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Treatment of acute rheumatic carditis and prevention of recurrence

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THE TREATMENT OF ACUTE RHEUMATIC CARDITIS AND PREVENTION OF RECURRENCE

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INTRODUCTION

The problem of the use of salicylates in the treatment of the acute phase of rheumatic fever will be discussed as regards massive dosage and the effectiveness of this therapy. No attempt will be made to completely review the history of the use of salicylates in its entirity.

The problem of prevention of recurrence of rheumatic fever will be discussed in considerable detail as regards the use of sulfonamide prophylaxsis of hemolytic streptococcal infections, diet, and tonsilectomy. The use of vaccines will not be reviewed as the clinical results have not been significant in the hands of clinicians with the exception of one clinic whose results have received no confirmation.

The problem of rest during the convalescent stage will be reviewed and an attempt to discuss criteria for ressumption of activity will be made.

The use of oxygen during the acute phase will also be discussed although this is relatively new in therapeutics.

All of these factors in rheumatic fever will be reviewed with emphasis on the treatment and prevention of recurrence of rheumatic carditis.

MASSIVE SALICYLATE THERAPY

The most important problem in the treatment of acute rheumatic fever is the prevention of organic heart disease. To effect this it is essential that the rheumatic inflammatory reaction be suppressed in the minimum of time and that polycyclic attacks of rheumatic fever be prevented. If rheumatic attacks were always monocyclic and short-lived, severe cardiac damage would rarely occur. For many years salicylates have been used in rheumatic fever in an attempt to attain these objectives. There is general agreement on the rapid antipyretic action of salicylate and on the efficient alleviation of pain and swelling of the joints with salicylate therapy. Whether salicylates prevent polycyclicattacks or reduce the incidence of permanent cardiac damage has been disputed for years.

As long ago as 1903, Lees suggested doses as high as 300 gr. of salicylate daily to obtain a "true anti-rheumatic effect" (2). In 1906 Clarke reported the treatment of rheumatic patients with 240 gr. of sodium salicylate per day, and felt that this shortened the duration of the disease and protected the heart.

In 1914, Miller (3) reviewed the literature on the action of salicylates in acute articular rheumatism. He found that with salicylate therapy, pain was relieved in an average of 5.3 days; without salicylates pain persisted for 13.4 days. Relapses occurred in 30.3 per cent of the 1,258 patients receiving salicylates, but only 6 per cent of the 974 patients who did not receive salicylates had recurrence of their symptoms. There was

no difference in the length of hospital stay in the two groups. Miller quotes Pribram on the incidence of cardiac complications; cardiac damage developed in 28.8 per cent of patients on salicylate and in 23.4 per cent of patients not receiving salicylate. During the period reviewed, Miller states that 15 to 20 grains of sodium salicylate every two or three hours was considered a moderate dose, and many physicians gave as much as 300 grains a day. In 1918, Hanzlik (4), Scott, and Gauchat in a study of the specific effect of salicylates on rheumatic fever concluded that while salicylate is effective it is not specific and that other drugs will produce the same results though perhaps not so consistently. They stated that salicylate was no more than a symptomatic remedy. They found no reduction in the occurrence of endocarditis with salicylate therapy. In 1925, Swift (5) stated that salicylates had a favorable effect on the exudative phase of rheumatic fever but that it failed to influence markedly the proliferative lesions. He felt that this explained why salicylates had no effect on chorea and did not prevent valvular lesions in patients receiving full dosage. He did emphasize that these drugs were of great assistance in reducing the fever and controlling the "toxic state." The tendency to lose weight was less marked in patients receiving salicylates. With the reduction in fever and toxicity there was a lowering of the heart rate. Swift pointed out that if salicylate eliminated the edema from the valves, as it does from the peri-articular tissues, some of the traumatic injury to the endocardium might be eliminated. He emphasized the importance, both to the physician and the patient, of continued care,

even after all symptoms are relieved by salicylate therapy, as otherwise the patient may in the end suffer more permanent injury than if he were untreated. In 1933, Graef (6), Parent Zitron, and Wyckoff reported a series of 105 cases of acute rheumatic fever treated only with opiates and local therapy to the affected joints. They stressed the tendency of the acute manifestations of rheumatic fever to subside spontaneously and often rapidly.

In 1943, Coburn (7) reopened the problem of salicylate therapy in rheumatic fever in his report of 101 cases treated with varying amounts of sodium salicylate. Sixty-three patients received only small doses of the drug, and 21 developed organic heart disease. Thirty-eight received 10 Gm. or more of sodium salicylate daily, and none of these developed heart disease. Coburn administered sodium salicylate by mouth and also intravenously in doses of 10 to 20 Gm. daily. He felt that by giving the medication by vein, a more rapid and sustained rise in the plasma concentration of the drug was obtained. His studies were controlled by estimations of the plasma level. He concluded that a plasma salicylate level of at least 35 mg. per 100 cc. may be required to suppress the rheumatic reaction and that plasma levels below 20mg. per 100 cc. may be sufficient to relieve symptoms while masking a progressive inflammatory process. Coburn's report of the clinical results of massive salicylate therapy deals chiefly with the shortening of the period of infection in patients so treated, as judged by the erythrocyte sedimentation rate. The cardiologic criteria used are not presented for valvular heart disease or for

physical signs of heart disease. His patients were young adults of 18 years or more, and in this age group cardiac manifestations and residua of rheumatic disease are less common and less severe that in children.

Hanzlik (8) credits Mendel with the first use of intravenous salicylate in 1904. Hanzlik quotes Matta, Lesne, Gilbert, Coury, and Bernard as using this method of administration. These clinicians claimed certain advantages in the intravenous method over the oral route; namely, the avoidance of gastric disturbances, emesis, and side reactions in general; more rapid absorption of the drug; and finally the prevention of cardiac complications. Coburn has revived the interest in this method and claims that a more rapid elevation of the blood salicylate is obtained and that the patient is more quickly brought under control.

McEachern (9) has reported his results in 350 cases of acute rheumatic fever treated between November, 1943, and June, 1944. Toxic reactions were frequent with intravenous medication and minimal in the orally treated group. Cardiac sequelae were present in both groups. He concluded that oral administration of 10 to 16 Gm. of sodium salicylate was the most satisfactory method of treatment. Taran and Jacobs (10) concluded that intravenous salicylate offered no advantages in treatment and that the technical difficulties and annoying symptoms outweighted the possible benefits of a more rapid rise in the plasma salicylate level.

Hanzlik, Goodman and Gillman (11), and, more recently, P. K. Smith (12) have concluded that intravenous administration is unwarranted because of the rapid and almost complete absorption of

sodium salicylate from the gastrointestinal tract. Smith has shown that peak plasma levels are reached about one hour after oral administration. Hanzlik states that the advantages claimed by the supporters of the intravenous method are unsupported by any evidence and that, when administered in this way, salicylate may cause considerable damage to the heart and other organs. Five patients given massive salicylate therapy intravenously for acute carditis died (25,26,10), either as a result of toxicity of salicylates or of failure of the treatment of carditis.

In June, 1945, Keith and Ross (13) reported their results in the treatment of two groups of patients with acute rheumatic fever in the Royal Canadian Navy. The sedimentation rate returned to normal in an average of four weeks in a group of 70 patients receiving 10 to 13.3 Gm. of salicylate per day and in four and one-half weeks in 33 patients receiving 0 to 1.7 Gm. a day. Three patients in the low dosage group and five in the high salicylate dosage group developed heart disease. Five patients who had pre-existing heart disease showed progression, two in the low and three in the high salicylate group. They could not conclude that large amounts of salicylates were of any more benefit than small doses.

