

THE GINGIVAL MANIFESTATIONS OF AVITAMINOSIS C, WITH ESPECIAL CONSIDERATION OF THE DETECTION OF EARLY CHANGES BY BIOMICROSCOPY^{1, 2, 3}

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IN previous papers we have described methods for detecting ariboflavinosis, avitaminosis A, and aniacinosis by gross and biomicroscopic examination of the ocular limbus, conjunctiva, and tongue, respectively (1, 2, 3, 4). This paper presents a preliminary report of observations on changes in the gums in avitaminosis C as seen macroscopically and biomicroscopically.

Following administration of ascorbic acid as specific therapy, the gingival lesions in two persons have now almost completely disappeared, as judged by microscopic examination. In all others, the gum lesions initially more severe have markedly receded under this therapy, in some nearly completely. These persons are still receiving the specific therapy, and their gingival lesions are continuing to undergo recession. Control groups receiving nicotinamide or vitamin A have had no improvement of their gingival lesions.

Gross and biomicroscopic examination of the gums is an advantageous method of detecting all states of avitaminosis C.

DESCRIPTION OF GROUPS AND PROCEDURES

Forty-nine adults were examined, and the personal details about them were presented in the preceding paper (4).

Their gums were examined, prior to therapy, with the biomicroscope as well as in the gross. Both types of examination were restricted to the labial aspect of the upper and lower gums between

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the first premolars on each side. Although Salle states that in adults the purely scorbutic gingivitis begins mostly on the anterior surface of the gums in the region of the incisors (5), our selection of this site was also determined by feasibility and convenience. It may be that lesions elsewhere in the gums appear first or are more severe, but changes are so prevalent in the frontal aspect that restriction of the examination to that site has proved practical and satisfactory.

The tongue, angles of the mouth, and skin were also examined as already described (4).

Thirty-two persons were selected at random to receive ascorbic acid therapy.⁴ They had various states of gum lesions. The remainder, forming a control group, were given nicotinamide. Another group, receiving vitamin A, served as an additional control group.

Each of sixteen persons in the ascorbic acid group was given a capillary resistance test by the method of Schultz (6) before the therapy was begun. On each of twenty-seven persons to receive ascorbic acid and fifteen to receive nicotinamide a determination for the concentration of ascorbic acid in plasma by the macro-method of Mindlin and Butler (7) was conducted prior to therapy. Two months after therapy had been started, determinations for the ascorbic acid level in the plasma were run on seven persons receiving ascorbic acid and six persons receiving nicotinamide.

The specific daily therapy, started on April 9 and 21, 1941, consisted of 500 mg. of ascorbic acid in four tablets of 125 mg., each being given at an interval during the day. Further details in the administration of the therapy are contained in a previous paper (4). The daily dosages of nicotinamide and vitamin A for the control groups were 200 mg. and 100,000 I.U., respectively.

Among those receiving the ascorbic acid therapy, seven have since become unavailable through departure and could not be further followed. For similar reasons, two from the control group had to

⁴ The ascorbic acid was generously furnished by Mead Johnson & Company, Evansville, Indiana.

withdraw. At regular intervals gum examinations have been conducted on the groups receiving the specific and control therapy, respectively. For the former, these examinations will form the basis for terminating therapy.

DESCRIPTION OF GINGIVAL LESIONS

In the development and resolution of its specific lesions, avitaminosis C was found to be analogous in behavior to avitaminosis A (3), aniacinosis (4), and ariboflavinosis (1, 2, 8), though each is a distinct entity. This common pattern gave rise to a concept of deficiency states (9). In a deficiency disease the specific pathological process in a tissue has velocity, intensity, and sequence which determine its state. Categorized most simply according to these characteristics, it may be a mild acute, mild chronic, severe acute, or severe chronic process in a particular stage. Actually, once the chronic form sets in, it usually constitutes a base on which may be superimposed a mild or severe acute process.

According to the form, intensity, and stage of the pathological process, the condition of the gums in avitaminosis C was appraised. Both the acute and chronic processes were graded in three degrees, with each combination of form and intensity being divided into four successive stages. The predominant characteristics determined the stage, since manifestations of the previous and following phases were often present. Status was expressed in terms of both acute and chronic processes.

In many of the persons, the manifestations in the gums were seen readily in the gross; in some, certain characteristic features were detected definitely only by biomicroscopy. The series presented most of the states. It is understandable that the early stages in the acute and chronic processes were least frequent; for the first examination was in April and the persons were adults. By arranging the gingival lesions in a progressive series, according to their states, and by the reverse sequence of changes upon therapy, the course of the process in evolution and recession has been reconstructed.

In the gums the pathological changes appear in definite sequence. But since the characteristic changes of one stage do not disappear before evidences of the next appear, manifestations of the preceding and succeeding phase may be seen concurrently with the predominant signs of a given stage. Furthermore, different parts of the gum may show different stages. Although all sites are subjected to the same sequence of changes, they may not be affected synchronously. Rather, they are involved in a definite order: interdental papilla, the marginal, and then the alveolar gingiva. Both gums are not always equally affected; often but not invariably the upper gum shows the more advanced process.

It is convenient to describe the sequence of pathological changes in both the acute and chronic processes by following the arbitrary divisions of the rating scheme.

The acute process in the first stage presents the subsurface vascular papillae in an engorged and dilated state. Under the microscope these enlarged, congested capillaries are quite readily perceptible. In the mild degree this change is restricted largely to the interdental papillae and then the marginal gingiva. In a more intense condition the vascular reaction occurring more diffusely may be seen over the entire gum. There is little or no swelling.

