C. Advancing.

1. Changes of early stage plus further destruction of cartilage.
2. Beginning of definite lipping of bone.

D. Late.

1. Slight (decreased) periarticular swelling.
2. Destruction of cartilage more or less complete.
3. Marked marginal lipping of bone.
4. One or both of the following: (1) subchondral bone; (2) areas of destruction and hypertrophy.

E. Later.

1. Deformation.

CONCLUSIONS

1. In arthritis, roentgenograms alone are rarely characteristic enough to be diagnostic of any specific ætiologic condition.

2. When the roentgenologist uses the terms "atrophic," and particularly "hypertrophic," he must be sure the clinician knows he is referring to the roentgenographic image and is not diagnosing a clinical syndrome—for example, "hypertrophic arthritis" (meaning senescent or primary osteo-arthritis). The two may or may not be synonymous. This may be important in medico-legal cases.

3. The roentgenographic "diagnosis" is not final, but always subject to correlation with the clinical data.

RHEUMATIC FEVER AND NUTRITION*

By JAMES F. RINEHART

THE factors controlling the development of rheumatic fever afford an intriguing medical problem and one of major importance to public health. Most investigators have concerned themselves with the bacteriological aspect of the disease. That an infective agent is operative in the development of rheumatic fever can hardly be denied. The work of numerous students strongly implicates the hæmolytic streptococcus.¹ The more recent work is particularly impressive. The common occurrence of respiratory infections with various strains of Group A hæmolytic streptococci preceding the onset of rheumatic fever

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strongly incriminates this organism as the infective agent. On the other hand evidence also indicates that some other factor or factors are operative. While respiratory infections with effective strains of hæmolytic streptococci are common, in only a small minority of cases are such infections followed by the rheumatic syndrome. A most promising line of investigation would appear to be a search for pre-disposing or conditioning influences. The difference in frequency of rheumatic fever at the extremes of the social economic scale has not received the thought and study which it merits. Most of such studies have come from England. Campbell and Warner² report that rheumatic fever is the most crippling affection of the poor. Glover³ believes that no disease has a more clean-cut social incidence than rheumatic fever and estimates the occurrence of acute rheumatism as 20 or even 30 times as great in the poor as in the well-to-do. Miller⁴ finds that, although the frequency does not seem to follow absolutely the variations in degree of poverty, "yet nothing is more certain than that it is a disease of the poorer classes." Coombs⁵ notes that it is quite certainly a rare disease among the well-to-do. Among 1,000 children from the Out-Patient Department of King's College Hospital, London, the incidence of those showing evidence of acute rheumatism was 13.1 per cent., whereas among 700 children from private practice the incidence was only 0.7 per cent.,⁶ a *ratio of 19 to 1*. Paul⁷ finds a less striking, though distinct, association with poverty in his New Haven studies. It seems probable that less marked differences in social-economic conditions were present in the New Haven groups. There are, of course, a number of factors which might be operative in the different social environments. To the writer it appears unlikely that hereditary influences would be responsible for striking differences in "social" incidence. Although little is known with regard to the incidence of hæmolytic streptococcal infections in various social categories it also appears extremely improbable that the organism would exhibit the striking social selectivity observed in rheumatic fever. One variable factor intimately associated with social environment is undoubtedly nutritional. This has been rather clearly shown with respect to vitamin C.⁸ As indicated below, very suggestive, if not conclusive, evidence has already accrued implicating nutritional deficiency as a contributory influence in rheumatic fever. If this is so, it would give the whole problem a hopeful outlook for ultimate control. Certainly this aspect of the problem deserves thorough investigation. It is the purpose of this paper to review the evidence implicating nutritional deficiency in rheumatic fever.

Vining⁹ emphasised the debilitated state of the pre-rheumatic child and suggested that vitamin B undernutrition might play a rôle in the development of rheumatic fever. McLean¹⁰ reviewed the early manifestations of the disease in 258 children. He observed that they were

commonly pale, high-strung, nervous, irritable children who were easily fatigued, had poor appetites, and who were either losing weight or not gaining it as they should.