Manchester (14) also treated in the manner of Coburn a group of patients in naval service. He found a smaller number of significant cardiac residua among patients given massive salicylate therapy than among controls, especially if the therapy was instituted before "signs of significant carditis" had appeared. Fulminating infections did not always respond favorably, and there were two deaths in the intensively treated group, on the 4th and

7th days, respectively.

Taran and Jacobs (10) gave massive doses of salicylates at the onset of rheumatic carditis to 8 children and treated 41 control patients in other ways. They concluded that "while it cannot be definitely stated that massive salicylate therapy unequivocally suppresses the rheumatic process and prevents the stigmata of heart disease, it is clear that this form of treatment makes the patients symptom-free."

Wegria and Smull (15) gave 21 patients massive salicylate therapy, with 19 control patients. They concluded that the course of acute rheumatic fever is not shortened by massive salicylate therapy, with the reservation that earlier institution of treatment might have resulted in shortening the rheumatic episode.

Murphy (16), in a recent report of careful studies in twelve patients receiving large doses of salicylate, questions the usually accepted view that salicylates promote the subsidence of rheumatic joint inflammation. In several patients characteristic lesions developed in a variety of sites during the course of heavy salicylate therapy. The size of inflamed joints was determined frequently, and the skin temperatures over these joints were compared with the rectal temperatures. The erythrocyte sedimentation rate was also determined. The results of these measurements did not indicate any subsidence of the inflammatory reaction under the influence of massive salicylate therapy. In addition, Murphy observed in patients receiving this treatment such phenomena as fresh rheumatic nodules and, in one case, fresh polyarthritis and electrocardiographic evidence of further cardiac involvement.

T.N. Harris (17) in a recent report attempts to evaluate the effect of salicylate therapy upon the inflammatory reaction in rheumatic fever. He concludes that large doses of salicylates may lower the erythrocyte sedimentation rate of non-rheumatic as well as of rheumatic patients. "It is very doubtful, therefore, that massive salicylate therapy suppresses the inflammatory reaction of the rheumatic patient or that the lowering of the erythrocyte sedimentation rate in rheumatic patients has the significance attributed to it by Coburn." He made no attempt to evaluate the effect of massive salicylate therapy in rheumatic carditis.

L. M. Taran (18), in a second report, states that results of two years' clinical experience with a special technic for giving salicylate show that none of 38 rheumatic patients treated with 10 grams of sodium salicylate daily developed valvular heart disease and that 21 out of 63 similar patients who received only small doses of sodium salicylate developed physical signs of rheumatic carditis.

Ten to 20 grams of sodium salicylate are given intravenously every day for one to three days depending upon fever and other symptoms. Usually on the third to the seventh day, oral medication replaces intravenous treatment and is continued through the thirtieth day of the salicylate regimen. Doses of 1.6 Gm. sodium salicylate and 0.6 Gm. sodium bicarbonate are given by mouth every four hours day and night.

Taran feels that if a patient develops an acute polyarthritis during the course of a long protracted rheumatic episode, salicylate therapy will fail to modify the course of rheumatic

activity even when given in adequate dosage and for long periods of time. It may indeed give symptomatic relief but will not shorten the duration of the activity of the disease.

Taran's observations seem to show that salicylate therapy fails under the following conditions:

1. Inadequate dosage to raise the salicylate serum level.
2. Failure to maintain the desired level.
3. Large doses of sodium bicarbonate inadequately covered by the administration of larger doses of salicylates.
4. The administration of salicylates in cases in whom rheumatic activity has been present for a long period of time.
5. Impatience with the continued use of the drug.
6. Sensitivity to salicylates and the early occurrence of signs of intoxication.
7. Unmindfulness of the fact, that, in addition to salicylate therapy, proper nursing and nutritional care is required to attain a favorable result.

Toxic reactions to high concentrations of salicylate in the blood are quite common according to numerous observers. Tinnitus, nauseau and vomiting are among the earlier toxic manifestations of salicylates. Taran feels that nausea, vomiting, slight abdominal pain, tinnitus and temporary deafness do not constitute contraindications to the continued use of salicylate therapy.

More severe manifestations have been reported, both as a consequence of massive salicylate therapy and otherwise. They include hypoprothrombinemia and hemorrhage (19,22,23,24), occasional mental changes (21,15), and some decrease in alkali reserve (19, 22). Taran states that symptoms more directly demonstrative of irritability of the central nervous system are ominous and call for an immediate interruption of salicylate administration. Hyperventilation, irritability, restlessness, insomnia and confusion

are distinct danger signals. Taran feels that the latter symptoms do not seem to be correlated with the above mentioned group of unconsequential symptoms of salicylism.

DISCUSSION:

Certainly the question of the effectiveness of massive doses of salicylates in the treatment of rheumatic fever and carditis is moot. The effectiveness small doses of salicylates is highly questioned. The salicylates given in adequate doses during polyarthritis or high fever are very effective antipyretics and analgesics. The analgesic effect of salicylates in the arthritis of rheumatic fever is indeed so rapid that its effect is occasionally taken as a therapeutic test in the differential diagnosis of the arthritides.

However, as regards the hypothesis that massive salicylate therapy suppresses the inflammatory reaction of the rheumatic patient, no definite statement can be made. The literature has been reviewed. Certainly the various investigators defend their views ably. The salicylates have lasted through five decades of therapy in rheumatic fever and carditis. Taran and Coburn feel that salicylates are specific in antirheumatic activity. In view of their evidence and the excellent symptomatic relief obtained with salicylates, the drug is the drug of choice in the treatment of acute rheumatic carditis.

Taran also offers interesting observations on the failure of salicylates to procure therapeutic success.

OXYGEN THERAPY

In 1939 Poulton (27) published a report on oxygen therapy with special reference to its use in rheumatic myocarditis. He postulates a local tissue anoxia in rheumatic myocarditis.

The points in favor of a local tissue anoxia in rheumatic myocarditis as postulated by Poulton are as follows:--

1. The histological picture of Aschoff node formation in the myocardium so often described, has been epitomised as a panarteritis with thrombosis of the lumen in places and peri-arterial fibrosis (Gadart 1938) (28). Associated with this there is cloudy swelling, diffuse or in patches, later fatty metamorphosis of the muscle cells, and latest of all a dystrophic change, seen best in the auricular wall in mitral stenosis, where the muscle substance disappears, leaving a delicate web of sarcolemma. Coombs (29) (1924), who described these changes, ascribed them to inflammatory toxins; but why should not they be due to anoxia secondary to the panarteritis?

2. Asphyxia in cats causes lengthening of the P-R interval, missed beats, and 2 to 1 heart-block (Lewis 1925) (30), conditions met with clinically in acute rheumatism, and recently the S-T deviation from the iso-electric line, which is also commonly met with in acute rheumatism, has been attributed to want of oxygen (Dietrich and Schwiegh 1933 (31) Büchner 1938 (32)).

3. Repeated small blood-transfusions are beneficial in rheumatic myocarditis (Horvath 1938) (33) and these would increase the supply of oxygen in a disease characterised by a low hemoglobin percentage.

If there is anoxia of the heart muscle, an increased production of lactic acid would be anticipated. This might show itself in an increase of the blood lactic and/or of the amount excreted.