In the second stage, the gum itself becomes red. In mild cases the heightened color is seen first at the points of the interdental papillae and then spreads to their bases and the marginal gingiva. It forms a serrated line across the free margin varying in intensity from light to vivid or dark red, but always deeper in shade than the less affected alveolar gum. In cases of more marked degree a pronounced redness extends uniformly over the entire gum. Very little or slight swelling is present at this time. The subsurface capillary papillae, beginning to show disturbance of their usual arrangement, become less discrete and distinct. The intense redness of the gums seems to be a diffuse coloration from engorged larger, deeper vessels. In the early part of this phase, however, many subsurface capillaries, much

congested, may appear as more intensely tinged points against a diffuse red background and impart to the gum a mottled appearance. The line of vascular demarcation usually present at the labial border of the gum, beneath which mucosal vessels disappear, may now be less distinguishable or entirely undistinguishable as the gingival surface assumes a near similar hue to the labial mucosa.

In the third stage, the reddened gum undergoes swelling. Here again, the intensity of the redness and swelling may be mild, moderate, or severe. In some instances these changes are restricted to the interdental papillae. More often the marginal gingivae, also affected, form a red, swollen collar projecting in high relief around the necks of the teeth. In such conditions the alveolar gingiva will be much less involved, usually showing more coloration than swelling. Very frequently the redness and swelling are present in the entire gum. The swelling may be so intense as to stretch the gum and give its surface a glossy, satiny finish. At the same time the tissue may be fiery red. Or when the swelling is disproportionately more marked than hyperemia, the emanation of redness from the underlying vessels may become so diffused by fluid as to give a pastel tint to the gum. The subsurface capillaries may not be seen.

At its free edge the gum may recede slightly, exposing more enamel surface of the tooth and increasing the length of the crown. If the gum is markedly swollen, its margin abutting against the tooth may form a trough. The gingival crevice may be enlarged and filled with calculus. Beginning formation of a pocket containing calculus and materia alba may be seen. Often the widened and deepened sulcus formed a well-developed pocket that was highly infected and filled with accumulated sordes and debris. At such a site the infection may be so destructive that the entire gum in that segment is broken down. From the resulting marked recession and thinness, a longitudinal groove appears in the gum. Infection of the gum is very common in this stage. Also most of the persons in this

series who had reported bleeding gums after brushing their teeth had changes typical of this stage.

More profound conditions seen in fully-developed scurvy, although not contained in the present series of cases, have been frequently described. The congested, spongy gums bleed readily, especially at their margin. In still more marked cases the enormously swollen gums are ulcerated and covered with a foul, necrotic material. Later the teeth become loose and may fall out; and the alveolar process undergoes necrosis. In such conditions, secondary infection with its added deleterious effects is especially conspicuous.

If the changes in the previous stage are not excessively severe or profoundly destructive, the acute process in its next stage shows beginning subsidence. At first the redness disappears with the swelling remaining. The gums appear greatly distended but pale in color. Probably infiltration takes place, either supplanting or masking the hyperemia and bringing about the disappearance of the redness. The interdental papillae and the marginal gingiva may be quite swollen and whitish in color, the distended tissue forming a collar around the tooth. In other instances the entire gum is greatly distended but exceedingly pale. In its pronounced form the tissue looks as though it were waterlogged. The subsurface capillaries are no longer visible.

In the chronic process the first stage is characterized by slight dilation and engorgement of the subsurface vascular papillae. The vascular reaction imparts a light redness to the gums. Shortly thereafter appears slight swelling. Coming first in the interdental papillae, the redness and swelling then extend to the gingival margin and finally, if of sufficient degree, over the entire gum.

In the next stage, the redness from the vascular reaction is gradually obscured by edema and probably by infiltration. At first seeming to contain excessive fluid and later to take on a more concentrated consistency and to be more opaque from a slight influx of light grey material, the gum is swollen but pale. The subsurface

capillaries are completely masked. The process may be confined to the interdental papillae and the margin adjacent to the teeth, or it may be present over the whole gum. It is probable that many of the acute processes subside into this stage and become chronic.

In the third stage, atrophy begins. The heavily infiltrated gum, which may show considerable distention and hypertrophy, now begins to manifest atrophy in the form of pitting. These pits are minute depressions. They appear first on the interdental papillae, then on the gingival margin adjacent to the tooth, and finally, may occur scattered over the entire gum. Although these pits, when large, can be discerned in the gross, they are best seen under the microscope. Indeed, only by this means can the beginning or smaller pits be observed. At first they are mostly subepithelial; they appear as funnel or cup-shaped depressions largely under the surface with the epithelium dipping only slightly at each point. Later, the epithelium is drawn in more deeply at each spot. In effect the surface seems to be studded with countersinks. Occasional isolated nodules may be seen. Along with these changes there is beginning retraction of the gum at its margin. In marked degrees of this stage the gum may be thick. Its general configuration then is rounded rather than modeled to the contour of the dental roots. In consistency, the gum is quite firm.

In the next stage, the atrophy becomes more profound. On the interdental papillae, the pits, which previously were so prominent, gradually disappear. The papillae show a decrease in size in all dimensions and gradually recede to the point of complete disappearance. The atrophic process may extend to the margin of the gum adjacent to the tooth. There may be extreme recession of the gum, leaving much of the cementum exposed. Consequently, the teeth show an increase in the length of their crowns and a loss of their root surface. Here again, pits that may have been present on the margin disappear, as the gum itself gradually recedes from its true position. In the most pronounced form, the entire gum is in-

volved. The interdental papillae have been lost, there is marked retraction around the neck of the tooth, and the remainder of the gum shows pronounced atrophy. Its color becomes white. In general, the contracted gums have a rounded contour. A few presented a rough nodular surface. Rotated, extruded, and loose teeth and diastema are very common. In this stage the line of vascular demarcation at the labial border of the gum is also undistinguishable.

