom which may be due to a variety of causes and it is questionable whether one is justified in making a diagnosis of riboflavin deficiency on the basis of slight vascularity of the cornea as the only symptom. The subject is one which needs further investigation."

It is clearly premature, therefore, to interpret the presence of corneal vascularity in every subject examined (Table 6), as evidence of riboflavin deficiency.

The original descriptions (13) of ocular changes in riboflavin deficiency are based on findings in cases of acute riboflavin deficiency. In long standing deficiency, even of a mild character, many months of massive riboflavin therapy may be needed before the corneal vessels are occluded and free of blood. Later studies of Kruse (24) indicate that this may be the case.

It is also possible that the corneal vascularity we have observed, while it originated when the subjects were on riboflavin deficient diets, once established was not cleared up because only massive doses can effect a cure although the diets may subsequently have been good in this respect.

Granting this possibility, the question arises whether the corneal vascularity found throughout the group we have under observation can ever be cleared up by adequate riboflavin therapy, *i.e.*, whether the condition is reversible. Another version of the same question is whether some degrees and forms of corneal vascularity can be caused to disappear by riboflavin therapy and others not. The same questions arise in connection with conjunctival opacity and thickening as criteria of vitamin A deficiency.

Having raised the question of the reliability of corneal vascularity as an index of riboflavin deficiency, it must be stated that Bessey

and Wolbach (12) observed the appearance of corneal vascularity in experimental ariboflavinosis in rats (it does not occur in the guinea pig); and that Johnson and Eckardt (25) found that orally administered riboflavin, 1.5 to 3.0 mg. daily, was effective in clearing up rosacea keratitis, including the corneal vascularity.

Evidences of Niacin Deficiency

The signs and symptoms which may be associated with chronic niacin deficiency are stomatitis, glossitis, diarrhea, bilateral symmetrical dermatitis with erythema, pigmentation without erythema, and mental aberrations. The oral, gastro-intestinal, skin, and mental lesions may each occur alone or in any of the possible combinations. Vincent's infection may be superimposed on a niacin deficiency stomatitis (14).

A mild (or early form) of niacin deficiency may manifest itself as soreness of the tongue without glossitis, gastric discomfort after meals, burning of the esophagus and stomach, flatulence and constipation, and anorexia. None of these, of course, is specifically pathognomonic; but the possibility of mild niacin deficiency as the etiological factor must be borne in mind.

Little evidence of severe niacin deficiency was found in the subjects of this survey. (Table 7.)

Table 7. Possible evidences of niacin deficiency observed upon examination of 1,153 employes of the Lockheed Aircraft Corporation.

Finding on Physical Examination	Number of Cases	Per Cent of Total
Total Examined	1,153	
Redness of Tongue	2	0.17
Atrophy of Papillae	6	0.52
Absence of Coating	9	0.78
Edema and Hypertrophy	11	0.95
Pellagrous Dermatitis	1	0.09
Number of Persons With One or More Signs	24	2.08

It is possible that had the more refined method of detecting early niacin deficiency, recently described by Kruse (26), been available, we would have recorded many more positive cases.

Evidences of Vitamin C Deficiency

The physical examination discovered no subject with any of the signs of scurvy.

On the other hand, a large number had low plasma ascorbic acid values. These values are summarized in Table 8.

Of our subjects, 32.5 per cent had plasma ascorbic acid levels below 0.4 mg. per cent. The prevailing opinion regarding the significance of a low plasma ascorbic acid is represented in the following quotation (28): "When the figure falls below .45 mg. per 100 cc. of plasma, it may be inferred—that the vitamin C depot is approaching dangerous depletion. In such circumstances, it would seem advisable to administer about 5 to 10, 200-mg. doses of ascorbic acid, as an initial step in preparing the patient for operation."

Ingalls (29) proposed the following classification of plasma ascorbic acid values:

1 - 2	mg. per cent	complete saturation
1 - 0.7		normal
0.7 - 0.5		low normal
0.5 - 0.3		suboptimal
0.3 - 0.15		asymptomatic scurvy
0.15 - 0.		scurvy

Similarly, Chu and Sung (30) concluded from a combination of saturation and blood level studies that plasma levels below 0.4 mg. per cent indicated a deficiency state.

The above conclusions are derived from studies on young children. Against them must be set the findings and conclusions of Crandon, *et al* (15) in an extremely thorough study of experimental scurvy on an adult man.

They came to the conclusion that plasma ascorbic acid is a poor

index of vitamin C status, concurring in the opinion of Butler and Cushman (31) that the white-cell-platelet level is a more accurate measure. Crandon *et al* found that although the plasma ascorbic acid fell to zero after 41 days on a vitamin C free diet, the white-cell-platelet level was zero only after 82 days. Ten days after this stage, *i.e.*, after 92 days on a vitamin C free diet, the first signs of scurvy, hyperkeratotic papules, appeared; and 20 days later the petechiae characteristic of scurvy appeared. The following quotation describes some of the findings on which Crandon *et al* based their conclusions: "At the end of three months, after the plasma ascorbic acid had been zero for 44 days, a sizable wound was made on the right mid-back of the subject. Ten days later biopsy of this wound showed good healing, as compared with a normal control; histological study showed ample intercellular substance and capillary formation." A second wound made after the plasma ascorbic acid had been zero for 141 days did not heal below the skin. Following intravenous 1,000-mg. vitamin C daily, good healing set in, in a few days.

Table 8. Plasma ascorbic acid values found among 1,160 employes of the Lockheed Aircraft Corporation.[1, 2]

Mg. Per 100 Ml. of Plasma	Number	Per Cent of Total	Cumulative Percentage
Total Examined	1,160	100.0	
Less than 0.20	124	10.7	10.7
0.20–0.39	253	21.8	32.5
0.40–0.59	231	19.9	52.4
0.60–0.79	206	17.8	70.2
0.80–0.99	164	14.1	84.3
1.00–1.19	97	8.4	92.7
1.20–1.39	55	4.7	97.4
1.40–1.59	16	1.4	98.8
1.60–1.79	8	0.7	99.5
1.80 or More	6	0.5	100.0

[1] Determined by the macro method of Mindlin and Butler employing a photoelectric colorimeter (27).