EXPERIMENTAL EVIDENCE

In 1933 we reported on a pathologic process resembling rheumatic fever, which developed in guinea-pigs subjected to the combined influence of vitamin C deficiency and infection with Beta hæmolytic streptococcus of guinea-pig origin. Heart valve and articular lesions developed which we considered to bear significant resemblance to those of rheumatic fever.¹¹ It is noteworthy that some of the animals even developed subcutaneous nodules analogous to those seen in the clinical disease. It is probable that this method has more closely reproduced the histopathology of rheumatic fever than any other experimental procedure.

Schultz¹² likewise produced non-purulent carditis by means of the synergistic influence of chronic scurvy and hæmolytic streptococcal infection. He said he considered that the changes only slightly resembled those seen in rheumatic fever. More recently McBroom, Sunderland, Mote and Jones,¹³ as well as Taylor,¹⁴ have recorded the occurrence of degenerative and proliferative reactions in the cardiac valves of scorbutic animals in which a factor of infection was not experimentally introduced. They observed no clear difference in those animals in which experimental infection was superimposed on the scorbutic state. It is of significance that for the most part the streptococci used by these authors were derived from human sources and were not satisfactory infecting agents for guinea-pigs. In our original work, streptococci derived from natural pathogens for guinea-pigs were used. In our own experience the virulence of the infecting organism is important in the production of the "rheumatic-like" pathologic picture. Stimson, Hedley and Rose¹⁵ reported the finding of a proliferative endocarditis in guinea-pigs subjected to scurvy and injected with a streptococcus toxin. They state that they had previously been attracted by the possibility of a conditioning nutritional factor in rheumatic fever. In a series of puppies in which vitamin A deficiency was followed by inoculation with streptococci derived from a case of rheumatic fever, the result was negative.

CLINICAL STUDIES OF VITAMIN C NUTRITION AND METABOLISM IN RHEUMATIC FEVER

In the clinical field the observations are conflicting, and to date are inconclusive. Perry¹⁶ (1935) determined the excretion of vitamin C in the urine of rheumatic children following a single test dose of 500 mg.

of ascorbic acid. He studied 5 acute cases and 6 quiescent cases. Three in each group showed no apparent deficiency; the others were soon brought to a state of saturation by repeated test doses of ascorbic acid. While finding that "mild degrees of deficiency are not uncommon in rheumatic children," he concluded that "vitamin C deficiency is not an important factor in the causation of acute rheumatism." Sendroy and Schultz¹⁷ reported observations on the metabolism of vitamin C in cases of rheumatic fever. Although they concluded that the results of this study did not support the concept that a condition of ascorbic acid deficiency is a predisposing factor in the causation of rheumatic fever, their results might be interpreted differently. It should be pointed out that the study was not one that evaluated the nutritional status relative to vitamin C at the *onset* of the disease. A number of the cases in the series had been given ascorbic acid supplements for one to four months prior to examination. This study, however, reveals the interesting fact that 7 of the 13 cases showed a significant metabolic abnormality, in that there was a marked discrepancy between intake and urinary excretion of ascorbic acid, indicating either a fault in absorption or enhanced destruction or utilisation of the vitamin in these cases. Abbasy, Harris and Hill¹⁸ reported findings in a large series of cases in a study based upon urinary excretion of ascorbic acid. They found that rheumatic subjects both in the *active* and *convalescent* stages were significantly undersaturated with ascorbic acid even though they were on a diet which they had found adequate to maintain saturation in control subjects. Based upon a body weight of 140 lb. the tissue deficit of ascorbic acid in the rheumatic subjects was in the range of 2 grammes. Studies which we have recently reported lead us to believe that this may represent a significant degree of deficiency.¹⁹ While they found a comparable condition in cases of active tuberculosis, the cases of convalescent tuberculosis reacted as the normal controls. The above findings were not borne out in a small series of cases reported by Keith and Hickmans.²⁰ The cause for these divergent findings is not apparent. In our experience there are many irregularities in data based solely upon urinary excretion, and a considerable urinary output may occur following a test dose of the vitamin in the presence of a low blood content and before tissue saturation has been achieved.²¹