Poulton cites evidence along this line of reasoning to support his theory of local tissue anoxia. An investigation took place at

the Birmingham Children's Hospital and Dr. E. M. Hickmans, biochemist to the hospital, reported the following to Dr. Poulton. The patients efebrile and in bed; 94 estimations of blood lactic acid at about 10 A.M. in rheumatic cases and 62 in controls were made by Friedmann's method and 26 in rheumatic cases and 11 in controlls by the method of Avery and Hastings. The lactic acid of the urine was determined 103 times in rheumatics and 68 times in controls, usually for a period of twelve hours. The average percentage of lactic acid by both methods and in the blood by both methods and in the urine excreted in twelve hours and the range (highest and lowest figures) were the same in the two groups; but the distribution curves differed. There were more high and low values for the blood lactic acid in the rheumatic series than in the controls. There were also more high values for the excretion of lactic acid in the rheumatics than in the controls. There was therefore a difference in the metabolism of lactic acid in the two groups, which might be explained by an increased production of acid in some cases of acute rheumatism.

Poulton cites investigation on the effect of oxygen on the metabolism of lactic acid which was being carried out in London by Mr. H. J. Taylor, Ph.D. Poulton cites cases of acute rheumatic carditis in which there was a considerable fall in the blood lactic acid while the patients were in oxygen tents.

This suggests that the oxygen relieved the local anoxia of the heart muscle. As might be predicted from the work in Birmingham, such striking changes do not take place in all cases of rheumatic myocarditis; nor were they present in the controls.

The remainder of his report is based on a study of 26 rheumatic patients (15 in their first attack), treated with oxygen for periods varying from abut a week up to eighty-two days, at Guy's Hospital, Lewisham Hospital, Queen Mary's Hospital, Carshalton, and the Downs Hospital, Sutton. The attempt was made to keep the oxygen percentage in the tent at 60-70; this could not be effected in a leaky tent. The patient usually remained in the tent continuously; but after two or three weeks some patients were allowed out once a day for an hour to prevent boredom. In wards where the technique was unfamiliar the patients came out twice a day for washing.

Subjective clinical condition.--In 17 of the 26 cases clinical improvement was noticed. The patients felt better; they were more active and ate more, and cyanosis disappeared; one could "breathe better." The improvement was most obvious in very ill patients, such as one with pericarditis, nephritis, and purpura, who was so ill that a note was made that oxygen had probably saved his life; another who had made but little recovery from a pericarditis; and another with pneumonia and pericarditis. All these were children.

In 8 cases there was no clear subjective improvement: 4 patients did not feel unwell beforehand. Another patient, who developed tachycardia after tonsillectomy fifty-three days previously, did not respond and only showed a temporary fall of the pulse-rate. Another patient's appetite failed, though there was a favorable effect on the pulse and he was taken out after fifteen days. Two patients had severe heart-failure. Barach and Richards (1931) noticed that oxygen did not cause much improvement in this type

of case, though one of their patients collapsed after removal from the tent and had to be put back.

This distinction was noted in a case in which an enlarged cardiac shadow indicated pericarditis. On Aug. 6, 1938, at Guy's Hospital, the patient did well in the tent, but the value of prolonged treatment was not realized, and he was taken out after two days. Two and a half months later, at Queen Mary's Hospital, he was put in the tent for thrity-five days; there was massive edema, scanty urine, and an enlarged liver; he died soon after coming out. Hence oxygen should not be left till the last stages of rheumatic heart disease. In 2 cases without pericarditis radiograms showed that the width of the heart became smaller after treatment with oxygen.

Temperature and pulse-rate.--In 14 cases there was nofever at the time the tent was used, though in most cases there had been recent fever. Fever was present in 12 patients, and all reacted with a fall of temperature in the tent, though in 2 the fall was slight.....In some the temperature rose again on removal of the tent, and it may rise again before the tent is removed.

A fall of pulse-rate was not brought about so readily as a fall of temperature, but it was observed in 22 cases, though in some the fall was slight.

Alteration of murmurs with oxygen treatment was noted in 15 cases--11 with a first attack and 4 of old standing: (1) there was a diminution of intensity or a disappearance of a systolic and/or mid-diastolic murmur in the tent in 10 cases, and reappearance with increased intensity outside the tent; (2) the first sound became

louder in the tent; and (3) the quality of murmurs changed. For instance, a systolic squeak disappeared, though it became faintly audible on occasions later on, while the patient was still in the tent. In ten cases no change was noted.

Electrocardiograms.--The rheumatic patients treated with oxygen and the controls showed improvement in the same proportion so far as low voltage was concerned; but this sign is rather uncertain, for it is readily produced by drying of the electrodes. There was frequently slight deviation of the S-T interval, which is taken to mean local want of oxygen. It was always much less than that commonly observed in coronary thrombosis or in old-standing myocardial disease. In all the four cases in which it was present it improved with oxygen, and in only 3 out of the 16 cases of the control series in which it was present.

In 16 cases treated with oxygen the P-R intervals could be compared. A length up to 0.18 sec. has been allowed as normal for a chold and 0.20 sec. for an adult. In 8 cases the interval was normal. In 6 it was long and became normal with treatment. One of these patients, just before going into the tent, had classical 2 to 1 heart-block with increasing P-R interval and pulsus bigeminus. Five days later, in oxygen, a normal P-R interval was observed.....The conclusion is that oxygen produces improvement in the electrocardiogram..

Later improvement with oxygen treatment.--For this assessment it is better to avoid cases with permanent cardiac damage but to consider patients in their first attack, in which improvement or recovery is more likely. Only 7 of the 15 cases in their first

attack are available, as in the others the time of observation since treatment has been shorter than two months. The result is considered to be good if (1) only a soft systolic murmur was present before treatment and this has disappeared; or (2) a canter rhythm or diastolic or presystolic murmur or a third or fourth heart sound (McKee 1938) (34) or a loud blowing or musical systolic murmur with a weak first sound has disappeared and the only auscultatory signs remaining are a soft systolic murmur with a good first sound and / or an accentuated and sometimes reduplicated pulmonary second sound, the reduplication being usually heard towards the end of inspiration; or (3) a pulse rate previously rapid now remains normal not merely as charted but also when the physician examines the patient. With these criteria the results in 6 or the 7 patients are good.

Leo M. Taran (18) feels that his observation of children with acute exudative carditis shows that failure to attain effective cardiac rest during the course of the acute inflammatory process of the myocardium may be responsible for the enormous heart damage observed at the end of the active period. Furthermore, he feels that it is obvious that even under the best physical and emotional environment of rest and relaxation, the heart muscle remains overactive during this phase of the disease. Overactivity of the acutely inflamed muscle fiber may be responsible for disturbance of the chemical and mechanical integrity of the heart muscle causing dilatation and impairment of cardiac efficiency. An accelerated cardiac action, a common finding in acute exudative carditis further depletes cardiac efficacy by diminishing diastolic coronary

filling. This accentuates an already existing anoxemia of the heart muscle.

Taran has utilized oxygen chambers in the treatment of acute exudative carditis. Children having acute rheumatic carditis reside in a 45 to 50 per cent oxygen atmosphere for ten to fourteen weeks. He states, "The marked improvement in the clinical behavior of the patient and the almost immediate removal of all the subjective and objective signs of apparent cardiac insufficiency reflect the profound effect of oxygen therapy upon the cardiac physiology which is so enormously disturbed during the course of acute exudative carditis."

