

A SURVEY OF NUTRITIONAL STATUS AMONG SCHOOL CHILDREN AND THEIR RESPONSE TO NUTRIENT THERAPY

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THIS paper describes the clinical changes which occurred in certain tissues in a group of school children that received specific nutrient therapy. The study³ was conducted under the direction of Dr. H. B. Pierce and under the auspices of the University of Vermont, College of Medicine, in Burlington. One hundred and twenty-four children were studied for about three years. These children were selected from 908 grade-school students who were screened for evidence of vitamin deficiency disease in the late fall of 1945 in Burlington.

The methods, data, and analyses of the chemical and dietary studies will be published in a subsequent paper.

These 124 children were given a physical inspection of the eyes, lips, gums, tongue, and skin in the fall of 1946. This was repeated each spring and fall, the final inspection being made early in the spring of 1949. Color photographs of all these tissues were made on each child on the occasions of the first, mid, and last physical inspections, about twelve months apart. Photographs of tissues under special observation in each group were taken at six-month intervals, to form a series of six photographs.

The children were divided into three groups on the basis of the clinical inspection. The commonly accepted changes in the conjunctiva, gum and tongue were the criteria for placing them

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in groups to study the effects of vitamins A, C and niacin, respectively (1, 2, 3, 4).

The children in each of the three groups were divided into two subgroups in which they were paired by stage and severity of lesions, by sex, and finally age. This was done to establish more comparable subgroups than might be achieved by a random selection. In each instance one subgroup then received vitamin therapy; its paired subgroup, placebos.

Therapy consisted of about four times the Recommended Daily Allowances of the Food and Nutrition Board of the National Research Council. Vitamin A was administered in a single daily dose of 25,000 International Units. A total of 200 milligrams of ascorbic acid was given daily in two divided doses. Niacinamide was given in the amount of forty milligrams, half the dose twice daily. The corresponding subgroups received comparable placebos. Four times the Recommended Allowances is a little less than some authorities administer as therapeutic dosage.

PLATES 1-6

Fig. 1. Initial photograph of a conjunctiva showing generalized thickening, with even greater thickening and opacity in a triangular area in the region at the junction of the limbus and horizontal meridian.

Fig. 2. The same conjunctiva as it appears seventeen months after the beginning of vitamin A therapy. No change is evident.

Fig. 3. Twenty-two months after the beginning of therapy, the first evidence of decrease in the generalized thickening of the conjunctiva is seen in the relatively greater prominence of the localized opacity, even though it, too, has shared in this recession.

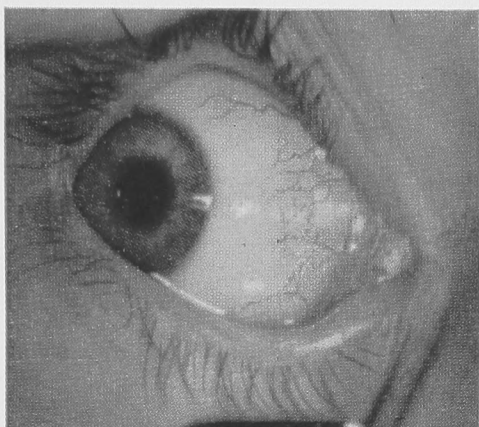
Fig. 4. After twenty-six months had elapsed since the beginning of vitamin A therapy, thinning and clarification has taken place over the entire conjunctiva. Most of the conjunctiva has become thinner and quite transparent superficially; the localized area, originally of greater thickness and opacity, though it has undergone thinning and clarification to the same relative extent under therapy, still shows at this stage some thickness and more or less opacity and consequently presents a seemingly circumscribed appearance.

Fig. 5. This conjunctiva is of a member of the control group. The photograph was made at the same time as Figure 1. The stage of the process is essentially the same.