It should be pointed out that these studies were not well adapted for determination of the degree of deficiency existing at the time of onset of the rheumatic fever. If a case of scurvy were given liberal supplements of vitamin C for several days before examination, excretion studies would naturally not reveal the pre-existing vitamin C deficiency. It is quite important, then, to take into consideration dietary modification that may have been made prior to such studies. We have attempted to do this and have based our work largely on the analysis

THE RHEUMATIC DISEASES

of the blood plasma concentration of vitamin C. It is well established that the concentration of ascorbic acid in the blood plasma clearly reflects the immediate nutritive status of the individual at the time of examination. In a series of adults¹⁹ we have found that fasting plasma ascorbic acid concentrations below 0.1 mg. per cent. usually indicate severe tissue depletion and in approximately 80 per cent. of such cases other evidences of significant vitamin C deficiency or sub-clinical scurvy can be demonstrated. Blood concentration between 0.1 and 0.3 mg. per cent. reflected lesser degrees of tissue depletion, and in a smaller percentage can be shown to be suffering from subclinical scurvy. This might be considered the range of "potential" deficiency. Adult patients with plasma concentrations varying from 0.3 to 0.8 mg. per cent. show only mild tissue depletion and it appears unlikely that they are suffering from vitamin C deficiency even though the tissues are not saturated. We have previously reported observations on plasma ascorbic acid values in rheumatic fever.²¹ Extended data regarding findings on rheumatic fever cases and control groups in adults are tabulated below (Table I).

TABLE I

	No. of Cases.	Average Plasma Ascorbic Acid.	Distribution of Plasma Ascorbic Acid Values mg./100 c.c.		
			0.0-0.09	0.1-0.3	Over 0.3
"Normal" adults ..	239	0.59	11 (5%)	29 (12%)	199 (83%)
Miscellaneous infections	176	0.37	43 (24%)	50 (29%)	83 (47%)
Acute rheumatic fever (unmodified diet) ..	19	0.16	9 (47%)	7 (36%)	3 (15%)
Acute rheumatic fever (modified diet) ..	5	0.55	—	—	5 (100%)
Acute rheumatic fever—Total	24	0.25	9 (37%)	7 (29%)	8 (33%)
Chronic rheumatic heart disease	44	0.32	12 (27%)	10 (23%)	22 (50%)

It can be seen that the average ascorbic acid concentration in the adult cases with acute rheumatic fever is strikingly low, particularly in those who had had no marked modification of diet prior to examination. In this group 37 per cent. showed the very lowest blood concentration (*i.e.*, below 0.1 mg. per cent.), which we have shown to indicate strong presumptive evidence of clinically significant deficiency,¹⁹ and most of the remainder showed ascorbic acid values in the borderline range of deficiency.

The data in children, shown in Table II, are less striking and cannot be interpreted as readily. The average normal plasma ascorbic acid concentration in children we have found to be higher than in adults,

and we do not yet know how to accurately evaluate the plasma concentration in children. These data, *per se*, are, of course, not conclusive, though they certainly are not inconsistent with the concept that deficiency of vitamin C or associated nutritional factors may be a contributory influence in the development of rheumatic fever (Table II).