It should be restated that in any state in the chronic process there may be an exacerbation. Consequently, an atrophic gum with retracted interdental papillae, retracted margin, and pale color may become red and undergo distention, as an acute process is ignited. If the swelling associated with an acute process intervenes, in the stage of pitting, the gums may become so distended as to completely extinguish almost all of the pits.

For both the acute and chronic processes, whether in the interdental papillae, gingival margin, or the entire gum, the changes were in general quite uniform from segment to segment in the field of observation in any one gum, though they were often accentuated by infection in one or two localized sites. Very frequently one gum was more severely affected than the other. It should be emphasized that both the acute and chronic gingival changes were noted in two edentulous adults.

None of the persons showed any skin lesion.

VALUES FOR ASCORBIC ACID IN PLASMA

From the group of forty-nine persons, blood samples for the determination of ascorbic acid concentration in the plasma were obtained from forty-two prior to therapy. It was found that 43 per cent of the latter had concentrations below 0.6 mg., the level frequently adopted as a significant dividing line; while 21 per cent had concentrations below 0.2 mg. per 100 ml. According to the usual interpretation of blood levels, 43 per cent of the persons might be suspected to have avitaminosis C. In contrast, it is to be remem-

GINGIVAL RATINGS	CONCENTRATION OF ASCORBIC ACID IN MG. PER 100 ML. PLASMA							
	0.00-0.19	0.20-0.39	0.40-0.59	0.60-0.79	0.80-0.99	1.00-1.19	1.20-1.39	1.4+
III Sl One							1	
III Sl Both					1		1	
III Mod One	3	2	1	4	2			1
III Mod Both	1	2	1	1		2		
III Mkd One	2					2		
III Mkd Both	3		2	2		2	1	
IV Sl Both		1			1			
IV Mod One				1	1			
IV Mod Both								1
TOTAL	9	5	4	8	5	6	3	2

Table 1. Values for concentration of ascorbic acid in plasma are arranged according to the corresponding ratings of the gums for their acute process.

bered that all had gum lesions; therefore, judged by tissue criteria, 100 per cent had avitaminosis C. It is interesting that 26 per cent, all with gingival lesions, had ascorbic acid levels of 1 mg. per cent or more.

When the values for the concentration of ascorbic acid are matched against the ratings from tissue changes in the acute process, it is seen that most of the values are on persons with lesions at the peak of an acute condition; and that of these persons with gingivae in this stage just as many had high as had low values for ascorbic acid (Table 1). When the values for ascorbic acid in the plasma are compared with the ratings for chronic gingival lesions, it is found that there is no evident relationship. In most stages and degrees the values are distributed just as frequently among the high as among the low levels (Table 2).

RESULTS FROM CAPILLARY RESISTANCE TEST

The capillary resistance test conducted on sixteen persons prior to therapy gave results which showed no relation to either the values for ascorbic acid concentration in the plasma or the status of the gums.

CHANGES ON THERAPY

At the outset it should be stressed that no scaling was done. In-

GINGIVAL RATINGS	CONCENTRATION OF ASCORBIC ACID IN MG. PER 100 ML. PLASMA							
	0.00-0.19	0.20-0.39	0.40-0.59	0.60-0.79	0.80-0.99	1.00-1.19	1.20-1.39	1.4+
III Sl Both							I	
III Mod Both				I	I			I
III Mkd One			I	3	2	2		
III Mkd Both	2	4	I	3	2	3		I
IV Sl One								
IV Sl Both			I					
IV Mod One	2	I		I		I	I	
IV Mod Both	I		I					
IV Mkd One	I	I	I				I	
IV Mkd Both				I				
TOTAL	6	6	5	9	5	6	3	2

Table 2. Values for concentration of ascorbic acid in plasma are arranged according to the corresponding ratings of the gums for their chronic process.

deed, no mechanical measures were applied to the gums and teeth other than whatever brushing the persons may have been accustomed to give them. For many persons brushing was probably somewhat infrequent; nor were they advised to be regular in it.

With most of the gums showing an acute imposed on a chronic process, the first response to ascorbic acid therapy was improvement and removal of the acute condition.

In the late stages of the acute process with infiltration and hypertrophy, either all the interdental papillae and collar or the entire gum lost much of its infiltration and swelling through therapy. Also, the usual pattern of the larger vessels was reestablished. Vascularity became quite pronounced in the labial mucous membrane and where it disappeared under the gum it formed a line of demarcation. In what was the most swollen part, namely, the interdental papillae and the collar, the tissue assumed a reddish hue, due to both removal of the infiltration and the reestablishment of vascularity. In many instances the color was heightened still more around the collar for a time when secondary infection had not yet been dispelled from very large crevices. Often this infection had been seemingly quiescent in this stage but became aroused with

reestablishment of the circulation. Thus, in a waterlogged tissue with slight redness in the interdental papillae and collar and rather pronounced crevices with a secondary infection, the removal of the swelling may at first increase the intensity of redness in the infected interdental papillae and collar, while the remainder of the gum will be freed of the acute process. Ultimately, if no devitalized teeth or foreign bodies are present, the infection is expelled and the acute process disappears.

In the stage characterized by hyperemia and swelling, there was diminution and removal of both manifestations. What in severe degree had been a red swollen gum became much thinner and paler. Here again, the vascular supply in the mucous membrane leading to the gum leaves a line of demarcation where it passes under the gum. Often, where originally there was intense swelling everywhere, but particularly in the interdental papillae and collar due to pronounced crevices with marked secondary infection, swelling was for a time only slightly diminished in the latter sites but almost entirely removed from the remainder of the gum. Here the secondary infection temporarily delayed the disappearance of the acute process. Where the crevice was not excessively large and the surrounding collar showed moderate swelling, there was a diminution in retraction and a disappearance of the swelling at the margin.