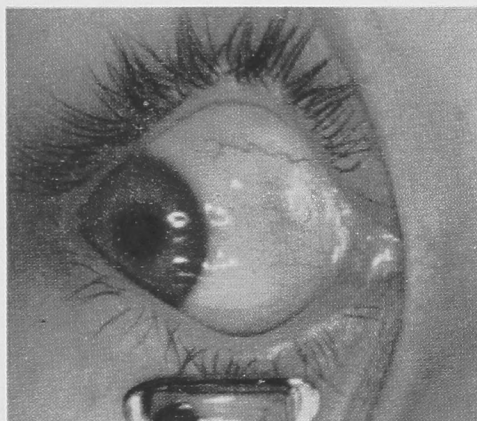
Fig. 6. The same conjunctiva of the control child shown in Figure 5 as it appears at the end of the therapy period. There is no change comparable to that in the conjunctiva of the child receiving vitamin A therapy.



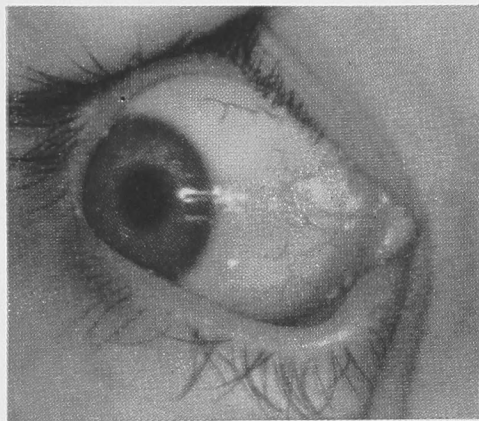
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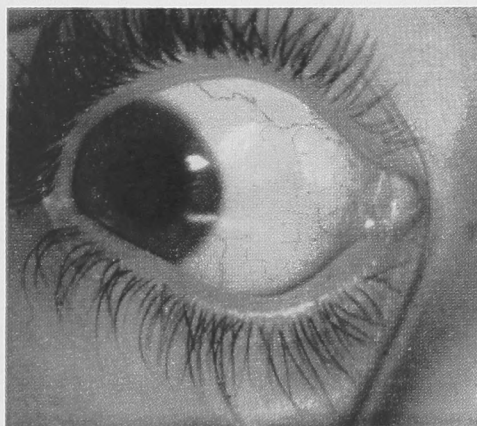
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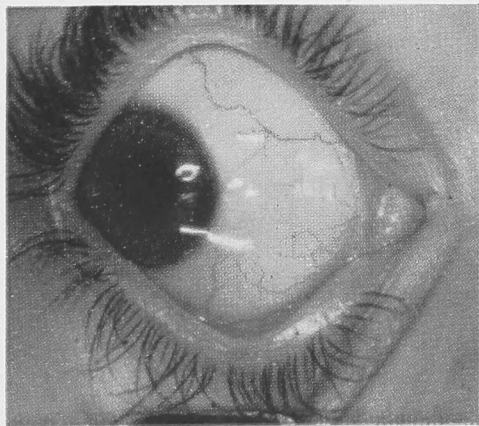
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PLATES 7-12

Fig. 7. Initial photograph of a lower gum which presents recession and superimposed acute changes of redness and swelling of papillae and margins.

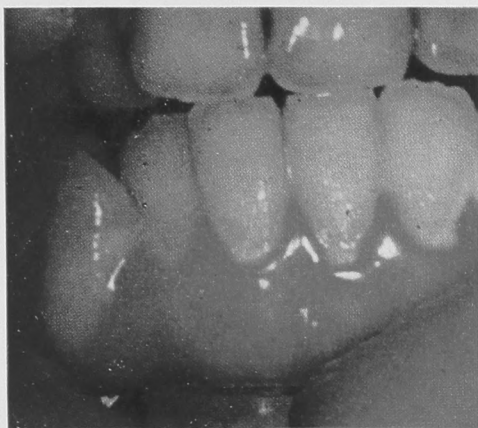
Fig. 8. Following four months of ascorbic acid therapy, the acute process is less intense and the swelling is more localized near the margins.

Fig. 9. The same gum shown in figures 7 and 8 at the completion of twenty-six months of therapy shows more tooth surface covered. There is a partial restoration of gum tissue.