[2] The subjects were instructed not to take any citrus fruit or tomatoes on the day of the examination. A few did, but their values are included in the tabulation.

The findings in the teeth and gums in this experiment are especially interesting: "During the first five months of the diet (devoid of vitamin C) no changes were grossly apparent in the teeth and gums. A competent dentist pronounced the gums to be normal in appearance at the end of this time.

"At the end of six months when clinical scurvy, as manifested by the perifollicular hemorrhages of the legs had been present for three weeks, examination of the gums and teeth was made . . . .; the gums were slightly more boggy on pressure than usual, but no other gross changes could be seen. A biopsy specimen of the gingiva at this time was absolutely normal. Of interest is the fact that although the gross findings were negative, X-ray films of the teeth taken at this time showed occasional interruptions of the lamina dura."

Nevertheless in the study of Crandon *et al* the white-cell-platelet level of vitamin C had fallen to one-third of its initial value on the day the plasma level first became zero. The curves of plasma and white-cell-platelet vitamin C indicate that when the plasma level falls below about 0.2 mg. per cent the white-cell-platelet level begins to fall. From the point of view of prophylaxis the conservative position would be that a plasma ascorbic acid below 0.2 mg. per cent is unsafe. Of the subjects we examined 10.7 per cent were in this state.

The study of Crandon *et al* dealt with a case of pure vitamin C avitaminosis, induced experimentally. Care was taken to provide adequate amounts of all other vitamins. A pure vitamin C avitaminosis is a rare clinical occurrence. Commonly it is complicated by deficiency of water-soluble vitamins of the B complex. This complication may aggravate the vitamin C deficiency and bring on the signs of scurvy earlier than in experimentally induced pure vitamin C deficiency. Crandon *et al* recognized this possibility.

Another factor to be considered in interpreting plasma ascorbic acid values is the length of time the subject has been subsisting on a low vitamin C intake, *i.e.*, an intake not so low as to give a vitamin

C plasma level of zero or nearly zero, but one insufficient to maintain a fair level, *e.g.*, above 0.4 mg. per cent. Some of the characteristics of mild scurvy may develop even though the plasma may still contain detectable amounts of vitamin C. The observations of Kruse (26) indicate that this may be the case, indeed that it is common.

Plasma ascorbic acid values reflect only recent dietary history (32). In the case of any one individual a low value may not indicate the habitual physiological state of the individual or reflect the character of his usual diet. When, as in the case of the present survey, 32.5 per cent of 1,160 men taken at random have plasma ascorbic values below 0.4 mg. per cent and 10.7 per cent below 0.2 mg. per cent, there is a high degree of probability that the low plasma vitamin C content which characterizes the group as a whole, does reflect the habitual diet of these men and indicates a low vitamin C content in their tissues.

It is remarkable that the vitamin C intake should be low in so high a percentage of men residing in this citrus-growing region, where citrus fruit and leafy vegetables are cheaper throughout the year than in most parts of the country. Eating habits appear to have changed for the worse in this region since 1938 when a nutrition survey in Pasadena indicated that even the poor, on relief, were obtaining in excess of 70 mg. of ascorbic acid daily, of which a little less than half came from citrus fruit, the remainder mainly from leafy vegetables.

One reason for the change in the picture since 1938 may be that the scanty breakfast of many of these men is responsible for the low consumption of citrus fruit and tomatoes. These fruits are commonly consumed either at breakfast or not at all.

Serum Albumin

Serum albumin was determined on 195 out of 200 consecutive subjects. The results are summarized in Table 9. They show that

all the values fell within the normal range of 3.95 to 5.24 (33). This result was to be expected; the protein intake of practically all of the subjects was adequate (5), and a lowering of the serum albumin follows only on severe and prolonged protein undernutrition (in the absence of organic disease).

We felt justified after finding that 195 consecutive subjects gave normal values in discontinuing the serum albumin determinations.

Range	Number	Per Cent of Total Number
TOTAL	195	100
3.90–3.99	5	2.6
4.00–4.09	8	4.1
4.10–4.19	17	8.7
4.20–4.29	28	14.4
4.30–4.39	25	12.8
4.40–4.49	22	11.3
4.50–4.59	27	13.8
4.60–4.69	25	12.8
4.70–4.79	21	10.8
4.80–4.89	9	4.6
4.90–4.99	7	3.6
5.00–5.09	1	0.5

[1] Determined by the method of Robinson and Hogden (34) after separating the serum albumin by the method of Kingsley (35).

Table 9. Serum albumin in 195 out of 200 consecutive subjects.[1]

Table 10. Hemoglobin values: grams per 100 ml. of blood[1] among 1,170 employes of the Lockheed Aircraft Corporation.

Grams Per 100 Ml.	Number	Per Cent of Total	Cumulative Percentage
TOTAL EXAMINED	1,170	100.0	
7.53	1	0.09	0.09
10.12	1	0.09	0.17
11.50–11.99	3	0.26	0.43
12.00–12.49	7	0.6	1.0
12.50–12.99	34	2.9	3.9
13.00–13.49	90	7.7	11.6
13.50–13.99	202	17.3	28.9
14.00–14.49	273	23.3	52.2
14.50–14.99	313	26.8	79.0
15.00–15.49	162	13.8	92.8
15.50–15.99	56	4.8	97.6
16.00 or More[2]	28	2.4	100.0

[1] Determined by photelometer—instrument calibrated by oxygen combining capacity determinations. Grams of hemoglobin per 100 ml. = oxygen combining capacity per 100 ml. multiplied by 0.736 (36).

[2] The highest value observed was 17.7 gm.

Hemoglobin

Table 10 contains a summary of the hemoglobin values. According to Wintrobe (37) the range of normal hemoglobin values for adult males is 16.0 ± 2.0 gm. per 100 ml. In 29 per cent of our subjects the hemoglobin value was below 14.0 and 3.9 per cent below 13.0.

Wintrobe chose 14.5 gm. per 100 ml. as a standard for 100 per cent hemoglobin. Taking this value as a standard, 52 per cent of our subjects had less than "100 per cent" hemoglobin.

There is a clear indication of a tendency to low hemoglobin values in this whole group of men, unless it be that the normal range of 16.0 ± 2.0 and a 100 per cent value of 14.5 gm. are too high. (*See* discussion below.)