In mild degrees in this stage, where redness and swelling was largely restricted to the interdental papillae and collar, these manifestations disappeared. When they were present over the entire gum, but were slightly more intense in the interdental papillae and collar because crevices with secondary infection were present, therapy at first removed the redness and swelling from the alveolar gingiva. Absolutely, much of the redness and swelling from the interdental papillae and collar were also removed; but in the presence of secondary infection, enough of the manifestations remained for a time so that the margin stood out in contrast to the remainder of the gum which had already been restored to its natural color and

thickness. Some time thereafter, the redness and the swelling disappeared from the interdental papillae and collar.

It is worth while to emphasize the conditions which retard the resolution of the acute process. These conditions occurred mostly in the stages just discussed, namely, those characterized by swelling and redness or infiltration. For one thing, in this series a secondary infection, almost always focal in disposition, was frequently associated with the acute deficiency process in its climactic stages and aggravated the gingival condition at its site. This infection had to be expelled before the acute deficiency process would disappear and normal gum tissue at that point show complete restoration. Under this circumstance disappearance of the acute deficiency process from there during ascorbic acid therapy was slowed. Where no devitalized tooth was present, the secondary infection localized and drained spontaneously in response to ascorbic acid therapy. When the infection was severe, it has taken a year in some instances to resolve it and extinguish the acute avitaminotic process. With no therapeutic measure other than ascorbic acid, the signs of localized infection and the acute process vanished. Another circumstance, a devitalized tooth in whole or fragment, located in the site of the secondary infection, was apt to slow the therapeutic response. When a devitalized tooth was present in the focus of infection, it was often found advisable to have it extracted. Thereafter, the acute process rapidly disappeared. The devitalized tooth perpetuated and prolonged the infection. Whether such a tooth acting as a foreign body was sometimes *per se* the retardant, or whether it furnished a nidus for infection which was always the retarding factor, cannot be said. Practically either situation is incompatible with healthy gingival tissue.

In the stage characterized mainly by redness, therapy reestablished vascularity, with its characteristic line of demarcation, and at the same time removed redness from the gums, leaving them in their natural color.

Since the acute process in many instances may mask much of the chronic changes, removal of the former then brings out the latter underlying condition with its full manifestations. Very often a gum swollen and showing only traces of pitting here and there, is seen to be heavily pitted upon dissipation of the swelling. Similarly, interdental papillae may, prior to therapy, be apparently normal in size and position, but upon removal of the acute process with its swelling, they may be left in their actual basic condition, atrophic and contracted.

After the acute changes are expelled, the chronic process undergoes recession.

In the advanced chronic stage characterized by atrophy of the entire gum, including the interdental papillae, with marked retraction, the response to therapy occurred first in the alveolar gingiva where a new material was laid down, giving increased thickness to the gum and imparting to it a whiter color. Teeth that were previously loose became firm. Where much of the infection had disappeared from the margin, the crevice became much smaller and the gum tended to move to its accustomed place, obliterating much of the crevice.

Persons with gums of marked degree in this stage usually also had an acute process and one or more heavily infected areas. Consequently, in these instances the acute deficiency and the infective processes have taken most of the year to disappear and the chronic process has just begun to undergo recession. But the changes on therapy in the less intensely involved gums in this stage give an indication of the course of events.

In moderate and slight degrees of this stage, after the acute process has withdrawn, the deposition of a new substance throughout the gum may be observed. Although this material was laid down over the entire gum, it seemed to appear first on the margin and interdental papillae sites which were most seriously affected. At this time also, not only may the crevices begin to be obliterated, but the

interdental papillae which were partially contracted may show extension to more nearly their normal length. With the deposition of a new substance throughout the gum, any pitting disappears.

Gingival tissue in an advanced chronic stage with little acute process is much less vascular than in the normal condition. Its heavy infection may be low grade. Then the first response to therapy is restoration of the vascularity. From this response, together with the reaction to the infection, the gum may temporarily take on pronounced redness. As the infection is overcome the gingival tissue then gradually assumes its natural, normal color which initially it had lacked.

In the cases of marked degree in the stage characterized principally by generalized pitting, there was laying down of material throughout the gum. Frequently this deposition was seen first in the depths of the pits, its whiteness giving the gums under the microscope a dappled appearance. With this material filling in the gum, the pitting on the surface then tended to disappear. Usually, it disappeared first from the alveolar area so that at one stage in the recovery period a gum that had previously been entirely pitted now showed pitting only in the interdental papillae. At this time, the interdental papillae also began to resume their normal height. Along with the extension of the papillae came the climbing of the collar to cover the tooth and the disappearance of the crevice. Also, the subsurface capillaries began to reappear in orderly arrangement, at first emerging only slightly but later to their usual position. In lesser degrees with the pitting limited to the interdental papillae and margin, the course in recession has been similar.

The gum in the stage marked by distention and infiltration lost its swelling. If in this change, pitting or slight atrophy of the interdental papillae was unmasked, the laying down of new material filled in the area and gave it more substance. The papillae and margin began to regain their usual positions, while the entire gingiva through deposition of new material added substance.

Control groups receiving nicotinamide or vitamin A have shown no improvement in their gums.