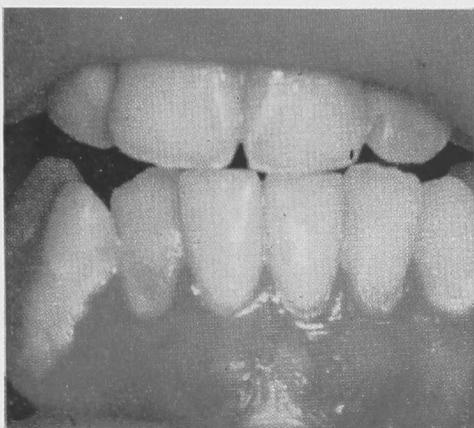
Fig. 10. The upper gum of a child in the control group showing recession, swelling, and redness. This is an initial photograph.

Fig. 11. The same gum as in figure 10 at the end of the study also shows recession, swelling, and redness. In fact, there is an increase in swelling and redness.

Fig. 12. This photograph, made before therapy was instituted, shows a red, swollen, and fissured tongue. The fungiform papillae are swollen and most of the filiform papillae are atrophied.



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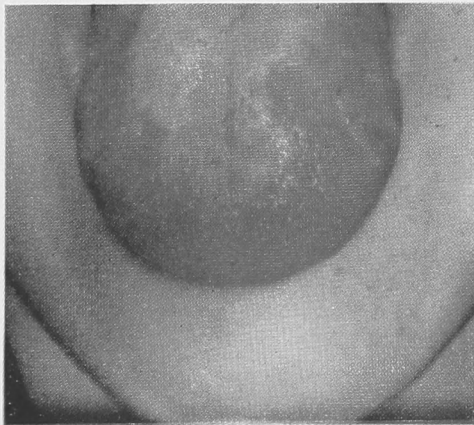
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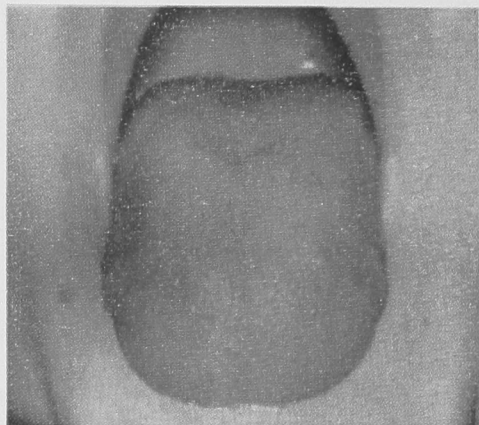
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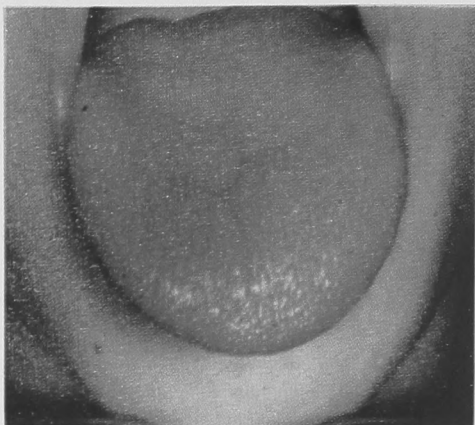
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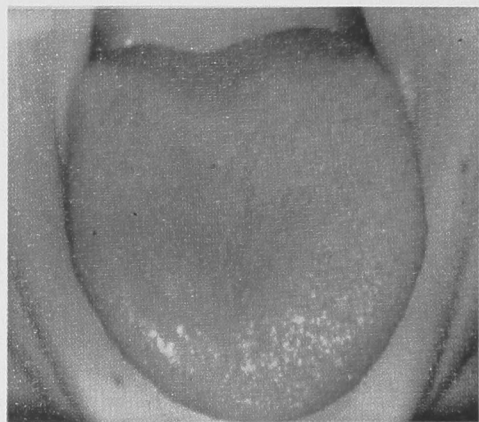
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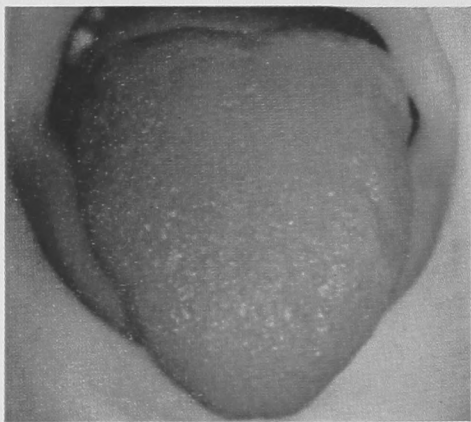
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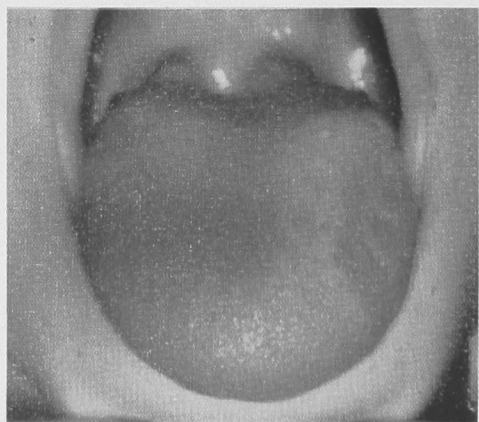
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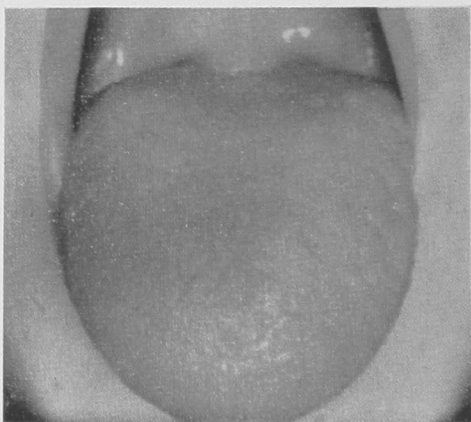
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VITAMIN A