Table 11. Volume of packed red cells.[1]

Volume Per Cent	Number	Per Cent of Total	Cumulative Percentage
Total Examined	1,170	100.0	
31	1	.09	0.09
38	1	.09	0.18
41	5	0.43	0.61
42	12	1.0	1.6
43	17	1.5	3.1
44	63	5.4	8.5
45	81	6.9	15.4
46	148	12.6	28.0
47	173	14.8	42.8
48	213	18.2	61.0
49	155	13.2	74.3
50	138	11.8	86.1
51	93	7.9	94.0
52	43	3.7	97.7
53	12	1.0	98.7
54	8	0.68	99.4
55	6	.51	99.9
58	1	.09	100.0

[1] Hematocrit tubes were centrifuged at 3,000 to 3,400 R.P.M. for 45 minutes after which time there was no further change in volume at this speed.

On the other hand, the volume of packed red cells tended to be higher than Wintrobe's normal range of 47.0 ± 7.0, with 43.2 as the "100 per cent" value as shown in Table 11. The median was 47.9, and the semi-quartile range was between 46.3 and 49.6. Only 0.2 per cent was below 40, and 97 per cent had cell volumes higher than Wintrobe's "100 per cent" value of 43.2.

Detailed Hematological Study of 228 Cases

It was not feasible in the time at our disposal to make a red cell

Table 12. Hematological determinations on 228 consecutive male subjects and on 110 men with hemoglobin values of less than 13.4 grams per 100 ml. of blood.

Hematological Determination and Class Intervals	Consecutive Subjects			Anemic Cases		
	Number of Cases	Per Cent of Total	Cumulative Percentage	Number of Cases	Per Cent of Total	Cumulative Percentage
HEMOGLOBIN, GMS. PER 100 ML. — RANGE OF NORMAL VALUES = 16.0 ± 2.0 GMS.						
Total	228	100.0		110	100.0	
16.20–16.79	3	1.3	1.3			
16.00–16.19	8	3.5	4.8			
15.80–15.99	2	0.9	5.7			
15.60–15.79	2	0.9	6.6			
15.40–15.59	6	2.6	9.2			
15.20–15.39	19	8.3	17.5			
15.00–15.19	15	6.6	24.1			
14.80–14.99	23	10.1	34.2			
14.60–14.79	19	8.3	42.6			
14.40–14.59	27	11.8	54.4			
14.20–14.39	21	9.2	63.6			
14.00–14.19	20	8.8	72.4			
13.80–13.99	24	10.5	82.9			
13.60–13.79	11	4.8	87.7			
13.40–13.59	7	3.1	90.8			
13.20–13.39	8	3.5	94.3	42	38.2	38.2
13.00–13.19	5	2.2	96.5	25	22.7	60.9
12.80–12.99	2	0.9	97.4	16	14.6	75.5
12.60–12.79	2	0.9	98.3	12	10.9	86.4
12.40–12.59	1	0.4	98.7	5	4.6	91.0
12.20–12.39	2	0.9	99.6	3	2.7	93.7
12.00–12.19			99.6	2	1.8	95.5
11.80–11.99	1	0.4	100.0	2	1.8	97.3
11.60–11.79				1	0.9	98.2
10.12				1	0.9	99.1
7.53				1	0.9	100.0
RED BLOOD CELLS[1], MILLIONS PER CU. MM. — RANGE OF NORMAL VALUES = 5.4 ± 0.8						
Total	228	100.0		110	100.0	
8.00–8.19	1	0.4	0.4			
7.00–7.19	5	2.2	2.6			
6.80–6.99	4	1.8	4.4	1	0.9	0.9
6.60–6.79	9	3.9	8.3			
6.40–6.59	15	6.6	14.9	1	0.9	1.8
6.20–6.39	17	7.5	22.4			
6.00–6.19	30	13.2	35.5	8	7.3	9.1
5.80–5.99	29	12.7	48.2	7	6.4	15.5
5.60–5.79	40	17.5	65.8	15	13.6	29.1
5.40–5.59	30	13.2	79.0	18	16.4	45.5
5.20–5.39	26	11.4	90.4	18	16.4	61.8
5.00–5.19	9	3.9	94.3	19	17.3	79.1
4.80–4.99	9	3.9	98.3	10	9.1	88.2
4.60–4.79	3	1.3	99.6	9	8.2	96.4
4.40–4.59	1	0.4	100.0	1	0.9	97.3
4.20–4.39	0			3	2.7	100.0

Hematological Determination and Class Intervals	Consecutive Subjects			Anemic Cases		
	Number of Cases	Per Cent of Total	Cumulative Percentage	Number of Cases	Per Cent of Total	Cumulative Percentage
VOLUME OF PACKED CELLS, PER CENT — RANGE OF NORMAL VALUES = 47 ± 7						
Total	228	100.0		110	100.0	
55	2	0.9	0.9			
54	3	1.3	2.2			
53	5	2.2	4.4			
52	14	6.1	10.5			
51	16	7.0	17.5			
50	32	14.0	31.6	1	0.9	0.9
49	27	11.8	43.4			
48	42	18.4	61.8	5	4.6	5.5
47	33	14.5	76.3	6	5.5	10.9
46	29	12.7	89.0	15	13.6	24.5
45	8	3.5	92.5	21	19.1	43.6
44	12	5.3	97.8	33	30.0	73.6
43	2	0.9	98.7	13	11.8	85.5
42	3	1.3	100.0	10	9.1	94.6
41				4	3.6	98.2
38				1	0.9	99.1
31				1	0.9	100.0

[1] The red cell counting chambers were set up in the usual manner in duplicate. The fields were photographed and the count made on the developed films.

Table 12 continued.

count on every subject. In order to get an impression of the range of red cell counts in this group, counts were made routinely on the first four cases examined each morning. A summary of the findings in this group consisting of 228 cases is given in Tables 12 and 13, and in Figure 1.

Table 12 shows that in these 228 consecutive subjects, the hemoglobin values tended to be lower than would be expected from Wintrobe's normal range of 16.0 ± 2.0 gm. There were only eleven cases, 6.1 per cent, above 16.0 gm. and 63 cases, 27.6 per cent below 14.0 gm. The tendency was the same here as in the whole group surveyed.