Two months after therapy had been started, determinations for the concentration of ascorbic acid in plasma were conducted on seven persons receiving ascorbic acid, five of whom had had initial values below 0.60 mg. per cent. After two months on this therapy, all seven persons had values higher than 1.25 mg. per cent, one as high as 1.76 mg. Yet, at this time, their gingival tissue had not appreciably changed in response to the therapy.

Of six control persons receiving nicotinamide who had initial values for ascorbic acid below 0.60 mg. per cent, only one had a concentration above that level two months later with their usual diet as their sole source of ascorbic acid.

DISCUSSION

Since scurvy arises from a deficiency or disturbance in ascorbic acid, it is pertinent to consider the recorded manifestations of that disease, especially changes in the gums. In the long recorded history of scurvy, many reports are on epidemics occurring among armies, naval- and merchant-vessel crews, and civilians of besieged cities.

In his celebrated treatise on scurvy, Lind reviewed critically all the previous writings on the subject (10). He says: "The first description of a true scurvy [in armies] that I have met with, is what occurred in the Christian army in Ægypt, about the year 1260, under Lewis IX. But there mention is made, not only of the legs being affected, but also of the spots. The fungous and putrid gums are particularly described."

From the records of an outbreak on Jacques Cartier's second voyage to Newfoundland in 1535, Lind quotes (11): "... some did lose all their strength, and could not stand upon their feet; then did their legs swell, their sinews shrunk, and became as black as a coal. Others had also their skin spotted with spots of blood, of a purple colour. It ascended up to their ancles, knees, thighs, shoulders, arms

and neck. Their mouth became stinking; their gums so rotten, that all the flesh came away, even to the roots of their teeth; which last did also almost all fall out." In subsequent accounts of the disease these signs are invariably mentioned, as well as less constant manifestations, although various observers placed them in different sequences.

Echthius in 1541 arranged the symptoms into two classes (12). The first, which appear at the beginning, comprise lassitude; weakness of the legs; itching, redness, and pain of the gums; and darkening of the complexion. He observes that where all these symptoms concur, an approaching scurvy may be foretold. Under the second class he enumerated the succeeding and more certain signs: a fetid breath; a spongy swelling of the gums, which are apt to bleed, with loosening of the teeth; eruption of spots on the legs.

Wierus in 1567 wrote that weakness and pain in the legs was felt at the approach of the disease; the flesh of the gums was often destroyed to the roots of the teeth; small hemorrhagic spots appeared on the legs (13). Similarly, Brunerus (14) stated that violent pains in the legs preceded the scurvy, and that the spots and putrefaction of the gums followed soon after. But Dodonaeus (15), reporting in 1581 on an epidemic of scurvy, stated that many persons did not manifest the spots, rather their gums were chiefly affected. Also, Eugalenus in 1604 listed putrid gums as the first sign and hemorrhagic spots as the next manifestation (16).

Dividing the course of scurvy into three stages, Lind himself (10) described the symptoms in the order of their appearance. As characteristic of the first stage he mentioned: change in complexion, lassitude, stiffness and weakness of knees, gum changes, hemorrhagic spots on the skin, and beginning edema in the legs. "Their gums," he reports, "... swell, and are apt to bleed upon the gentlest friction. Their breath is then offensive; and upon looking into their mouth, the gums have an unusual livid appearance, are soft and spongy, and become afterwards extremely putrid and fungous, one of the

most distinguishing signs of the disease." He asserts: "These are the most constant and essential symptoms of the malady in the progress of its first stage. But a diversity is sometimes observed in the order of their appearance." In the succeeding stages, the condition of the gums grew worse.

Early in the disease, Himmelstiern noted (17), the gums were pale and less turgescient than in their healthy condition; later in the spring and summer months they showed livid, soft swelling, to the point of thick puffiness. Then pain, swelling, and spots appeared in the knees. Arranging the signs of scurvy into four classes or stages, Curran cited gingival changes in all classes (18). Of the gums in the first class, he stated that they were never natural. He described pale, thin, as well as red, swollen gums. He wrote: "A diseased condition of the alveolar margin of the gums seems to be the most constant of the characteristics of scurvy." Krebel, dividing the disease into three stages or degrees, likewise mentioned pale, thin or red, swollen gums (19). Other clinicians in the same era regarded gum affections, edema in the legs, and hemorrhagic spots as a basis of diagnosing scurvy (20-23). Immerman stated that after an initial or prodromal period, the scorbutic condition appeared in the majority of cases, but not always, in the gums (23). Gingival lesions are regarded as remarkably constant by some present-day observers (24, 5, 25).

Besides the main characteristics of scurvy in adults, just presented, the disease as it occurs in infants has been especially studied. In 1878 for the first time, Cheadle (26), reporting on the concurrence of swollen or bleeding gums and swollen tender thighs in three infants, characterized the condition as scurvy. Barlow, in 1883, reviewing the literature on twenty previous cases and presenting observations on eleven new cases, demonstrated that the involvement of the thighs was subperiosteal hemorrhage (27). In fifteen cases there were changes in the gums; in six, none; in the remaining ten, the gums were not mentioned. Barlow believed that the absence

of sponginess in the latter instances was the reason his colleagues had dismissed scurvy as a possible diagnosis, an interesting indication of the diagnostic emphasis placed on gingival changes at that time. For the condition he proposed the name infantile scurvy, "which is distinguished from adult scurvy by the greater incidence of the disease of the bone." It was found to be most prevalent between the ages of nine and eighteen months.