The bulbar conjunctiva in its reported relation to vitamin A was studied. Normally it is a thin, transparent tissue covering the anterior surface of the eyeball except at the cornea. The term sclera is very often mistakenly applied to the white of the eye, which actually includes both conjunctiva and sclera. It should also be mentioned that the epithelial layer exclusively has been commonly regarded as being affected in the conjunctiva in avitaminosis A; but that more recently the subepithelium containing the vascular network has been shown to undergo change always and often predominantly. Most of the changes described in this report are in the subepithelium.

It has been shown (1) that in vitamin A deficiency the conjunctiva becomes thickened, its vascularity increased and its transparency lost. It becomes translucent and then opaque. This process is not uniform over any zone of the conjunctiva. The initial site and therefore the most advanced area is at the junction of the horizontal meridian with the limbus with the process originating in the deeper layer. This describes briefly the pathology of the underlying chronic process on which may be superimposed from time to time an acute or subacute proc-

PLATES 13-18

Fig. 13. Following niacin therapy, the tongue shown in Figure 12 has decreased in redness. There is less swelling of the fungiform papillae and a beginning restoration of the filiform papillae.

Fig. 14. This pre-therapy tongue presents moderate fissuring.

Fig. 15. Following niacin therapy the most striking difference from Figure 14 is the substantial amount of filling in of the fissures.

Fig. 16. The initial photograph of the tongue of a control child. There are "slashes" on the tongue margins and the fungiform papillae are swollen.

Fig. 17. The same tongue fifteen months later in which a more acute process is superimposed. The tongue is red and swollen. The marginal "slashes" are more evident and there is an area in which most of the papillae have disappeared.

Fig. 18. In the final picture of the same tongue shown in Figures 16 and 17, the acute process has subsided. However, the swelling remains in the tongue. In addition to the marginal "slashes," fissures have appeared on the dorsum. In this photograph taken at the end of the study, the tongue is very little different than it was initially.

ess which appears and recedes much more rapidly (5). The acute manifestations include hyperemia and congestion of the conjunctiva, followed by swelling and finally infiltration.