Table 13. Derived mean values for red blood corpuscles for 228 consecutive male subjects and for 110 men with hemoglobin values less than 13.40 grams per 100 ml. of blood.

Mean Corpuscular Volumes	Consecutive Subjects			Anemic Cases		
	Number of Cases	Per Cent of Total	Cumulative Percentage	Number of Cases	Per Cent of Total	Cumulative Percentage
VOLUME, CUBIC MICRONS,[1] — RANGE OF NORMAL VALUES = 87 ± 5						
Total	228	100.0		110	100.0	
102.0–104.9	3	1.3	1.3	3	2.7	2.7
99.0–101.9	4	1.8	3.1	1	0.9	3.6
96.0– 98.9	4	1.8	4.8	2	1.8	5.5
93.0– 95.9	12	5.3	10.1	3	2.7	8.2
90.0– 92.9	12	5.3	15.3	6	5.5	13.6
87.0– 89.9	22	9.6	25.0	12	10.9	24.5
84.0– 86.9	41	18.0	43.0	21	19.1	43.6
81.0– 83.9	44	19.3	62.3	20	18.2	61.8
78.0– 80.9	45	19.7	82.0	20	18.2	80.0
75.0– 77.9	19	8.3	90.3	8	7.3	87.3
72.0– 74.9	15	6.6	96.9	11	10.0	97.3
69.0– 71.9	5	2.2	99.1	1	0.9	98.2
66.0– 68.9	1	0.4	99.6			
63.0– 65.9	1	0.4	100.0	1	0.9	99.1
60.0– 62.9				1	0.9	100.0
HEMOGLOBIN, MICRO-MICROGRAMS[2] — RANGE OF NORMAL VALUES = 29 ± 2						
Total	228	100.0		110	100.0	
31	1	0.4	0.4	1	0.9	0.9
30	2	0.9	1.3	1	0.9	1.8
29	7	3.0	4.4	1	0.9	2.7
28	8	3.5	7.9	2	1.8	4.5
27	17	7.5	15.4	7	6.4	10.9
26	31	13.6	29.0	14	12.7	23.6
25	42	18.4	47.4	18	16.4	40.0
24	51	22.4	69.8	19	17.3	57.3
23	37	16.2	86.0	19	17.3	74.5
22	22	9.6	95.6	14	12.7	87.3
21	7	3.1	98.7	10	9.1	96.4
20	1	0.4	99.1	2	1.8	98.2
19	1	0.4	99.6			
18	1	0.4	100.0			
15				2	1.8	100.0

Mean Corpuscular Volumes	Consecutive Subjects			Anemic Cases		
	Number of Cases	Per Cent of Total	Cumulative Percentage	Number of Cases	Per Cent of Total	Cumulative Percentage
HEMOGLOBIN CONCENTRATION, PER CENT[3] — RANGE OF NORMAL VALUES = 34 ± 2						
Total	228	100.0		110	100.0	
33	1	0.4	0.4			
32	8	3.5	3.9			
31	23	10.1	14.0	2	1.8	1.8
30	80	35.1	49.1	26	23.6	25.5
29	82	36.0	85.1	49	44.5	70.0
28	31	13.6	98.7	21	19.1	89.1
27	3	1.3	100.0	8	7.3	96.4
26				2	1.8	98.2
25						
24				1	0.9	99.1
23				1	0.9	100.0

[1] Mean corpuscular volume = $\frac{\text{volume packed red cells per 1000 ml.}}{\text{red cell count, millions per cu. mm.}}$

[2] Mean corpuscular hemoglobin = $\frac{\text{hemoglobin, gms. per 1000 ml.}}{\text{red cell count, millions per cu. mm.}}$

[3] Mean corpuscular hemoglobin concentration = $\frac{\text{hemoglobin, gms. per ml. x 100}}{\text{volume packed red cells per 100 ml.}}$

Table 13 continued.

The question arises: What is a proper normal hemoglobin value? This question has been discussed by Leslie (38). In 928 adult males living in New York, Leslie found a mean average value of 14.7 gm., a median value of 14.7 gm., a semi-quartile range of 14.1 – 15.5, and the complete range to be 11.2 – 18.2. In the age range 20 to 60, no effect of age was observed.

In the subjects of the present survey the median hemoglobin value is 14.45 gm. Increasing this value by 1.4 per cent (to make our values comparable with Leslie's, since we used the Van Slyke coefficient for converting oxygen combining capacity to grams of hemoglobin, and Leslie used the Hufner value) it becomes 14.65, a value identical with that found in the New York series.