SUMMARY

Certainly Taran is enthusiastic concerning the use of oxygen therapy in acute exudative carditis. His report, however, is as yet unpublished. There is a discouraging paucity of other observations on the use of oxygen therapy. Taran feels that the duration of rheumatic activity is not measurably altered by oxygen therapy, but that cardiac disability is significantly minimized.

Barach and his associates (35,37) concluded from their study that in congestive heart failure and in acute coronary thrombosis oxygen therapy is often a life-saving measure. They observed that successes with oxygen therapy occurred more frequently in the degenerative type of heart disease than in the acute inflammatory type of rheumatic carditis.

The exact status of oxygen therapy in acute exudative carditis is unknown.

SULFONAMIDE PROPHYLAXIS

The relationship of the beta hemolytic streptococcus to the etiology of rheumatic fever has long been a controversial subject. Although many students of this disease are of the opinion that both the initial attack and subsequent recurrences of rheumatic fever are usually preceded by streptococcal upper respiratory infection, others believe that this association is merely accidental. Kuttner (38) believes it is more than mere accident. It seems too constant to be completely disregarded.

Several articles have been published as to the effect of sulfanilamide administration during the course of acute rheumatic fever and chorea. Massel found no beneficial effects from prontosil in two patients with frank rheumatic fever or in two other patients with chorea. In 1937, Massel and Jones (39) employed sulfanilamide in primary doses of 6-7 grs. per 10 lbs. body weight during the first twenty-four hours, followed by 4-5 grs. per 10 lbs. body weight daily thereafter. They administered the drug to fifty-eight rheumatic fever patients. In no case did sulfanilamide produce any symptomatic relief or shortening of the disease. In fact, in some cases the drug seemed to increase the severity of the disease.

Swift (40) also showed that sulfanilamide has little if any detectable beneficial effect on the course of rheumatic fever once the condition is well established. Too, the toxic effects of the drug were especially marked in these patients and as a result certain rheumatic manifestations seemed to be intensified.

The value from sulfanilamide was still invisioned and prophylactic use of this drug was studied. Thomas and co-workers (41, 42) reported a four year study on ninety patients all of whom had had one or more major rheumatic episodes, the last one occurring within three years of entering the study. They define a major episode as "one in which the patient is ill enough to be confined to bed at home for at least a week or to be hospitalized and in which fever, polyarthritis, active carditis, chorea or other signs are unequivocal. Outspoken chorea is considered a major episode only when the patient affected had had other forms of rheumatic fever as well."

The dosage of sulfanilamide given was 15 grs. divided into two daily doses during the 1936-37 season and 20 grs. divided into two daily doses during the three following seasons.

The effect of treatment, during the eight months of treatment and the control period, showed that pharyngeal cultures positive for beta streptococcus were more and more numerous and strongly positive among the control patients than among those treated. Also, during the free drug interval in summer, a noticable increase in beta streptococcus took place in the treated patients.

No major rheumatic episodes appeared in the treated group during the four year study but in the control group fifteen appeared. In all, fifty-five patients received prophylactic doses during seventy-nine seasons while sixty-seven patients were observed as controls during one hundred and fifty seasons. Of the control group thirty-five never underwent a season of

prophylactic treatment. Eight major episodes occurred among them. The remaining thirty-two had sulfanilamide at some time and were then shifted to the control group. Among these patients seven major episodes occurred. This indicates that a sulfanilamide course has no statistically demonstrable effect on subsequent appearance of acute rheumatic fever after the sulfanilamide has been discontinued.

Two minor rheumatic episodes appeared in the treated group but only a short time after the treatment was started in the fall. Six appeared in the control group. No deaths occurred in those patients treated but four occurred in the control group. One of these was from acute rheumatic fever, two from subacute bacterial endocarditis and one from uncertain nature.

It is striking that while major rheumatic recrudescences occurred in 10 per cent of 150 person-seasons observed in the control group, none occured in 79 person-seasons in the treated group. Notable too is the fact that the treated group contained a slightly higher percentage of patients with organic and functional cardiac disability.

Coburn and Moore (43) in their primary report of prophylactic use of sulfanilamide found that the drug did not prevent rheumatic manifestations after the onset of streptococcal pharyngeal infections but continuous administration in seventy-nine out of eighty patients throughout the winter prevented hemolytic streptococcal infection and signs of rheumatic activity.

Their next report showed an incidence of rheumatic fever of less than 1 per cent in a group of one hundred and eighty-four

patients studied over a three year period. The expectancy level was 35 per cent. Thinking that possibly the age factor of the group might be responsible for the decrease in incidence, for many of the children had passed puberty, they withdrew sulfanilamide from the patients who received prophylactic doses in the period 1936-1939 during the 1939-1940 period. This group consisted of one hundred patients, mostly adolescents. None of the one hundred patients had had streptococcal pharyngitis or manifestations of rheumatic activity while on sulfanilamide. Since the discontinuence, thirty-two of these one hundred contracted hemolytic streptococcal pharyngitis during the first twelve months and in 40 per cent of these thirty-two, rheumatic fever developed.

The above studies of Thomas and France, begun in September, 1936, and of Coburn and Moore, begun about the same month, were reported simultaneously in January, 1939. Thereafter similar studies were conducted in several other American Clinics (74, 56,41,42,55,44,45,43,46,47,48,49,50,51,52,53, and 54).

Among the rheumatic patients protected by sulfonamides over 1,037 seasons only twenty-two acute rheumatic exacerbations occurred, an incidence of 2.2 per cent, and only three patients died from rheumatic fever. But among the rheumatic patients who received no sulfonamide during 1,340 seasons, there were 183 acute attacks (an incidence of 13.7 per cent) and five deaths from rheumatic fever. In other words among the rheumatic patients not given sulfonamides there were six times as many acute recurrences and almost twice as many deaths as among those who received sulfonamide prophylaxis.

Because sulfonamides sometimes accentuate the symptoms of an acute attack, most investigators refrained from starting sulfonamide prophylaxis until four to six weeks after all signs of activity of the latest rheumatic attack had disappeared. Other physicians, caring for patients hospitalized during attacks, preferred to start the prophylactic doses of sulfonamide before the patient left the hospital, even though the disease was still slightly active. Thus the patient might be better protected against possible carriers of hemolytic streptococci in his home environment. (57)

To date practically all of the patients were treated only during the fall and winter months. But Dodge (57), Kuttner (57) and Thomas (53) expressed the belief that it is a better plan to administer sulfonamide throughout the year, in order not only to minimize the likelihood of drug sensitivity which might result from interrupted dosage, but chiefly to provide more complete year round protection.

To date sulfanilamide has been used in most cases, sulfathiazole or sulfadiazine in a few (50). Sulfadiazine has been considered preferable to sulfanilamide. Sulfamerazine has been regarded as potentially the sulfonamide of choice. Since sulfamerazine is excreted slowly by the kidneys, it should be possible to maintain an effective blood level by giving one small daily dose (57). No further reports on sulfamerazine prophylaxis are available at present.

In general, the daily dose was, for children, about 0.5 to 1 gm. of the sulfonamide; for adults, 1 to 2 gm. To maintain

an even saturation of the tissues of the drugs were given at regularly spaced intervals, either three doses daily, each at eight hour intervals, or two doses daily, each twelve hours apart, for example, 7 A.M. and 7 P.M.

Occasional determinations of the level of sulfonamide in the serum or qualitative test of the urine for sulfonamides were made to show whether patients were taking the drug. Most workers attempted to maintain a level of 1 to 3 mg. per 100 cc. of serum.