Figure 1 presents a photograph of a conjunctiva exhibiting the changes indicative of a chronic process as it appeared before therapy. The area with the most advanced change is in the region of the horizontal meridian at its intersection with the limbus. This roughly triangular area is thicker than the remaining conjunctiva and is completely opaque. Only the most superficial vessels are seen with any degree of clarity. One can look a little deeper into the rest of the conjunctiva; but the vessels appear progressively fainter. Increased vascularity is a part of this process. However, in the advanced stage, the opacity of the conjunctiva effectively hides any but the uppermost vessels from view.

From a photograph (Figure 2) of the same zone in the same child taken seventeen months after the beginning of therapy, no demonstrable change in the conjunctiva can be seen. However, in Figure 3, taken twenty-two months after the beginning of therapy, the opacity is seen to be clearly demarcated. It is the first demonstrable change. In the final picture (Figure 4) of this conjunctiva, taken about twenty-six months after the beginning of therapy, the opacity in the site of most advanced change is definitely circumscribed. The vessels in the areas just above and below are seen more clearly as a result of thinning and superficial clarification of the conjunctiva (1).

Photographs of the same zone in the conjunctiva of a member of the vitamin A control group are presented for comparison. Figure 5 is of a picture taken at the beginning of the study; Figure 6, at the completion. Between these two pictures there is no evident difference in any way corresponding to the changes seen in the conjunctiva of the child receiving vitamin A therapy.

VITAMIN C

The gums were under observation for the effects of vitamin C therapy on them. Normally the gum extends slightly over

the enamel and, as interdental papillae, between the teeth for half the distance of their exposed length. It is thin, pink, and elastic in consistency. Hugging the teeth rather tightly, it provides some measure of support for them.

It has been shown (2) that when the gingival tissue is deficient in vitamin C for a period of time, it becomes more or less swollen and pale, followed by atrophy of its substance. The interdental papillae lose in height, and sometimes even their identity. The marginal gingiva gradually recedes, exposing more and more tooth surface and providing less support.

Usually this process is masked by more acute changes. These consist of redness and swelling of the gum, often with secondary infection.

In the age group under observation the shedding and eruption of teeth brought into play terrific stresses on the gums and therefore added to the nutrient demands of the tissue.

Figure 7 shows the pathological changes in a lower gum prior to therapy. There is a marked recession of the gingival tissue with a superimposed acute process of a moderately severe nature. Figure 8 presents the same gum as it appeared four months after therapy was begun. Although there is no apparent rebuilding of the gum substance in this short time, the stage is being set. The swelling is more localized near the margins and the acute process is less intense.

In Figure 9 this gum is shown at the termination of therapy (2). What was suggested by the previous photograph is now seen to have progressed to a partial restoration of gum tissue. The gums cover more tooth surface; the pathological process has actually undergone reversal. But not until about twenty months had elapsed from the beginning of therapy was any significant improvement of this nature noted.

Figures 10 and 11 are of the lower gum of a child in the control group. The former was taken at the beginning, the latter at the end of the study. In both, recession, swelling, and redness may be seen. No changes comparable to those noted in the gum of the child receiving vitamin C therapy have oc-

curred. In fact, the gum is obviously in much poorer condition at the conclusion of the study.

NIACIN

The tongue was observed for effects of niacin therapy. Normally, the anterior two-thirds of the tongue is covered predominantly by filiform papillae. Of the fungiform papillae, 90 per cent are in the interior fifth, with the remainder distributed throughout. It has been shown (3) that with a long time deficiency of niacin in this tissue, the papillae at first hypertrophy, then atrophy. In undergoing this sequence of changes, the fungiform precede the filiform papillae. Those at the tip and on the margins are affected first and then those on the dorsum are reached. If the pathological process reaches a later stage, fissures may appear.

At any time during this sequence of events, acute manifestations may arise and may effectively hide the underlying process. These changes consist in redness and swelling of the tongue substance as well as of the papillae.