The conclusion is justified, therefore, that our group may be

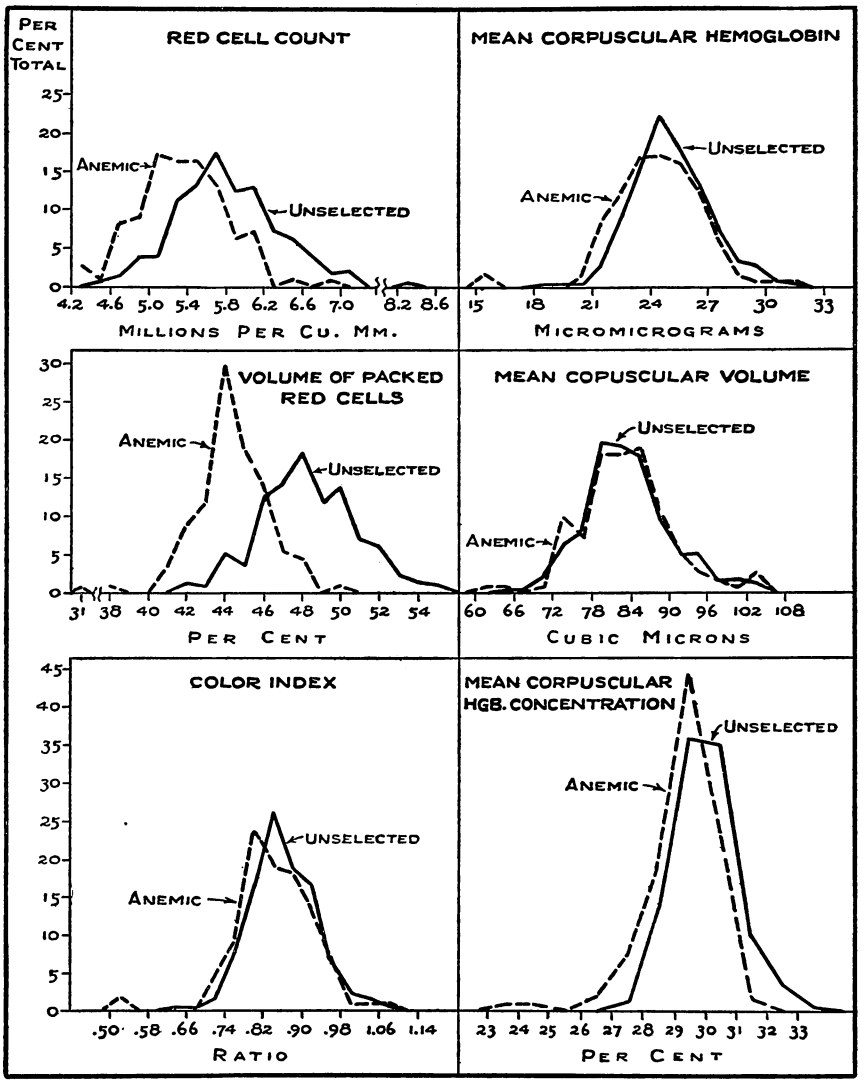

Fig. 1. Percentage distributions of hemotalogical values for an unrelated group of employes and for employes having hemoglobin values of less than 13.4 gms. per 100 ml. of blood.

considered "normal" with respect to hemoglobin concentration although they tend to be lower than Wintrobe's normal range of 16.0 ± 2.0.

The red cell counts on the other hand, tended to be higher than would be expected from Wintrobe's normal range of 5.4 ± 0.8.

Fifty-one cases, or 22.4 per cent, were 6.2 or above, and only one case, 0.4 per cent, was below 4.6. We cannot state, at present, the reason for the range of values in our group being higher than the range proposed by Wintrobe; it may, possibly, reside in the counting technique we used.

The range of red cell volumes also was higher than Wintrobe's normal of 47 ± 7, and was similar to that found in the whole group. The distribution curve is skewed toward the side of higher values; forty, or 17.5 per cent, were 50.5 or above and five, or 2.2 per cent, below 43.5, with none below 41.5.

A summary of the findings in this group of 228 consecutive subjects is therefore that the hemoglobin values tended to be lower and those for red cell count and red cell volume higher than suggested by the normal ranges proposed by Wintrobe. If one uses the latter's criteria for normality, there is a tendency in nearly all our subjects toward subnormal filling of the red cells. The question whether this tendency is real or an artifact arising from the inapplicability of Wintrobe's normal standards to our group, or to the techniques we have used, must, for the present, be left in abeyance.

Prevalence of Anemia

There were 126 subjects with hemoglobin values less than 13.4 gm. A hemoglobin value of less than 13.4 gm. is subnormal by any of the accepted standards for the "normal" hemoglobin of adult men. In this group, 10.8 per cent were, therefore, anemic, in degrees varying from mild to moderately severe.

The significance of this finding to the appraisal of the health of workers generally in this country is heightened by the following ancillary facts. This group of men, of whom 10.8 per cent were anemic, were selected in part by a pre-employment medical examination. The health of the group must be considered, therefore, as having been above the average of the population at large. They were young; 71 per cent were under 30 and 86 per cent under 35.

Their original homes were in most of the middle and western states. Finally the criterion by which the 10.8 per cent were diagnosed as anemic is far from one of perfection. If, for example, the range of normal values given by Wintrobe, 16.0 ± 2, had been used, there would have been 29 per cent with subnormal (*i.e.*, below 14.0 gm.) hemoglobin.

Red blood cell counts were also made on 110 subjects whose hemoglobin values were below 13.4 gm. per 100 ml. The hematological data on this group also are given in Tables 12 and 13, and Figure 1.

The red cell counts in all but four of the 110 anemic subjects were within, or higher than, the normal range, 5.4 ± 0.8 millions per cu. mm., 20.9 per cent were below 5.0 million; none were lower than 4.2 million. But the values in this group, taken as a whole, were definitely lower than in the unselected series of 228 consecutive subjects.

Similarly the red cell volumes were also definitely lower than in the unselected series. The tendency toward lower red cell volumes almost exactly balanced the tendency toward lower red cell counts. As a result the percentage distribution of mean cell volumes was almost identical in the unselected and anemic series (Table 13 and Figure 1).

One difference between the unselected and anemic series, therefore, is that the latter subjects had fewer red cells. Another difference is that the degree of filling of the red blood cells was less in the anemic than in the unselected series. This is shown in Tables 13 and 14 and Figure 1 by the comparisons in the values in the two groups of the mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and color index.

It will be observed in Tables 13 and 14 that the values in the unselected series for mean corpuscular volume, hemoglobin, hemoglobin concentration, and color index all tend to be lower than the normal ranges cited. These normal ranges are those proposed by

Color Index[1]	Consecutive Subjects			Anemic Cases		
	Number	Per Cent of Total	Cumulative Percentage	Number	Per Cent of Total	Cumulative Percentage
Total	228	100.0		100	100.0	
1.06–1.09	1	0.4	0.4	1	0.9	0.9
1.02–1.05	4	1.8	2.2	1	0.9	1.8
.98–1.01	6	2.6	4.8	1	0.9	2.7
.94– .97	16	7.0	11.8	8	7.3	10.0
.90– .93	38	16.7	28.5	15	13.6	23.6
.86– .89	43	18.9	47.4	20	18.2	41.8
.82– .85	60	26.3	73.7	21	19.1	60.9
.78– .81	37	16.2	89.9	26	23.6	84.5
.74– .77	17	7.5	97.4	10	9.1	93.6
.70– .73	4	1.8	99.2	5	4.5	98.2
.66– .69	1	0.4	99.6			
.62– .65	1	0.4	100.0			
.58– .61						
.54– .57						
.50– .53				2	1.8	100.0

[1] Normal, or 1.0, is taken as 14.5 gms. per 5.0 million red cells, and the color index = $\frac{\text{hemoglobin (gm.)}}{14.5} \div \frac{\text{red cell count}}{5{,}000{,}000}$.