For how many years should sulfonamides be administered? Sufficient time has not elapsed to permit an answer to this question. Some physicians have expressed the belief that administration of the drug should be continued at least five years or, in the case of a child, until the child reaches the age of sixteen years. Once administration of the drug is discontinued, protection against relapses does not long continue. In contrast to this belief Baldwin (58) has reported on the follow-up of a small group of children who had received chemoprophylaxis. She found no evidence of increased susceptibility to streptococcal infection and rheumatic activity at the time sulfanilamide was withdrawn. However, the majority of studies indicate that protection against recurrences does not continue once the drug is discontinued.

Toxic reactions from sulfonamide prophylaxis were not excessive either in number or in severity. They were generally described as "infrequent and unimportant", "Mild and rare" or "generally mild".

Most of the toxic reactions consisted of rashes, drug fever, leukopenia or mild hemolytic anemia. They cleared promptly when

administration of the drug was stopped.

Although the patients were treated with sulfonamides during 1,037 seasons, only one death presumably due to sulfonamides was reported (55); that of a boy twelve years of age, who had active rheumatic carditis. After the boy had taken sulfonamides for one month, fatal "agranulocytosis with secondary septicemia" developed.

Unfortunately this patient did not report for appropriate treatment until sixty hours after the onset of symptoms; otherwise recovery might have been effected. (Such a danger from sulfonamides is now notably reduced in view of the excellent results of penicillin in agranulocytosis: prompt recovery without a single death among eleven patients so treated (59).)

Epidemiology Units Number 22 and 89 of the Navy (60) and Damrosch (61) report the appearance of resistant strains of beta hemolytic streptococci after the use of sulfadiazine prophylaxis. Their's arethe reports of this occurrence. Should such strains develop, penicillin will probably be effective against them.

Jackson (62) feels that if the disease is definitely inactive, an excellent diet and wholesome living conditions will practically eliminate the chances of a recurrence with carditis; and that sulfonamide prophylaxis is indicated for children recovered from rheumatic fever who have had definite carditis and are forced to live in an environment which does not provide a good diet and at least a fair level of general care.

Wilson and Lubschez (63) have stated their belief that many of the reported statistics are misleading. According to them, the likelihood that a major exacerbation will occur depends not

so much on such factors as the number of previous attacks, the severity of the disease and the particular year in which a given study was made as it does on the age of the patient and the length of time since the last attack, factors which, although more important, were not adequately considered in the choosing controls for study.

Rosenberg and Hench (64) in an excellent review of sulfonamide prophylaxis submitted the data of Wilson and Lubschez and those of several proponents of sulfonamide prophylaxis to Dr. Joseph Berkson for statistical analysis. Statistical adjustment for the difference in age in the groups compared showed, if anything, a greater average difference of rates, favorable to the treated patients, than reported by the original authors.

Since 1943 sulfonamides were administered to great numbers of persons in the armed services as a prophylactic measure against respiratory infections. An appreciation of the size of these experiences is obtained from reports such as those of Watson and his co-workers (65); who treated "several thousand" persons; of Hodges (66), who treated 10,000 persons; of Holbrook (67), who studied the course of 40,000 persons; of Coburn (68); who studied 30,000 persons, and of Lee (69), who reported studies on 25,000 persons.

The results of this work are not completely analyzed but preliminary reports indicate that the plan worked remarkably well (70,71,72,73,65,75). All who made these studies agreed that the incidences of hemolytic streptococcal respiratory infections, of scarlet fever, of meningococcal infections and of

gonorrhea were greatly reduced. With regard to rheumatic fever, Carter (76), Coburn (68), and Holbrook (67) reported reductions paralleling those in the incidence of respiratory infections caused by the hemolytic streptococcus.

These reports on mass prophylaxis should engage the early attention of institutional physicians in attendance at schools, colleges and camps.

THE ROLE OF ASPIRIN

For many years physicians have attempted to lessen the number of rheumatic recurrences by the use of a salicylate given between attacks. Some physicians (77,78) gave small doses daily for several months; others (79) gave a salicylate one week of each month. But little evidence has been obtained to indicate that salicylates, thus given, prevent rheumatic relapses. A different program of salicylate prophylaxis was recommended in 1938 by Schlesinger(80), who gave acetylsalicylic acid to rheumatic children as soon as an infection of the upper part of the respiratory tract developed and continued its administration until three or four weeks after the infection had subsided. He expressed the belief that the number of relapses and the mortality rate were definitely reduced. Among twenty-seven patients given acetylsalicylic acid thus, twenty-one recovered and six died; the mortality rate was 22 per cent. Among twenty-four patients not so treated thirteen recovered and eleven died; the mortality rate was 46 per cent.

Recently Coburn and Moore (81) have advocated a somewhat similar plan. Four to six grams of sodium salicylate were administered daily depending on the size of the patient. Administration of the drug was started as soon as acute pharyngitis appeared. If throat cultures revealed hemolytic streptococci, salicylates were continued for four weeks; otherwise, administration of the drug was stopped. Of forty-seven rheumatic patients having hemolytic streptococcal pharyngitis so treated, only one (2

per cent) developed rheumatic fever. Among 139 untreated controls, fifty-seven (41 per cent) developed rheumatic fever. The number of patients treated in this manner is small. The work must be extended before it can be properly evaluated. With this plan, salicylates are given at a time when sulfonamides are powerless to prevent recurrences; that is, between the onset of the acute hemolytic streptococcal infection and the usual time for the appearance of the rheumatic attack (82). If the claims of Schlesinger and of Coburn and Moore can be confirmed, this method may prove to be a needed supplement to sulfonamide prophylaxis.

TONSILLECTOMY AS REGARDS RECURRENCE.

Clinicians have long considered the tonsils as a very important focus in the persistence of rheumatic infections. Numerous surveys have been made on this relationship but the interpretation of these results have not been uniform. Most authorities concede, however, that the tonsils bear a certain relationship to rheumatism and rheumatic endocarditis. Observations indicate that infection in the tonsils frequently precedes one of the rheumatic manifestations but it is as well known that many children subject to attacks of tonsillitis, or sore throat, do not develop evidences of rheumatic disease. Enucleation of the tonsils has frequently been recommended with a hope of preventing a recurrence of the rheumatic manifestations and also attempting to curtail the acute phase.

To evaluate the effect of tonsillectomy as a therapeutic agent several questions arise. The first of these is whether or not an acute attack of rheumatic infection develops for the first time as frequently in children whose tonsils have not been removed as it does in those who have had a tonsillectomy. Secondly, does a tonsillectomy have any influence in determining the course and duration with a possibility of recurrences after the disease is once established. Thirdly, does the presence or absence of tonsillar tissue influence the outcome of this disease? Is the incidence of carditis greater or less? Is the mortality rate lowered?

In answering the first question I might review the work

of Kaiser (83) who in a study of two separate groups of children; 48,000 in one and 4,400 in the second, equally divided into tonsillectomized and non-tonsillectomized patients, found that the tonsils do have some influence on the incidence of rheumatic disease as recongnized in children. The attacks occur 30 per cent less often in those children who have had their tonsils removed. The method used to arrive at this conclusion was to analyze a large child population in which the incidence of rheumatic fever and chorea were known.