Photographs of the tongues of two children before and after niacin therapy are presented in Figures 12-15. In Figure 12 the tongue of a child before therapy is seen to be red, swollen, and fissured. The fungiform papillae are swollen as well, and most of the filiform are atrophied. In the picture taken after termination of therapy (Fig. 13), the redness is shown to have decreased. The fungiform papillae are less swollen, and there is beginning restoration of the filiform papillae (3). In the tongue of another child the most striking difference between its appearance before (Fig. 14) and after therapy (Fig. 15) is in the substantial amount of filling in of the fissures that has occurred.

In each of these two sets of pictures a beginning reversal of the chronic process is noted. From comparison of the last picture in each set (Figs. 13 and 15), it may be observed that the status of the tongue in Figure 15 is closer to a normal appearance than is that in Figure 13. This observation brings out

the fact that the final status attained after therapy within a given time period is dependent on the status of the tissue at the outset. This holds true not only for the tongue, but for the other tissues as well.

Changes in the tongue of one of the niacin controls receiving placebos illustrates the waves of exacerbation and subsidence that may occur in the natural course of a deficiency state. In contrast to the status before therapy (Fig. 16), six months later a subacute exacerbation appeared, superimposed on the underlying chronic process (Fig. 17). Five months thereafter the exacerbation abated but not to the point that the status was similar to that at the beginning of the study. In an additional five months, another exacerbation appeared which was not so intense as the previous one. Four months subsequently the subacute process is intensified; while in another seven months it shows a slight subsidence. (Fig. 18.)

AMOUNTS TAKEN

Therapy was begun in mid-December, 1946, and was terminated at the end of January, 1949, a total of twenty-six months or seven hundred and seventy days. Therapy and placebos were given under supervision on school days, but this supervision frequently was not as close as desired. The children were encouraged to take therapy or placebos when school was not in session. Some took advantage of this; many did not.

If there is any discrepancy between the records submitted and the actual performance—and it is reasonable to suppose that there is—the actual performance is apt to be poorer than the figures indicate. Also some of the performances were consistent throughout; on the other hand, some took more of their therapy in the first half of the study, others in the second half. These variations were very great. Since both omission and variation in taking therapy have a direct bearing on the results, tending to minimize them, data on performance takes on considerable significance.

Table 1 shows the performance, according to the records

NUMBER OF DAYS	VITAMIN A		ASCORBIC ACID		NIACIN	
	Number of Children	Number Improved	Number of Children	Number Improved	Number of Children	Number Improved
TOTAL	24	11	21	7	19	13
< 300	1	0	2	0	0	0
300-424	6	1	7	4	6	4
425-549	7	4	6	1	9	7
550-674	8	5	3	0	4	2
> 675	2	1	3	2	0	0

Table 1. Approximate number of days on which specified therapy was taken by all children and by those showing improvement.

submitted, of the children on vitamin A, ascorbic acid, and niacin therapy. The performance is expressed in number of days that therapy has been taken. Although these children had the opportunity of taking therapy for twenty-six months, the performances ranged from twelve to twenty months. Therefore, in no sense did this study provide a measure of effectiveness of certain amounts of therapy over a period of two years; but rather of therapy for about one and one-half years in the one instance and for about one year or slightly more in the other two instances. In the vitamin A group, the mode is between 550 and 674 days; that is, the children in this group took therapy equivalent to somewhat more than eighteen months. An almost equal number fell in the ranges of 300-424 and 425-549 days, or the equivalent of somewhat more than twelve months. The mode for ascorbic acid falls in the 300-424 day range; and for niacin, in the 425-549 day grouping.

RESULTS

All pictures were examined without knowing whether they were of persons receiving therapy or of controls. In the case of the conjunctiva, the comparison was made on the complete series of six pictures. With the gums, however, the comparisons were made on the series of three pictures only. The

tongues were examined by both of these two procedures. The complete series of six pictures for the children in the therapy and matched control groups were examined first for evidence of improvement. When other control groups were used as well as the matched controls, the series of three pictures per child were studied for all children. The therapy and control segments of the group under study were always unidentifiable in the total number. It should be pointed out that the examination conducted in this manner became a test, not only of the actual change occurring in the tissues, but also of the diagnostic acumen of the examiner. This should be borne in mind in evaluating the results.