Table 14. Color index of red blood corpuscles for 228 consecutive male subjects and for 110 men with hemoglobin values of less than 13.40 gms. per 100 ml. of blood.

Wintrobe. If the latter's criteria of normality be accepted, then most of the subjects in the study, probably over 90 per cent, regardless of how high the hemoglobin level, had hypochromic anemia, because their values for mean corpuscular hemoglobin concentration were below the normal range of 34 ± 2. This is highly improbable. A more reasonable conclusion is that the normal values proposed by Wintrobe are not applicable in the present study.

Table 15 summarizes the morphological classification of the anemias. This classification is based on that of Wintrobe using, however, instead of Wintrobe's normal values those derived from data obtained by the same techniques on 207 non-anemic men, *i.e.*, with higher hemoglobin values. There were 43.6 per cent in the

Class of Anemia	Definition of Class of Anemia[1]				Number	Per Cent of Total
	Number of R. B. C.	Mean Corpuscular Values				
		Volume	Hemoglobin Content	Hemoglobin Concentration		
Macrocytic	Subnormal	Above Normal	Above Normal	Normal or Subnormal	3	2.7
Macrocytic Questionable					2	1.8
Normocytic	Subnormal	Normal	Normal	Normal	37	33.6
Normocytic Questionable	Borderline	Normal or Borderline	Normal	Normal	11	10.0
Simple Hypochromic	Normal or Subnormal	Normal	Normal or Subnormal	Subnormal	22	20.0
Hypochromic Questionable	Normal or Subnormal	Normal	Normal or Subnormal	Borderline	4	3.6
Microcytic	Normal or Subnormal	Subnormal	Subnormal	Normal	19	17.3
Microcytic Questionable	Normal	Borderline	Borderline	Normal	4	3.6
Microcytic & Hypochromic	Normal or Subnormal	Subnormal	Subnormal	Subnormal	8	7.3
Total					110	100.0

[1] For each hematological value, "normal" means within limits of a standard range; borderline means close to lower limit of range; and subnormal means less than lower limit of range. Lower limits for normal or standard value were: red cell count, 5.3 million; volume, 79 cu. microns; hemoglobin content, 23 micro-micrograms; hemoglobin concentration, 29.0 per cent. Mean cell volumes for macrocytic cases were 102 or 103 cubic microns; for questionable cases, 98 and 99.

Table 15. Morphological classification of anemias for 110 men with hemoglobin values of less than 13.4 gms. per 100 ml. of blood, using standards for normal levels derived from data obtained by same techniques for 207 men with higher hemoglobin values.

category of normocytic anemia, 23.6 per cent with simple hypochromic anemia, 20.9 per cent with microcytic anemia, and 7.3 per cent with microcytic and hypochromic anemia. It must be emphasized that most of these anemias are mild.

SOME FEATURES OF THE MEDICAL HISTORIES NOT INCLUDED ABOVE

A. Gastro-Intestinal Function

	Per Cent
Appetite—a. Good	60
b. Fair	33
c. Poor	8
Indigestion	23
Diarrhea	6
Constipation	21
No Gastro-Intestinal Complaints	60

There are many indications in the literature (39, 40, 41) that gastro-intestinal discomfort or malfunction of the so-called "functional" type, can frequently be relieved by administration of one or more components of the vitamin B complex. It is a reasonable surmise, therefore, that the frequency of gastro-intestinal discomfort in this group, is in part a consequence of malnutrition.

B. Eyes and Vision

In the Company's pre-employment examination, the vision of the men was examined and classified as "good," "fair," or "poor." From the Company's records, we obtained the following summary: good, 85 per cent; fair, 14 per cent; poor, 1 per cent.

Nevertheless, as discussed above in the section on evidences of riboflavin deficiency, there were many complaints of visual and ocular discomfort.

C. Colds

Continuous or frequent colds were reported by 14 per cent, in addition to 64 per cent who reported one or more colds in the preceding three months. There were only 22 per cent who reported they had no cold during this time.

D. Fatigue and Irritability

Twelve per cent found their work excessively tiring. Nine per cent stated that they were easily irritated by their companions at work, and 11 per cent were easily irritated at home. Fourteen per cent believed their work was injurious to their health.

Summary of the Findings in the Medical Histories

The medical histories disclosed that there was in this group of men a great deal of what has appropriately been called "dis-ease." Many are not comfortable at their work or at home. The complaints were most commonly of the gastro-intestinal tract or of the eyes. It is true that these disturbances are minor; nevertheless, they rob the men of a feeling of well-being.

It is a challenge that 40 per cent of the men examined complained of gastro-intestinal discomfort. It is a challenge because these men would be rated as healthy young men; most of them are under 30. They are a selected group; they all underwent a pre-employment examination, and their health was an important item in their selection for employment. The factor of selection is real, because at the time these men sought employment there were many applications for employment, and accordingly the standards on which selection was based were high.

Summary

1. A nutrition survey among workers in an aircraft industry in Southern California was begun in November, 1941.

2. The objectives in this survey are:

An appraisal of present nutritional condition.

A study of the effects on health and working ability of nutritional supplements.

3. The medical and laboratory examinations consisted of the following: medical history, physical examination, biomicroscopic examination of the conjunctiva and cornea, plasma ascorbic acid,

serum protein concentration, hemoglobin, red cell count, red cell volume, and serological tests (Kahn and Kolmer) for syphilis.

4. The reliability of some of the above tests as diagnostic methods of mild or chronic nutritional deficiency are discussed.

5. This report summarizes the findings on the nutritional condition of the men at the time they were first examined (November, 1941-February, 1942).

6. Most of the men were relatively young, under 30.

7. Only two cases of definitely positive, and two cases of questionably positive serology for syphilis were found among 1,205 subjects examined.

8. The distribution of weight to height and age was within the standard normal range.

9. The serum protein concentration was normal in every subject examined.

10. Nearly every subject showed evidence of vitamin A deficiency (past or present), by the criterion that thickening, opacity, or localized elevation of the conjunctiva is evidence of vitamin A deficiency.