Secondly, what influence does a tonsillectomy have on the recurrence of rheumatic manifestations? Wilson, Lings and Crosford (84) in their survey of four hundred and thirteen rheumatic children in 1938, with careful correlation between the age at tonsillectomy and age at which recurrent attacks occurred, brought out that recurrences occur in young children under 9 years of age whether the tonsils are removed or not while after 10 years of age recurrences are less common in both groups. It is well known that recrudescences of rheumatic fever become less after the teen age. Kaiser (85) in his analysis of four hundred and thirty-nine rheumatic children found recurrent attacks only 10 per cent less in tonsillectomized children than in non tonsillectomized. Allen and Baylor (86) find the incidence of recrudences of rheumatic fever is 43.15 per cent after tonsillectoy as compared with an average recurrence of manifestations in non-operative patients of 50-60 per cent.

Lastly, is the outcome of the disease influenced by tonsillectomy. Kaiser and Hill (87) do not show a noticeable decrease in

cardiac involvement but as indicated in reports by Robey and Finland (88) there is a decrease in its severity. Allan and Baylor were encouraged to find that tonsillectomy in their series showed a decrease in cardiac involvement and that of forty-nine patients not having cardiac involvement at the time of tonsillectomy only six (12.2 per cent) developed rheumatic heart disease subsequent to operation.

Is the outcome of the disease influenced by tonsillectomy? Kaiser in noting the outcome in five hundred and ninety-seven children found that the mortality rate was 13 per cent among the children whose tonsils were in during the rheumatic infection and 7 per cent among those whose tonsils were out at the time of the initial attacks. These percentages only suggest that the most serious type of rheumatic infection is more likely to occur in those children with tonsils.

If benefit were derived from a tonsillectomy, one might ask the question as to whether or not it would be wise to perform such an operation during the active stages of the disease. Roby and Finland (88) state that it should not be done while an active acute tonsillitis is present but since acute rheumatic fever is a sequelae it can and has been safely done.

DIET IN PREVENTION OF REUCURRENCE

In 1943, Coburn and Moore (89) investigated the role of nutrition as a conditioning factor in the rheumatic state.

They selected one group of children in whom rheumatic fever did not occur for controlpurposes. They selected students in a private day school for girls. The school selected had an annual matriculation of over 500 children and for at least six years had been free of rheumatic fever. The group of subjects from this private school consisted of 50 girls in good health.

For the rheumatic group city school children and adolescents they selected a group who had been under the care of a ph ysician for at least five years. They chose a group of young ambulatory rheumatic subjects on whom continuous clinical and bacteriologic observations had been made for five years or longer. Erythrocyte sedimentation rates and antistreptolysin titers were determined after every infection of the respiratory tract caused by hemolytic streptococci. Patients in whom rheumatic activity developed were admitted to either the Babies Hospital or thePresbyterian Hospital. The city school group consisted of 100 children, all of whom had one or more attacks of rheumatic fever with cardiac involvement.

The results of the study were as follows:

Calories.--Most of the diets of both the more susceptible and the less susceptible subjects were moderately low in calories. The median requisite for the 50 patients was - 24 per cent. It was not statistically significant.

Protein.--The study indicated that the association between greater susceptibility and a deficient intake of protein was statistically significant.

Calcium.--There was an almost statistically significant association between calcium deficiency and greater susceptibility.

Iron.--Results here were similar to that of protein ingestion.

Vitamin A.--Of the vitamins computed, the ingestion of vitamin A only showed a striking difference in the diets of the two groups. Ninety-six per cent of the more susceptible and only 48 per cent of the less susceptible patients were deficient in Vitamin A intake. The median deviation from the requisite for 50 patients was - 30 per cent.

The rarity of rheumatic fever among children receiving the advantages of life in the higher economic stratum is well recognized. Occasionally, however, a wealthy child enjoying the privileges of the best hygienic environment contracts rheumatic fever following streptococcic pharyngitis. They have collected data on a small group of rheumatic children whose family budgets could supply the best diets to determine whether there was anything unusual in their dietary histories.

The histories of these 14 unselected rheumatic children show a high incidence of feeding problems in early childhood.

Of some interest is the possible significance of a low intake of calcium throughout childhood. Calcium plays an essential role in the normal irritability of nerve and muscle tissue, in the clotting of the blood and perhaps in the permeability of membranes, all of which may be altered in rheumatic fever. The

absorption of calcium from the gastrointestinal tract is dependent on ingestion of adequate amounts of Vitamin D or on exposure of the body to sunlight, neither of which is sufficiently available to rheumatic children. Althrough severe rickets is not common in rheumatic children, the striking prevalence of poor musculature and dental development among these children may well reflect a mild prolonged deficiency of calcium.

That a lack of those proteins most useful in growth and repair may be important in conditioning a subject to rheumatism is compatible with all observations made during the study of Coburn and Moore.

It is not known at present whether Vitamin A has a function in the metabolism of mesodermal cells. Shank et al (90) observed that regardless of the concentration of Vitamin A in the plasma prior to the onset of active exacerbations of the disease, there was a fall in the level of Vitamin A in the plasma with the development of acute rheumatic fever, the degree of decrease varying directly with the intensity of the rheumatic attack. Similar observations were made by Race (91), Ellison and Moore and Hall (92) etal.

Kuttner (93), in 1940, indicated that the re-enforcement of the diet with Vitamin A will not protect against rheumatic fever.

It was also in the article of Coburn and Moore that an interesting theory of the factors essential to the genesis of the rheumatic state was postulated. They felt that three factors appeared to be essential. The first of these is a constitutional factor, transmitted by the genes as a mendelian

recessive which modifies the metabolism of the host in some manner as yet unknown (94). So far as can be determined in a mixed metropolitan population about 5 per cent of human subjects are constitutionally susceptible to the development of rheumatic fever. Maturation of the rheumatic process in this5 per cent depends, however, on at least two other concomitant factors. One of these, the factor of infection, is hemolytic streptococci, whose products precipitate the rheumatic attack.

There is the factor of "conditioning of the host" by a poor diet. Paul (95) indicated the importance of conditioning of the host in his valuable epidemiologic studies when he concluded:

"Any appreciation of this process tends to minimize the idea that the clinical entity of rheumatic fever may be precipitated in a normal individual as a result of his first contact with the infectious agent (presumably the hemolytic streptococcus). It tends to magnify the importance of susceptibility in this disease as an evolved characteristic. One almost concludes that the infant must grow up to be a rheumatic."

Thus, Moore and Coburn formulated the equation of the etiology of rheumatic fever and carditis.

The significance of diet and environmental care has been studied rather thoroughly by Jackson et al. (62) at Iowa City, Iowa, as regards rheumatic fever recurrences.

In that study 266 children were included who met the requirements of having an established diagnosis of rheumatic fever, and were under observation and supervision of the University clinic

for some time after the disease had become inactive. Only cases which could definitely meet the diagnostic criteria of Jones were included in the study. A large group of children with questionable diagnosis were eliminated. The criteria of Taran were followed to establish that the disease had become inactive.

Because of the marked variability in manifestations and for comparative purposes, the recurrences were classified as major, minor or possible recrudescences according to the description of Hansen.

One hundred ninety-five (73 per cent) were under close medical supervision, that is, they made regular visits to the clinic. Seventy-one (27 per cent) were under indirect supervision, that is, they made an occasional visit to the clinic, and were followed by their local physicians and a public health nurse, who reported the condition of the children to the authors.