TABLE II

	No. of Cases.	Average Plasma Ascorbic Acid.	Distribution of Plasma Ascorbic Acid Values mg./100 c.c.		
			0-0-0-09	0-1-0-3	Over 0-3
Normal (children) ..	31	0-75	1 (3%)	2 (6%)	28 (91%)
Miscellaneous infections	144	0-49	22 (15%)	32 (22%)	90 (63%)
Tuberculosis: active ..	28	0-49	5 (19%)	5 (18%)	18 (62%)
Tuberculosis: latent ..	61	0-76	2 (3%)	5 (8%)	54 (88%)
Acute rheumatic fever (unmodified diet) ..	49	0-34	8 (17%)	19 (39%)	22 (44%)
Acute rheumatic fever (modified diet)* ..	19	0-67	—	—	19 (100%)
Acute rheumatic fever—Total	68	0-44	8 (11%)	19 (27%)	41 (60%)

Abt and his associates²² recently reported average plasma ascorbic acid values which were slightly higher in cases of acute rheumatic fever than in scarlet fever. It must be noted, however, that the data in the two groups are not comparable, and not comparable to those reported by us. Most of the 26 children in their group with rheumatic fever and carditis had been in the hospital on a diet, which is described as excellent, for some time prior to the vitamin assay. The cases of scarlet fever were observed in another hospital, and in all instances the study was begun on, or shortly after, admission. Plasma ascorbic acid values in their cases of chronic rheumatic heart disease in a third hospital were low.

THERAPEUTIC VALUE OF VITAMIN C

Although no exhaustive study has been made of the therapeutic value of vitamin C in rheumatic fever, results recorded to date have been disappointing. Sendroy and Schultz,¹⁷ in a carefully executed but relatively short experiment, failed to find any therapeutic benefit from administration of ascorbic acid. Several recurrences of rheumatic activity were noted in cases that had received adequate supplements of ascorbic acid for periods of 1 to 4 months. Their studies of capillary

* This group represents cases in which it was *known* that the vitamin C intake had been very considerably augmented prior to chemical assay of ascorbic acid in the blood. It is not unlikely that some in the other groups likewise had received supplements.

resistance suggested the existence of vitamin C deficiency in some but not all of the rheumatic children. Abt²² likewise observed recurrences in cases which were receiving liberal supplements of ascorbic acid.

In a group of rheumatic children Kuttner²³ found that large doses of vitamins A, B complex, C and D *added to an ordinary well balanced diet* did not reduce the incidence of upper respiratory infection, and noted that 3 children who had received the additional vitamins for some period of time developed rheumatic manifestations following a streptococcic pharyngitis.

Faulkner²⁴ reported the influence upon blood formation of ascorbic acid administered in doses of 200 to 300 mg., or of orange juice in equivalent amounts, in 27 cases of rheumatic fever, 8 cases of bone tuberculosis, and 2 cases of Still's disease. Thirty of these cases showed significant reticulocyte rises following administration of the supplementary vitamin C. Although Faulkner stated that the ætiology of the infection was not the controlling factor in the reticulocyte response, it is evident that the only disease category of sufficient number to be statistically significant is the rheumatic group. It is of interest that the cases studied were receiving at least a fair supplement of vitamin C prior to the study. It is my belief that the cases showing reticulocyte rises were suffering from subclinical vitamin C deficiency. The reticulocyte responses were analogous to the reaction which follows the administration of vitamin C to patients with the anæmia of scurvy.²⁵ It is becoming generally recognised that administration of vitamins produces a physiological response only in the presence of deficiency.²⁶ No specific therapeutic effect on the course of the disease was observed by Faulkner during the one-month period of increased vitamin C administration.

The failure of vitamin C to exert a direct curative action does not imply that it is without therapeutic value. Jones²⁷ has observed the recent marked reduction of distressing hæmorrhagic manifestations of rheumatic fever—*i.e.*, epistaxis and purpura. He notes that "Ten years ago in a ward of 7 or 8 children with active rheumatic fever, 3 or 4 nasal packings daily were frequently necessary. This picture is now completely altered. Nose bleeds are so reasonably mild and less frequent that packing of the nose is unusual." This changed picture he is inclined to ascribe to the more liberal and intelligent use of vitamin C rich foods or ascorbic acid in the management of cases.