Table 2 summarizes the effects of each type of therapy as determined by the examination. The results are expressed by the probability of exceeding by chance alone the observed dif-

Table 2. Comparison of therapy and control groups at end of study.

GROUP	NUMBER OF CHILDREN	TISSUE IMPROVED		DIFFERENCE IN PER CENT IMPROVED		
		Number	Per Cent	(Th.-C.) Per Cent	Probability	Significant
Vitamin A Therapy Controls—Matched	CONJUNCTIVAL STATUS					
	24	11	45.8			
	23	4	17.4	28.4	.01-.05	Yes
Ascorbic Acid Therapy Controls—Matched Controls ¹ —Other Groups	GUM STATUS					
	21	7	33.33			
	16	1	6.25	27.1	.05	Borderline
	113	2	1.8	31.5	<.001	Yes
Niacin Therapy Controls—Matched Controls ¹ —Other Groups ²	TONGUE STATUS ²					
	19	13	68.4			
	21	3	14.3	54.1	<.001	Yes
	96	0	0	68.4	<.001	Yes

¹ Includes children in matched control group and other therapy and control groups.

² Improvement in tongue includes consistent recession of the subacute process. The total number for controls is smaller because of unreadable pictures.

³ The absence of the three improved cases among total controls is due to failure to classify these as improved when read on three pictures only.

ference between the therapy and control groups. The arbitrary level of 5 per cent is taken customarily as the upper limit of significance, significant in that these differences would be exceeded by chance not more than once in twenty times that this procedure might be performed.

With vitamin A therapy the findings are significant. When the ascorbic acid therapy group is compared with the matched controls, the difference is at the 5 per cent level. When all children not receiving ascorbic acid, with gums comparable initially to those in the ascorbic acid group, that is, the gums showed at least beginning recession, are included as controls, the difference between the ascorbic acid therapy group and control group is very significant. The differences between the niacin group and matched controls as well as all other groups were both significant. Here, however, because of the masking effect of the subacute process, it frequently was necessary to consider consistent recession of this process indicative of improvement, as the chronic process did not emerge sufficiently until the end of the study.

SUMMARY

Twenty-four children with conjunctival changes, twenty-one children with gum changes, and nineteen children with tongue changes received therapeutic amounts of vitamin A, ascorbic acid, and niacin, respectively, for varying periods of time less than two years. In the A group, eleven had demonstrable improvement in the lesions; in the ascorbic acid group, seven improved; and in the niacin group, thirteen improved. In comparing these responses with the various control groups, it was found that these responses were statistically significant.

This study then presents confirmatory evidence that the changes noted by Kruse are the results of chronic deficiency in these specific tissues (1, 2, 3, 5). It also demonstrates that tissues reflecting deficiency states undergo recession and restoration upon provision of therapeutic amounts of the appropriate nutrients.

REFERENCES

1. 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. *Milbank Memorial Fund Quarterly*, July, 1941, xix, No. 3, pp. 207-240.
2. Kruse, H. D.: The Gingival Manifestations of Avitaminosis C, With Especial Consideration of the Detection of Early Changes by Biomicroscopy. *Milbank Memorial Fund Quarterly*, July, 1942, xx, No. 3, pp. 290-323.
3. Kruse, H. D.: The Lingual Manifestations of Aniacinosis, With Especial Consideration of the Detection of Early Changes by Biomicroscopy. *Milbank Memorial Fund Quarterly*, July, 1942, xx, No. 3, pp. 262-289.
4. Council on Foods and Nutrition, American Medical Association: Vitamin Deficiencies: Stigmas, Symptoms and Therapy. *The Journal of the American Medical Association*, June 22, 1946, 131, pp. 666-667.
5. Kruse, H. D.: A Concept of the Deficiency States. *Milbank Memorial Fund Quarterly*, July, 1942, xx, No. 3, pp. 245-261.