In 1894 Barlow (28), advancing an explanation of this seeming variance between gums and subperiosteal manifestations in infantile and adult scurvy, laid more stress on the gingival changes. He wrote: "The condition of the gums is very important. Defective observation on this point has led to frequent misconceptions as to the nature of the disease. Stated generally, the gum condition may be said to bear a definite relation to the number of teeth which have appeared. If several teeth have appeared, considerable sponginess of the gums may be manifest. Fleishy swellings form, which even project from the mouth and give rise to bleeding and foeter. But if only a few teeth have appeared the sponginess may be slight though definite, forming a narrow, fleishy ridge round each tooth. If no teeth have appeared the gums may be normal or may present small, bluish extravasations over the sites of the on-coming teeth."

Continuing, he stated: ". . . with respect to the gums, we may classify the infantile cases into those which have limb symptoms with spongy gums, and those which have limb symptoms without spongy gums, and we have found that the state of spongy gums is practically conditioned by the presence of teeth. If there are several teeth the sponginess is efflorescent, and in the severe cases the foeter, the bleeding, and the protruding tumours are indistinguishable from what we find in typical scurvy. If there are no teeth there is no sponginess, though there may be found on careful inspection minute ecchymoses. Now the greatest stress has been laid upon the gum condition in adult scurvy; but there is abundant evidence that a toothless man may present the limb weakness, the cachexia, and

anemia, and yet show no sponginess of gum whatever. In mild cases of land scurvy also it is constantly observed that the sponginess is limited strictly to the neighbourhood of those teeth which remain; and if there be large intervals where the teeth have been lost no sponginess appears in those intervals. I may here refer to a series of five cases which have been under my observation at different periods, but which in age were beyond the limit of infancy. In these five cases—children from two to ten years of age—there was undoubted scurvy, produced, I believe, by a curious hysterical antipathy to vegetables and meat. The gum affection was generally more severe than that of the infantile cases above described. The limb affection resembled that of the infant cases, but was less severe. The study of these cases occurring in childhood shows, I believe, a middle term (so far as the symptoms are concerned) between the infantile group and adult scurvy.”

Subsequent investigators have, in the main, subscribed to this view (29-34). But Netter (35) and Bardin (36) have particularly stressed changes in the gum, in addition to the swelling in the leg. Epstein (37) has declared: “. . . in the edentulous jaw the gingivitis is usually not absent. It is only less distinct and makes itself manifest in a slight reddening, swelling and edematous condition of the gum over the alveoli of the upper incisors. As a rule the gingivitis is detectible simultaneously with the bone swelling, exceptionally it first appears later.” In a like vein Holt and McIntosh (34) assert: “Changes in the gums are commonly found in the early stage, although they are rarely the first symptom to attract attention.”

Characteristic changes of scurvy in the bone during infancy as well as later during the period of growth have been studied in human beings (38, 39) and experimental animals (40-43). Both macroscopic and microscopic observations have been made. Moreover, the scorbutic manifestations perceptible in roentgenograms of the skeleton have been described (44, 45).

Many clinicians have attempted to describe the sequence of mani-

festations in scurvy; several have tried to divide the course of the disease into stages (10, 18, 19, 46). Most of the investigators, interested in early diagnosis, set down their observations on the earliest sign of scurvy. Moreover, they distinguished a period before the disease proper appeared, before its well-known signs could be recognized. Others later conceived that scurvy might exist below the level of clinical detection for a prolonged duration. Despite the variety of names by which these states were designated—premonitory signs, prodromal period, *forme fruste*, prescurvy, abortive scurvy, latent state—despite the differences in concepts about the states and their points of identification, all agreed that most of the scurvy occurred in these states (10, 12, 13, 14, 18, 23, 41, 47-57).

Still later with the recognition that scurvy appeared in still another state, the so-called monosymptomatic state, the aim was to elicit or detect that sign by appropriate methodology before it became grossly perceptible. As was generally agreed, the three principal manifestations of scurvy were: hemorrhages on the skin, bone changes, and gum lesions. Methods for detecting the first two manifestations in their early or mild state have already been widely applied. Detection of the third, gingival changes, forms the content of the present paper.

Latent fragility of the capillary walls, a state predisposing to hemorrhage, has been tested by determining whether petechiae or ecchymosis could be produced on a skin site by application of measured pressure. Originally, capillary fragility was described in association with a variety of pathological states (58-62). In 1914 Hess described tests with positive pressure showing impaired capillary resistance in scorbutic infants (63). Using the same procedure and counting petechiae, Göthlin suggested that it be used as a measure of vitamin C status (64). Meanwhile, a method applying negative pressure had been developed (65) and applied to detection of avitaminosis C (66).

The limitations of this procedure have been fully discussed (67,

68). Besides yielding a high degree of variation in values, it has proved disappointing in the most important respect, the detection of early or mild avitaminosis C. In the present work, as in numerous instances, the results from the method were entirely inconclusive.

In an excellent paper on the recognition of scurvy, Park and co-workers have described the early changes in bone as seen in the roentgenogram (69). In the practice of pediatrics this means of revealing early scorbutic changes has been extremely valuable. As a procedure for detecting avitaminosis C in the general population, however, it has certain limitations. It is applicable to a narrow age period, infancy and childhood. Indeed, it has never been asserted that detection of bone changes by x-ray, in its present application, would be sufficiently sensitive to allow appraisal of vitamin C status.

In considering gum lesions as a basis for detecting avitaminosis C, it is essential to recognize that they present manifestations other than hemorrhage. In fact, when hemorrhage occurs the pathological process in the gum is far advanced; for bleeding is preceded by a sequence of definite changes. Furthermore, hemorrhage is a contingent phenomenon; the expression "apt or tend to bleed" appears repeatedly in the literature. Therefore, if hemorrhage was the only criterion, if earlier changes were ignored, the full value of observations on the gums in detecting incipient and low-grade states would be impaired; with its range of application and sensitivity thereby greatly restricted, the true usefulness of the procedure in appraising vitamin C status would be misjudged. A minority of observers based their diagnosis solely on hemorrhage, and apparently accepted anything prior to that as insignificant or normal. However, most, as will have been noted, distinguished a course of changes in the gums. Indeed, some rightly designated these manifestations as gingivitis (31, 35, 37, 39).