PARENTERAL ASCORBIC ACID IN CARDIAC DECOMPENSATION OF RHEUMATIC FEVER

In 1938²² we reported a case of recurrent rheumatic carditis with cardiac decompensation who exhibited a persistently lowered plasma ascorbic acid concentration in spite of considerable excretion of ascorbic

acid in the urine. Intravenous administration of the vitamin was followed by significant improvement in cardiac function accompanied by diuresis. A striking physiological effect was noted in a second case of fulminant rheumatic carditis in a 12-year-old girl. The plasma vitamin C concentration 5 days after admission to the hospital was zero. At this time the child was very dyspnoeic and cyanotic in spite of oxygen administration. The sodium salt of ascorbic acid in dosage of 111 mg. was given intravenously every 4 hours. Within 48 hours there was marked improvement in respiration and relief of cyanosis. The plasma vitamin C concentration remained at zero 4 days after the administration of ascorbic acid was started, even though approximately 2 grammes had been given. The child succumbed one month after the onset of the recurrent attack with an acute rheumatic pancarditis. The clinical relief of dyspnoea and cyanosis in the case was, however, most striking. I believe that parenteral administration of ascorbic acid is worthy of clinical trial in desperate cases of decompensation in active carditis of this type.

THE POSSIBLE INFLUENCE OF VITAMIN P IN RHEUMATIC FEVER

Szent-Györgi and his co-workers²⁸ reported the presence in extracts of Hungarian red pepper, and later in lemon juice, of a substance other than ascorbic acid which exerted a control over the number of hæmorrhages in cases of "vascular" purpura. Experimental observations in animals have been conflicting and inconclusive. However, a considerable amount of clinical data has accumulated supporting the physiological activity of this substance in increasing the capillary strength in certain types of purpura. In addition to the original work of Szent-Györgi and his co-workers, Jersild,²⁹ Scarborough³⁰ and others have contributed supporting data. It is Szent-Györgi's concept that this substance, called by him "vitamin P" (permeability factor), acted with vitamin C in maintaining the integrity of the capillary wall. He expressed the opinion that vitamin P acts in conjunction with ascorbic acid as a part of an oxidation reduction system. For several years we have been interested in the capillary strength in rheumatic diseases, and it has seemed desirable to explore the possible rôle of vitamin P. While it is clear that we have insufficient data to justify any conclusion, it seems pertinent to report briefly suggestive preliminary observations in a field that appears to be worthy of further exploration. We have administered vitamin P to 3 children suffering from acute rheumatic fever. The case records are set forth below.

Case 1.—The first case studied was that of a girl 11 years of age who entered the hospital on November 3, 1940, with a recurrent attack of rheumatic fever with manifestations of active carditis. The first episode of rheumatic fever had occurred at 7 years of age. The recurrence was of 2 months' duration on entry. The sedimentation rate on admission was accelerated (18 mm. in 17 minutes)

The plasma ascorbic acid concentration was 0.23 mg. per cent. Subcutaneous nodules were present in the scalp. The child exhibited some improvement on rest in bed. For a period of 2 months between November 21, 1940, and January 20, 1941, she was given daily intravenous injections of 500 mg. of the sodium salt of ascorbic acid. Some improvement was noted during the first month, but a mild upper respiratory infection due to a hæmolytic streptococcus precipitated a recurrence. On January 24 the rheumatic process was still active, as evidenced by an accelerated sedimentation rate (18 mm. in 30 minutes), although there had been some improvement in the cardiac function and the quality of the heart sounds. At this time the child was given vitamin P by mouth and ascorbic acid was given by mouth (150 mg. daily). From this time on there was progressive improvement. The 18 mm. sedimentation time slowed to 1 hour and 56 minutes in one month. The capillary strength as measured by the Dalldorf³¹ suction method also rose.

Case 2.—This 9-year-old girl was admitted to the University of California Hospital on December 27, 1940, suffering from an acute rheumatic fever of one month's duration. On admission the plasma ascorbic acid concentration was 0.94 mg. per cent. On inquiry it was found that the child had received a daily supplement of 8 oz. of orange juice for the past 3 weeks. The sedimentation rate was rapid (18 mm. in 25 minutes), and the capillary strength was found to be low. The child was given a preparation of vitamin P by mouth. Improvement was progressive during the ensuing month. The child was discharged one month after entry with a normal sedimentation time and with no clinical evidence of active disease. The capillary strength was elevated.