The management of these children will be outlined in some detail because the therapeutic program is excellent and an impression of an adequate dietary program is given. As soon as a child with rheumatic fever comes under the supervision of the University Hospital or the mobile clinics of the State Services for Crippled Children, an investigation of the child's home environment is made by a trained medical social worker, and every effort is made to insure the child a good level of environmental care. About half of the children were hospitalized in the University Hospital. About a third received sanatorial care in the sanatorium connected with the Hospital. The remaining children were cared for in their own homes or in local hospitals during

the acute phase of the disease.

The family of each child was instructed by the doctor and nurse and often by a dietitian regarding the importance of an adequate diet which should include the daily consumption of: one quart of milk; one or two eggs; one serving of meat, fish, chicken, or liver; two vegetables (one-half cup is considered a medium serving); one orange, apple, or tomato; one other fruit in addition; one teaspoonful of cod liver oil; six teaspoonfuls of butter or margarine. They were also told that other foods such as bread, cereal, and potatoes could be added to satisfy the appetite and maintain correct weight, but under no circumstances were they to replace any of the above; cereal was not to be served more than once daily. Rather, the child was to be encouraged to eat larger quantities of fruits and vegetables; varieties of these were to be used so the child would not form likes and dislikes.

The above dietary instructions are relatively simple; yet provide for adequate dietary essentials which are lacking in the diets of numerous rheumatics.

In addition, each family was advised to have the child sleep in a room of his own whenever possible or at least to sleep alone, and to have about ten hours of rest each night. The importance of proper clothing was stressed, as well as control of temperature and humidity of the home. With regard to the care of intercurrent infection, the family was advised to have the child go to bed if there was any sign of infection, and to consult the family physician as early as possible. If another member of the family has a cold, sore throat, or any other infectious disease, the child was to

be kept away from that person, and the family physician notified. The family was told to have the child play with other children in the normal way, but to plan his activities to avoid fatigue. In addition, psychologic advice was given to prevent overprotection.

An individual public health nursing report regarding the child was sent to the local public health nurse or school nurse before the child returned to his home after institutional care and after each clinic visit. The local nurse was advised to make home visits as often as she felt it was necessary, and to instruct the family and to consult the family physician if any further difficulty should arise.

Under the above therapeutic program for the age group 4 to 13 years, there were forty recurrences for a rate of 7.9 per cent; for the age period 14 to 16 years, there was a rate of 10.5; for the age period 17 to 21 years, there were seven recurrences for a rate of 4.5 per cent.

The recurrence rate of Iowa-treated groups shows a significant deviation from the natural course of the disease. This difference is evidenced during childhood and is not present for the groups 14 years and older.

Of the enviornmental factors rated, themost significant association is seen between the level of dietary care and the rheumatic recurrences. All ten of the children who had recurrences with carditis were receiving inadequate diets and living in poor social situations. In Jackson's dietary data, the essentials most commonly deficient were protein, vitamin D, thiamine, and minerals. The dietary information in this study was insufficient

to allow quantitative computation, but the majority of the children were receiving inadequate diets at the time they developed their attack of rheumatic fever. Again, dietary insufficiency was incriminated by Jackson et al. as a conditioning factor in the rheumatic state.

Jackson also believes that the degree of deficiency of the diet appears to be related to the incidence and degree of heart damage.

As regards other environmental factors Jackson felt that the economic situation of the home showed no direct association with the distribution of recurrences. His experience was that whenever poverty was present it was exceedingly difficult to provide the essentials of care, particularly an adequate diet.

It has been reported that the recurrence rate of rheumatic fever for a random sample is lower after puberty than before. In Jackson's series the recurrence rate after puberty was not significantly different from that reported for a random sample. The boys and girls who comprised the group (14 to 18 years) were those from who little cooperation could be obtained because of the many instances of poor home social situations. The habits of living of these children will be well established and they have the expected adolescent revolt against a supervised program. These factors make the success of any therapeutic program in this age group doubtful. Jackson fould all the adolescent children with carditis having poor diets and living in poor home social conditions.

In the age group from 18 to 21 years, there was no recurrence with carditis as reported by Jackson, In evaluating this report,

it is important to remember that carditis is more common during childhood and adolescence, when nutritional requirements are high. When the heights and weights of rheumatic patients are plotted on growth charts, it has been noted that many fall in the out groups of body build, as undersized, obese, or tall - thin.

The evidence presented in the literature is both for and against the existence of a definite correlation between nutrition and rheumatic susceptibility. The same is true concerning environmental care. Taran (96) found the incidence of recurrence of rheumatic fever after convalescent care to be four times as high in children who return to poor home environment as in those who return to good living conditions at home. Coburn and Moore in the dietary study discussed previously found a close association between nutrition in childhood and rheumatic susceptibility. A preliminary report by the same authors on the results of re-enforcing the diets of a small group of rheumatic children with eggs shows none of the subjects experienced a recurrence.

SUMMARY:

The literature indicating a definite correlation between nutrition and rheumatic susceptibility has been reviewed in some detail. The studies of Jackson et al. at Iowa City have been reviewed insome detail and his dietary and therapeutic scheme outlined.

Jackson's series does not include patients receiving sulfonamide prophylaxis. The recurrence rate for major episodes for the accumulated reported groups of rheumatic patients who have received sulfonamide prophylaxis is 1.5 per cent. The recurrence rate for major episodes for Jackson's group of patients between 4 to 21 years is 5.2 per cent. The recurrence rate of Jackson in his study group of rheumatic subjects is significantly different from that reported by Wilson for a random sample and from a comparable Iowa group that did not receive improved environmental care the first year after onset. It is noteworthy that the age from 4 to 13 years is a period in which nutritional requirements of the child are high and a time in the child's life when his habits of living can be controlled with less difficulty than from approximately age 14 years and older.

CONVALESCENT FOLLOW-UP

In reviewing the literature it is striking that the various authors have used various criteria for definition of rheumatic recurrence. Also these authors have utilized various definitions and criteria for cessation of rheumatic activity.

It has been the common experience of students in the field of rheumatic fever that many patients, without obvious clinical or laboratory evidence of rheumatic activity, continue to show progressive cardiac damage. These patients have been suspected of having mild, clinically undetectable, active rheumatic disease. "Subacute carditis, which is insidious and subclinical occurs more frequently than the acute phase of the disease." (97)

It is also widely held that the recurrence risk in rheumatic disease is significantly higher, the shorter the lapse of time from the cessation of the active rheumatic episode. (98) In addition, it is well known that patients having had active rheumatic carditis, have a greater recurrence risk than those without a history of carditis. Those observations would seem to point to the necessity for a clear definition of rheumatic recurrence, with special reference to the reactivation defined as carditis.

Does a patient have an early recurrence of rheumatic disease after an active episode or are the new clinical manifestations a continuation of the active process? The so-called "quiescent interval" might thus be considered as a form of mild rheumatic activity, presenting none of the classical and accepted criteria for rheumatic activity. The latter view has been very ably

defended by Leo M. Taran.

Recently Taran (99) has reviewed the criteria used in evaluating the status of rheumatic activity. His report will be discussed in some detail.

He feels that it is significant that, while all cases having a leukocytosis had obvious manifestations of clinical rheumatic activity, nine out of every ten cases continued to show clinical evidence of active rheumatic disease after the total white blood count had returned to normal.