More recent evidence points even more specifically to gum changes as an integral part of avitaminosis C. In addition to the epidemics of scurvy with gingival manifestations already cited, nu-

merous outbreaks occurred during World War I. Reports on them described gingivitis in various stages. The changes in the gum were characterized as early (46, 70), constant (71), and very marked (37, 72-76). By a few observers they were represented as prominent but absent in some cases (77-80); by one, as early or late and often absent (81).

It is interesting that as early as 1878 Cheadle with long-range vision anticipated that scurvy with only gingival lesions might occur (26). He wrote: "I have said that cases of scurvy are rare amongst children in large towns, and instances of the fully-developed disease undoubtedly are so. It seems to me possible, however, that the cases of ulcerative stomatitis, which are not infrequent amongst ill-nourished, neglected children, may be due to the scorbutic condition—i.e., imperfectly-developed scurvy. The foul ulceration of the gums closely resembles the condition of these parts presented by cases of scurvy where the swelling of the severest stage has subsided, and the general cachectic condition is analogous to that which exists in scorbutic disease."

In 1941 Crane and Woods (82) reported an outbreak of avitaminosis C, among a group of children, characterized clinically by gingival changes. Similarly, in a dental clinic, a group of outpatients affected only with periodontal disease were found to have avitaminosis C (83).

Prominent among the signs of scurvy produced experimentally in animals by a vitamin C-deficient diet were typical gum changes (40, 84, 85). Furthermore, periodontal disease comprising alveolar atrophy was diagnosed histopathologically in animals with restricted intake of vitamin C (86-88). Most convincing of all, numerous reports asserted that gingivitis, in many instances far advanced, severe and complicated by secondary infection, was cured in persons by administration of vitamin C. In the first studies lime juice (77), lemon juice (54), and orange juice (89) were used; in later investigations, pure ascorbic acid (82, 90-97).

These various lines of evidence support the thesis that gum lesions are specific and invariable manifestations of avitaminosis C. It is evident that reports on the occurrence of gingival changes depend on the examiners' concept and criteria. Furthermore, because of these differences in diagnostic standards and because many observations were on fully-developed scurvy, with its several manifestations already present, it is not possible to conclude from the literature on scurvy in persons which sign was first in appearance. Evidence from experimental animals, if applicable, indicates that tooth pulp is the site of initial change (41, 98). Zilva and Wells stated (98): "Our animal experiments show definitely that the scurvy may be of an extremely mild form, and yet produce very marked changes in the teeth." Practically, however, the present work shows that the gums are affected sufficiently early to serve as a useful manifestation.

In all respects, therefore, examination of the gums forms a satisfactory basis for appraisal of vitamin C status. The gingival tissue is readily accessible to observation. Its changes are specific and constant in occurrence. They are present in all states of avitaminosis C: they appear early, persist and reflect its course. From them any state may be rated in terms of form, stage, and degree. The biomicroscope is exceedingly sensitive in revealing the very early and slight tissue changes. Low-grade states, whether prolonged or not, may be detected by it. The slighter the change and the closer it approaches perfection, the more the biomicroscope is required.

With the development of accurate methods for determining the concentration of ascorbic acid in blood and urine, analyses were conducted on these fluids, after a fasting period or a test dose, as a means of appraising vitamin C status. There has been a strong trend towards general acceptance of the results from these procedures as the true index of bodily status with respect to vitamin C. Indeed, the reliability of other methods of appraisal has been gauged by comparison with blood values as the criterion. Yet Greenberg,

Rinehart, and Phatak cautioned (99): “. . . the estimation of the reduced plasma ascorbic acid is only a measure of the immediate nutritive or metabolic level relative to vitamin C, and is dependent on recent dietary habits to a large degree. Although it is an index of the vitamin C nutrition at the time of the test, in a single case a low level does not imply tissue injury or scurvy (either clinical or subclinical). The latter results from the operation of suboptimal or low metabolic levels over some period of time. Conversely, a good or high level would not indicate that deficiency had not operated to produce tissue injury in the past.”

In line with this statement, Crane and Woods, studying an acute outbreak of scurvy in children by comparing gingival condition with ascorbic acid concentration in plasma, both in the autumn and the following spring, found that seven of seventeen children with consistently high ascorbic acid values on both occasions had gingival inflammation at one or the other examination; while fourteen of twenty-five children with inflammation of at least six months' duration had high values on one or the other occasion. Similar data in the present paper from comparison of ascorbic acid values with the states of the gingival lesions—with a more sensitive method of detecting and more rigid criteria of rating pathology in the gums—reveal an even less constant relationship. These results, far from demonstrating that the blood level is a trustworthy criterion for comparison of other methods, show that it has very marked restrictions as a method for appraising vitamin C status.

The reasons why blood values may not show a very close relationship to the tissue rating have already been explained (9). The following points are mainly responsible: the blood value may change seasonally as well as fluctuate very frequently, responding quickly to change in intake of ascorbic acid; the concentration of ascorbic acid in the blood changes sooner and much more rapidly than the tissue state, both in the evolution and recession of the deficiency disease; avitaminosis C is widely prevalent in the tissues in

the chronic state; improvement in the diet may raise the blood values with very little effect on the status of the chronic tissue lesion.