11. Between 17 per cent and 26 per cent, depending on the criterion, showed evidence of thiamin deficiency (past or present).

12. In 9 per cent of the subjects, a seborrheic condition of the face, or fissures of the lips or angles of the mouth were found, indicative of riboflavin deficiency. 35 per cent complained of ocular symptoms commonly found in cases of riboflavin deficiency.

13. Some degree of corneal vascularity was found in every subject. By this criterion nearly every subject showed evidence of riboflavin deficiency (past or present).

14. Evidence of severe niacin deficiency was found in only 2.1 per cent of the subjects.

15. 32 per cent of the subjects had a plasma ascorbic acid concentration below 0.4 mg. per cent; and another 20 per cent below 0.6 mg. per cent.

16. The red cell counts and red cell volumes were "normal" (or higher) in nearly all the subjects examined. About 11 per cent (126 out of 1,170) had hemoglobin values of less than 13.4 gm. per 100 ml. These must be considered as anemic. The red cell counts were subnormal in only four of 110 anemic cases. There were three cases of macrocytic anemia.

17. 40 per cent complained of gastro-intestinal discomfort or disturbances. The commonest complaints were of indigestion and constipation.

18. 63 per cent reported that they had had one or more colds in the preceding three months.

19. 12 per cent found their work excessively tiring.

20. Attention is drawn to the challenging circumstance that there is so much gastro-intestinal and ocular discomfort in a group of young, selected, presumably healthy men, and also to the relatively high incidence of anemia.

References

1. Stiebeling, Hazel K. and Phipard, Esther F.: Diets of Families of Employed Wage Earners and Clerical Workers in Cities. Washington, D. C., United States Department of Agriculture, Circular No. 507, January, 1939.

2. National Research Council, Committee on Food and Nutrition: Recommended Dietary Allowances, May, 1941. Mimeographed report distributed by the Federal Security Agency, Washington, D. C.

3. Food and Nutrition of Industrial Workers in Wartime. Report of the Committee on Nutrition and Industry. Washington, D. C., National Research Council Reprint and Circular Series Number 110, April, 1942.

4. Borsook, Henry and Halverson, Wilton L.: Nutrition and Health in Pasadena. *American Journal of Public Health,* August, 1940, 30, No. 8, pp. 895-900.

5. Wiehl, Dorothy G.: Diets of a Group of Aircraft Workers in Southern California. The Milbank Memorial Fund *Quarterly,* October, 1942, xx, No. 4, pp. 329-366.

6. Williams, R. D. and Mason, H. L.: Further Observations on Induced Thiamine (Vitamin B_1) Deficiency and Thiamine Requirement of Man: Preliminary Report. *Proceedings of the Staff Meetings of the Mayo Clinic,* 1941, 16, pp. 433-438.

Williams, R. D.; Mason, H. L.; and Smith, B. F.: Induced Vitamin B_1 Deficiency in Human Subjects. *Proceedings of the Staff Meetings of the Mayo Clinic,* 1939, 14, pp. 787-793.

Williams, R. D.; Mason, H. L.; Wilder, R. M.; and Smith, B. F.: Observations on Induced Thiamine (Vitamin B_1) Deficiency in Man. *Archives of Internal Medicine,* 1940, 66, pp. 785-799.

Williams, R. D.; Mason, H. L.; Smith, B. F.; and Wilder, R. M.: Induced Thiamine (Vitamin B_1) Deficiency and the Thiamine Requirement of Man: Further Observations. *Archives of Internal Medicine,* 1942, 69, pp. 721-738.

7. Pett, L. B. and Le Page, G. A.: Vitamin A Deficiency. III. Blood Analysis Correlated with a Visual Test. *Journal of Biological Chemistry,* February, 1940, 132, pp. 585-593.

8. Kruse, H. D.: Medical Evaluation of Nutritional Status. IV. The Ocular Manifestations of Avitaminosis A, with Especial Consideration of the Detection of Early Changes by Biomicroscopy. *Public Health Reports,* June 27, 1941, 56, No. 26, pp. 1301-1324; and The Milbank Memorial Fund *Quarterly,* July, 1941, xix, No. 3, pp. 207-240.

Kruse, H. D.: Methods of Detecting Mild Cases of Vitamin A Deficiency. *Science,* June 19, 1942, 95, No. 2477, pp. 623-624.

9. Callison, E. C.: Consideration of the Adequacy of Biomicroscopy as a Method of Detecting Mild Cases of Vitamin A Deficiency. *Science,* 1942, 95, pp. 250-251.

10. Brenner, S. and Roberts, L. J.: The Effects of Vitamin A Depletion on Young Adults. FEDERATION PROCEEDINGS. Federation of American Societies for Experimental Biology, March, 1942, 1, No. 1, p. 188.

11. Sebrell, W. H. and Butler, R. E.: Riboflavin Deficiency in Man. A Preliminary Note. *Public Health Reports,* December 30, 1938, 53, No. 52, pp. 2282-2284.

Sebrell, W. H. and Butler, R. E.: Riboflavin Deficiency in Man (Ariboflavinosis). *Public Health Reports,* December 1, 1939, 54, No. 48, pp. 2121-2131.

12. Bessey, O. A. and Wolbach, S. B.: Vascularization of the Cornea of the Rat in Riboflavin Deficiency, with a Note on Corneal Vascularization in Vitamin A Deficiency. *Journal of Experimental Medicine,* 1939, 69, pp. 1-12.

13. Kruse, H. D.; Sydenstricker, V. P.; Sebrell, W. H.; and Cleckley, H. M.: Ocular Manifestations of Ariboflavinosis. *Public Health Reports,* January 26, 1940, 55, No. 4, pp. 157-169.

Sydenstricker, V. P.; Sebrell, W. H.; Cleckley, H. M.; and Kruse, H. D.: The Ocular Manifestations of Ariboflavinosis. *Journal of the American Medical Association,* June 22, 1940, 114, pp. 2437-2445.

Sydenstricker, V. P.: Clinical Manifestations of Ariboflavinosis. *American Journal of Public Health,* April, 1941, 31, No. 4, pp. 344-350.