Case 3.—This 15-year-old Chinese boy entered the San Francisco Hospital on May 7, 1941, with a history of onset of acute rheumatic fever 6 weeks previously. Examination revealed a pale, undernourished Chinese boy with evidence of an active rheumatic carditis. The sedimentation rate was rapid (18 mm. in 13 minutes). The blood plasma ascorbic acid value was zero. He was given a high vitamin diet and a daily supplement of 75 mg. of ascorbic acid. The rheumatic process continued to be active during the ensuing 2 months. On July 3 a tonsillectomy was done. Two weeks later the sedimentation rate remained accelerated (18 mm. in 19 minutes). On July 20 a preparation of vitamin P was administered and continued daily. The sedimentation rate progressively slowed, being 18 mm. in 40 minutes one month later. At this time he was sent to a convalescent home and the study was concluded. No effect upon the capillary strength was demonstrated.

The capillary strength has been reported as lowered in acute rheumatic fever³² as well as in numerous other conditions. The hæmorrhagic manifestations commonly seen in rheumatic fever are well known. In view of its supposed action in conjunction with vitamin C as a part of an oxidation reduction system, and its influence on capillary strength, the possibility that vitamin P might prove useful in prevention or treatment of rheumatic fever would appear to warrant further study. Such studies are being continued by us.

PROPHYLACTIC VALUE OF VITAMIN C

The observations of Glazebrook and his associates^{33, 34} are particularly interesting and afford the first direct clinical observations indicating that vitamin C deficiency may be a major disposing influence and that correction may be of great prophylactic usefulness. In 1939, Roff and Glazebrook³³ described cases of gingivo-stomatitis among

boys in a training establishment of the Royal Navy. "The gums were congested and spongy, the surfaces having a gelatinous feel. Bleeding did not occur on simple palpation, but if one pierced with a probe the hæmorrhage was more copious than usual. The congestion was uniform, from the gums into the sulci on to the buccal mucous membrane, extending backwards and involving the tonsils and pharyngeal wall as far as the eye could see." In all cases vitamin C deficiency was found, with an average ascorbic acid deficit of approximately 4 grammes. The condition responded to administration of ascorbic acid. These authors also recorded prominent symptoms of lassitude with rheumatic pains in and around the larger joints and noted that exactly similar symptoms occur in cases in which there is evidence of infection, and that such cases may later develop rheumatic fever, with true arthritis; or carditis may develop silently without further manifestations of rheumatism. They state: "It is often impossible to differentiate from the description of the symptoms of the patient a case which will clear up on saturation with vitamin C, from one which will tend to progress to rheumatism and carditis."

In a subsequent report Glazebrook and Thomson³⁴ recorded observations of unusual interest. The study was conducted at a training school for young men between 15 and 20 years of age. The circumstances presented a unique opportunity for study of hæmolytic streptococcic infection in a population that might be considered to be in a state of subclinical scurvy. It was estimated that the average daily intake of vitamin C per student was between 10 and 15 mg.* Recurrent waves of hæmolytic streptococcic tonsillitis afforded the factor of infection. Of the approximately 1,500 students observed in the study, 335 were given liberal daily supplements of ascorbic acid, which was added to milk and cocoa. In sample studies it is noteworthy that these youths required a total supplement of approximately 4 gm. of ascorbic acid to achieve saturation. This is the approximate tissue depletion in cases of clinical scurvy.

No significant difference in *incidence* of common colds and tonsillitis

* "The diet of the institution allowed over 4,000 calories per student per day. The food distributed was badly managed. Electric ovens were used to reheat the food, and to keep it hot whilst awaiting distribution. Often 8 hours elapsed between the time the food was cooked and its arrival on the dining tables. The minimum time that heat was applied to the food, including the original cooking and subsequent reheating, was 2 hours.