If the tissue is normal a low blood value is significant. In the initial attack, the lowered concentration of ascorbic acid in the blood would be the first demonstrable change and would be followed shortly thereafter by tissue change. But with widespread prevalence of avitaminosis C, particularly in the chronic form, and its establishment early in life in most persons, a normal state in the gingival tissue is relatively infrequent. Hence, the blood method as a primary screen for the appraisal of vitamin C status has in reality a very limited range of application. Furthermore, when chronic changes are present—and this is the common eventuality—they recede very little upon any sustained improvement in diet and only very slowly under persistent therapy, while the ascorbic acid concentration rises immediately in response to either event. Temporarily or consistently, therefore, the blood value may be moderate or high without demonstrable recession in the existing lesion. Appraisal from the blood value alone would be entirely misleading.

From the concept of deficiency states (9) it may be seen that avitaminosis C includes all forms, degrees, and stages. Scurvy represents the severe acute state. It is interesting that several investigators have mentioned one or another of the various other states embraced by this concept. Hess (49) recognized three types of scurvy: the florid, with well-developed signs of the full-blown condition; the subacute, the commoner form, presenting a group of incompletely developed symptoms; the latent, resulting from a negative balance in ascorbic acid during the period prior to the onset of clinical manifestations. According to his conception of the course of events, the latent "may advance no further, . . . it may gradually merge into subacute scurvy and develop no further," or "the typical gradation may ensue, of latent, subacute and florid infantile scurvy." Several investigators have graded avitaminosis C into three degrees: one rated scurvy, using changes in the gums as a

principal part of the basis (72); the others distinguished degrees of gingivitis (89, 82).

In scurvy produced in animals, Tozer differentiated the chronic from the acute form on a time basis (100). She stated that the chronic form varies in severity according to the degree of deprivation of vitamin C. Using a different terminology to express intensity, she described mild and severe degrees for both the acute and chronic forms. Recognizing these various states, Höjer (41) employed still another nomenclature. Ferrario (101, 102) also produced acute and chronic scurvy in guinea pigs. Clinically periodontal disease is classified into gingivitis and alveolar atrophy, according to Boyle (86-88). He pointed out that gingivitis and marked alveolar rarefaction occur in acute scurvy. Upon producing chronic avitaminosis C, he noted that similar changes took place at a slower rate, particularly was diffuse alveolar atrophy a conspicuous feature.

It will be noted that in the present work many of the persons showing most marked atrophic changes in the gingiva manifested signs of alveolar atrophy. Indeed, the changes observed in the acute and chronic states, respectively, include the two aspects of periodontal disease. Earlier investigators observed pale, thin gums without distinguishing them as chronic gingival changes. Most of the literature on avitaminosis C, however, pertains only to the severe acute form. Generally the mild acute, mild and severe chronic states, the most common states of avitaminosis C among the population, have not been recognized, differentiated, and appreciated.

Considerable evidence shows that there is a high prevalence of avitaminosis C (103), including much of rather severe degree. Few persons have throughout life faithfully observed a dietary regimen satisfactory in its vitamin C content, or escaped the many other causes contributing to the deficiency state. Of the many with tissue affected, few have taken measures to restore it completely. In the gums are registered the cumulative changes, an arrested, incompletely receded, or progressive chronic as well as a fresh acute

process. Furthermore, the standard of perfection in the tissue is highly exacting and biomicroscopic detection is very sensitive. All these points make the high prevalence of avitaminosis C understandable.

Various criteria of recovery have been reported in the treatment of avitaminosis C with ascorbic acid. In some studies on gingivitis, therapy was terminated when the gums no longer bled on application of pressure. In treatment of scurvy, therapy was discontinued when the body was presumably saturated with ascorbic acid, as judged by analyses on blood and urine. But saturation does not mean restoration of tissue. It has been seen in the present work that all the blood values on the persons receiving ascorbic acid became very high in two months while the gums had as yet shown only slight improvement. If recovery is judged by hemorrhagic or saturation criteria, the patient would be discharged incompletely treated. Furthermore, there is much chronic avitaminosis C, some with secondary infection, and a long period is required for recession. It should be observed that in treating gingivitis with ascorbic acid for only a short period, even several months, and noting little or no apparent improvement in some instances, investigators may be misled in their conclusions on the effectiveness of the therapy, because they are dealing with a chronic condition, perhaps also secondarily infected, for which a long period of therapy is necessary. All these points suggest that, in the past, avitaminosis C has not been completely treated. To be complete the therapy should be continued until the gums show no abnormality.

It should be mentioned that the prevalence of secondary infection noted in the present work among some of the persons with advanced or severe gingival conditions parallels previously reported occurrences in association with gum lesions in avitaminosis C (24, 33, 39, 78).

SUMMARY

Of forty-nine persons in a low-income group, all had gross or

microscopic gingival lesions characteristic of avitaminosis C.

Following administration of ascorbic acid to twenty-five persons in this group, the gingival lesions in two have now almost entirely receded, as judged in all instances by biomicroscopic examination. The initially more severe lesions in the others of the therapeutic group have receded markedly, some nearly completely.

In all cases the striking feature is the very long period of time required for complete recovery, more than a year even with therapy of high potency. In this respect, avitaminosis C is similar to avitaminosis A, ariboflavinosis, and aniacinosis. This common feature, the slow response, leads to a concept of the deficiency states in which the importance of chronicity, as well as mild states, is emphasized.

Those persons receiving vitamin A or nicotinamide have shown no improvement in the gums.

For detection of avitaminosis C, examination of the anterior gums is recommended as a simple, convenient, objective method. When biomicroscopic is combined with gross examination, all forms, degrees, and stages of avitaminosis C may be noted and graded.

The marked prevalence of avitaminosis C is explained.

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