14. Sebrell, W. H.: THE VITAMINS (Chapter XVI). Council on Pharmacy and Chemistry and the Council on Foods of the American Medical Association. Chicago, American Medical Association, 1939, 637 pp.

15. Crandon, J. H.; Lund, C. C.; and Dill, D. B.: Experimental Human Scurvy. *New England Journal of Medicine,* September 5, 1940, 223, pp 353-369.

16. Kruse, H. D.: The Gingival Manifestations of Avitaminosis C, with Especial Consideration of the Detection of Early Changes by Biomicroscopy. The Milbank Memorial Fund *Quarterly,* July, 1942, xx, No. 3, pp. 290-323.

17. Wood, T. D.: Bureau of Publications, Teachers College, Columbia University, quoted by Rose, M. S.: A Laboratory Handbook for Dietetics. New York, 1937.

18. Frazier, C. N. and Hu, Chu' Uan-K'uei: Nature and Distribution According to Age of Cutaneous Manifestations of Vitamin A Deficiency: A Study of Two Hundred and Seven Cases. *Archives of Dermatology and Syphilology,* May, 1936, 33, pp. 825-852.

19. Straumfjord, J. V.: Lesions of Vitamin A Deficiency; Their Local Character and Chronicity. *Northwest Medicine,* July, 1942, 41, pp. 229-233.

20. Wolbach, S. B. and Bessey, O. A.: Tissue Changes in Vitamin Deficiencies. *Physiological Review,* July, 1942, 22, pp. 233-289.

21. Youmans, J. B.; Patton, E. W.; Robinson, W. D.; and Kern, R. M. S.: 57th Annual Meeting of Association of American Physicians, May 5, 1942.
Youmans, J. B. and Patton, E. W.: Laboratory Diagnosis of Nutritional Deficiencies. *Clinics,* August, 1942, 1, pp. 303-345.

22. Jolliffe, N. and Goodhart, R.: Vitamins in the Practice of Medicine. FEDERATION PROCEEDINGS. Federation of American Societies for Experimental Biology, September, 1942, 1, No. 3, pp. 316-319.

23. Sebrell, W. H.: Vitamins and the Public Health. FEDERATION PROCEEDINGS. Federation of American Societies for Experimental Biology, September, 1942, 1, No. 3, pp. 319-323.

24. Kruse, H. D.: Personal communication.

25. Johnson, L. V. and Eckardt, R. E.: Rosacea Keratitis and Conditions with Vascularisation of Cornea Treated with Riboflavin. *Archives of Ophthalmology,* 1940, 23, pp. 899-907.

26. Kruse, H. D.: The Lingual Manifestations of Aniacinosis, with Especial Consideration of the Detection of Early Changes by Biomicroscopy. The Milbank Memorial Fund *Quarterly,* July, 1942, xx, No. 3, pp. 262-289.

27. Mindlin, R. L. and Butler, A. M.: The Determination of Ascorbic Acid in Plasma; a Macromethod and Micromethod. *Journal of Biological Chemistry,* February, 1938, 122, pp. 673-686.

28. Lanman, T. H. and Ingalls, T. H.: Vitamin C Deficiency and Wound Healing. An Experimental and Clinical Study. *Annals of Surgery,* 1937, 105, pp. 616-625.

29. Ingalls, T. H.: Ascorbic Acid Requirements in Early Infancy. *New England Journal of Medicine,* 1938, 218, pp. 872-875.

30. Chu, F. T. and Sung, C.: The Vitamin C Content of the Blood Plasma in Normal and Sick Children. *Chinese Medical Journal,* 1937, 52, pp. 791-806.

31. Butler, A. M. and Cushman, M.: Distribution of Ascorbic Acid in the Blood and Its Nutritional Significance. *Journal of Clinical Investigation,* 1940, 19, pp. 459-467.

32. Greenberg, L. D.; Rinehart, J. F.; and Phatak, N. M.: Studies on Reduced Ascorbic Acid Content of the Blood Plasma. *Proceedings of the Society for Experimental Biology and Medicine,* 1936, 35, pp. 135-139.

33. Peters, J. P. and Van Slyke, D. D.: QUANTITATIVE CLINICAL CHEMISTRY. Vol. I. Baltimore, The Williams and Wilkins Company, 1931, p. 662.

34. Robinson, H. W. and Hogden, C. G.: The Biuret Reaction in the Determination of Serum Proteins. 1. A Study of the Conditions Necessary for the Production of a Stable Color Which Bears a Quantitative Relationship to the Protein Concentration. 2. Measurements Made by a Duboscq Colorimeter Compared With Values Obtained by the Kjeldahl Procedure. *Journal of Biological Chemistry,* 1940, 135, pp. 707-725 and pp. 727-731.

35. Kingsley, G. R.: A Rapid Method for the Separation of Serum Albumin and Globulin. *Journal of Biological Chemistry,* 1940, 133, pp. 731-735.

36. Peters, J. P. and Van Slyke, D. D.: QUANTITATIVE CLINICAL CHEMISTRY. Vol. I. Baltimore, The Williams and Wilkins Company, 1931, p. 544.

37. Wintrobe, M. M.: CLINICAL HEMATOLOGY. Philadelphia, Lea & Febiger, 1942, 792 pp.

38. Leslie, C. J.: Notes on Hemoglobin Values; Average Range for Males in New York Metropolitan Area; 1,095 Cases. *Proceedings of the Life Extension Examiners,* May-June, 1940, 2, pp. 51-56.

39. Borsook, H.; Dougherty, P.; Gould, A. A.; and Kremers, E. D.: The Vitamin B Complex and Functional Chronic Gastro-Intestinal Malfunction: A Study of Two Hundred and Twenty-Seven Cases. *American Journal of Digestive Diseases,* 1938, 5, pp. 246-251.

40. Chesley, F. F.; Dunbar, J.; and Crandall, L. A. (Jr.): The Vitamin B Complex and Its Constituents in Functional Digestive Disturbances. *American Journal of Digestive Diseases,* 1940, 7, pp. 24-27.

41. Bean, W. B. and Spies, T. D.: Vitamin Deficiencies in Diarrheal States. *Journal of the American Medical Association,* 1940, 115, pp. 1078-1081.