"The daily ration of potatoes was 12 oz. The vitamin C content of potatoes varies, but this quantity in the raw state should contain approximately 50 mg. A full ration of potatoes, as served on the dining tables, after cooking and reheating, was found to contain, on the average, about 4 mg.

"The other vegetables suffered an equal loss, with the exception of turnips, portions of which contained up to 6 mg. The milk was pasteurised, and $\frac{1}{2}$ pint of it contained about 1.5 mg. The other cooked foods contributed negligible amounts. The total intake of vitamin C varied from about 10 to 15 mg. per student per day."

was demonstrated. The duration of illness with the common cold was not different in the two groups, averaging 6.32 days in the vitamin C treated classes and 6.4 days in the controls. However, the *duration* of illness due to tonsillitis was significantly different in the two groups. In the vitamin C treated classes the average stay in the hospital was 10.05 days and in the control groups 16.7 days.

The most striking influence of vitamin C was in the reduction of the incidence of two complications of the streptococcic infection. There were 17 cases of "pneumonia" and 16 cases of acute rheumatism among the 1,100 controls and no case of either disease among 335 youths having vitamin C. Analyses showed that a difference as great or greater than this would be expected once in fifty times in a homogeneous population. The authors felt that there was some relationship between the cases of pneumonia and those of rheumatic fever. They noted the occurrence in the institution of a low-grade basal lung consolidation or pneumonitis which appeared to be related to both rheumatism and vitamin C deficiency. "It was characterised on the one hand by its tendency to progress into rheumatism, and on the other hand by its disappearance when treated with ascorbic acid. This pneumonitis, apart from a vague picture of ill-health, gave little clinical evidence of its presence, but it probably predisposed toward the development of acute pneumonia."

Hedley³⁵ has recorded an apparent diminution of the incidence of rheumatic heart disease among persons 5 to 24 years of age during the period 1930 to 1936 compared with 1922 to 1929. It is possible that increased knowledge of the importance of nutrition to health and the emphasis upon the possible rôle of nutritional deficiency in rheumatic fever may be responsible for this decline.

SUMMARY

Evidence is strong that respiratory infections with effective strains of Beta hæmolytic streptococci commonly precede the development of acute rheumatic fever. However, it is almost clear that some other factor enters into the ætiology of the disease. It is only a relatively small proportion of such infections that are followed by rheumatic fever. This suggests an environmental influence. The social incidence definitely associates the disease with poverty. It is doubtful that streptococcic infection would show such striking social selectivity. One of the basic environmental factors associated with poverty is, of course, nutritional inadequacy. That vitamin C undernutrition is frequently seen in the poorer classes is well attested by recent surveys. The accumulated evidence cited makes an undeniably strong case for a contributory scorbutic influence in rheumatic fever. The concept has the solid foundation of experimental evidence. Vitamin C de-

iciency combined with streptococcic infection in the guinea-pig produces a pathological picture with many similarities to that of rheumatic fever. Both scurvy and rheumatic fever basically involve degenerative changes in connective tissues.

Studies of nutritional status relative to vitamin C in rheumatic fever, while not conclusive, certainly are not inconsistent with the concepts. While it has been shown that vitamin C does not exert a specific curative effect upon rheumatic fever it is likely that the frequency and severity of the hæmorrhagic manifestations have been reduced. It is not known to what extent vitamin C or related factors might further protect the patient. Maintenance of *rheumatic* patients on adequate amounts of ascorbic acid will evidently not prevent recurrence of the disease. However, data are cited which strongly suggest that adequate intake of vitamin C exerts a protective effect in an unselected group even though they are subjected to the influence of hæmolytic streptococcic infection.

Preliminary report is made of encouraging observations relative to the possible influence of vitamin P upon the course of the illness. It is evident that there is much data indicating that nutritional deficiency factors may be of major importance in favouring the onset of rheumatic fever. In view of the great importance of this disease studies in the field of nutrition should be extended.

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