It is generally appreciated that an increase in the erythrocyte sedimentation rate is found in most toxic and infectious diseases. In rheumatic disease, an increase in the erythrocyte sedimentation rate has been considered as the most useful finding in evaluating the presence of rheumatic activity, and some observers are inclined to look upon it as of specific diagnostic, as well as prognostic, significance in rheumatic fever. Coburn, in his preliminary report in 1943, utilized the erythrocyte sedimentation rate as his index of rheumatic activity.

Taran notes that many patients had definite active rheumatic disease, with a normal sedimentation rate. All children in his series showed marked elevation during the first eight weeks from the onset of the illness, the elevation being most marked during the first four weeks. At the end of eight weeks 15 per cent had normal sedimentation rates but many of these continued to show evidence of active rheumatic disease.

Harris (100) in a study of 328 patients who were under observation until the quiescence of the infectious process noted

that in only less than 2 per cent did the leukocyte count remain above 8500 after the erythrocyte sedimentation rate had descended to the plateau level normal for that child. These findings on the comparative sensitivity of the ESR and WBC count in rheumatic fever agree with those of Ernstene (101). If the finding of a shift to the left in the peripheral blood as having the same implication as leukocytosis these findings agree also with Rogartz (102) and with Struthers and Bacal (103). There is an apparent disagreement between these comparative data and those of Massell and Jones (104), and Wilson. These authors found the ESR and WBC count of approximately equal sensitivity as indications of an inflammatory reaction, but this apparent disagreement is probably due to the standards used. Massell and Jones, and Wilson, considered as normal any corrected ESR of 23 mm. per hour or less, since that value is approximately the upper limit of normal for the population.

Accordingly, in Harris' laboratory, the ESR is considered normal for any given convalenscent rheumatic when the falling curve of ESR versus time reaches a plateau.

Also of interest are Harris' observation that in some cases under massive salicylate therapy that the ESR reached normal limits, while the white blood cell count still afforded evidence of continuing activity of the rheumatic process. The differential white blood cell count showed a shift to the left, or an abnormal number of non-filamented polymorphonuclear leukocytes, as additional

evidence of a persisting inflammatory process.

Both in private and hospital practice, a low-grade fever in a rheumatic patient is looked upon as a highly probable manifestation of rheumatic activity. A flat temperature curve is the commonest measurement upon which physicians rely in the assessment of the cessation of active rheumatic disease. Taran noted that while it is true that all the patients during the febrile period, showed obvious signs of active rheumatic disease, the greatest majority (90 per cent) continued to demonstrate rheumatic activity after the temperature was completely normal.

Disturbance in auriculoventricular conduction time has been considered as reliable evidence of the presence of active rheumatic disease in the auricular muscle. It has been suggested that this finding may be seen in the greatest majority of active rheumatic cases if frequent tracings are taken (105). However, 75 per cent of Taran's series of cases showed clinical evidence of active rheumatic disease when the auriculoventricular conduction time had returned to normal.

The first three weeks after the onset of illness, the pulse rate was found to be higher than at any time thereafter. None of Taran's two hundred cases showed a pulse rate of less than 100 before the end of the ninth week from the onset of the acute episode, and none had an elevated pulse rate twenty-seven weeks after the onset. It is noteworthy that four of ten children whose pulse rates remained normal, continued to show evidence of active rheumatic disease. On the other hand, a few cases that were apparently quiescent, showed an occasional sinus tachycardia.

Consistent gain in weight has been considered as indicative of the onset of the quiescent phase of the rheumatic disease (106). At the end of seven and one-half months from the onset, all children had reached a normal weight gain level (107), although at this time, 40 per cent of them still showed mild rheumatic activity.

Secondary anemia is usually present during rheumatic activity, the degree of anemia being related to the severity and the duration of the manifestations of the disease. It is considered a characteristic finding during active rheumatic carditis (108, 109).

In Taran's series none showed a normal hemoglobin at the beginning of the illness; the lowest hemoglobin level was found in the period from the second to the fifth week of the illness; and all the children showed a normal hemoglobin eight months after the onset of the illness. In a great many instances, the hemoglobin did not return to normal until the activity had subsided. On the other hand, 40 per cent of the cases showed clinical evidence of rheumatic activity after the hemoglobin had returned to normal.

Judging by the report of Taran the various laboratory criteria are not entirely reliable. One can apparently depend upon one laboratory procedure to determine the duration of rheumatic activity.

Taran discusses the importance of clinical observations and criteria. Fatigability, without evidence of cardiac insufficiency, is the symptom which can be adjudged best from careful observation of the patient, rather than from a provocative inquiry into symptoms

of fatigue.

Emotional instability, which is a concimitant of active rheumatic carditis, capricious appetite, restless sleep, and disturbance in the habits of evacuation and urination, form part of the syndrome of mild rheumatic activity. Marked and frequent fluctuations of expressions of elation and depression are, according to Taran, obvious manifestations during this phase of the disease.

From time to time, there appears in the literature, the observations on the part of the clinician that the rheumatic patients present a typical appearance. The pallor of active rheumatic during the acute stage is well known. This is often far greater than one would expect from the level of the hemoglobin.

Taran states, "The discrepancy between the degree of pallor and the level of the hemoglobin continues during the entire active rheumatic process, even in the smoldering phase, when other signs of activity seem to have come to an end. A close paralellism exists between the degrees of pallor and of fatigability."

A marked tachycardia with a tumultuous rhythm has long been recognized in acute rheumatic disease as auscultatory evidence of carditis. A clearly defined gallop rhythm with a rapid or slow cardiac rate has also been considered as evidence of acute carditis. And, in recent years, a rapid evolution of progressive cardiac damage, i.e., cardiac dilatation and hypertrophy, and increase in the extent of the valvulitis with rapidly advancing signs of cardiac insufficiency, has been looked upon as criteria of acute rheumatic carditis.

Frequent and careful observation of large groups of children from the onset to the end of an attack of acute cardits gave the impression that the criteria as described are inadequate in making the diagnosis of a "mild smoldering carditis" as defined by Taran. In his series one of every three cases of carditis failed to show this evidence. Continuous and detailed follow-up studies of his group showed other ausculatory signs, not clearly defined but apparently significant of an active process in the heart muscle.

The cardiac rates in this group of children were rapid or slow, but always markedly labile. Stimuli, which in quiescent hearts did not disturb the cardiac rate, caused, in this group, marked fluctuations. Furthermore, this fluctuation was of long standing. Physical exertion and emotional disturbance produced a sinus tachycardia of the ticktack type, lasting several hours. Continued bed rest might slow the heart rate to the normal average, only to be markedly accelerated when bed rest was terminated. When, however, active carditis had subsided, this disturbance in cardiac rate was of distinctly lesser degree and of markedly shorter duration. In a quiescent carditis, the return to normal of the accelerated heart rate was measured in terms of minutes; in active carditis, it was measured in terms of hours and, not infrequently, in terms of days.

Cardiac sounds and murmurs in mild carditis were everchanging. The volume and pitch of both first and second heart sounds varied from day to day and often from beat to beat. Murmurs changed in quality, direction, and extent of transmission. The evanescent character of cardiac murmurs in rheumatic hearts is well known. The frequency and multiplicity of changes observed in Taran's series

of children were noted only in the actively inflamed hearts.

The cardiac rhythm in active carditis simulates that of an embryocardia, irrespective of the rate. The normal ratio of the duration of systole and diastole is definitely disturbed. The usual one-to-two rhythm is lost and approaches more nearly, a one-to-one rhythm. On auscultation, it would seem that the time between the first and second heart sounds is equivalent to the interval between the second and first sounds. It is well known, that during exercises, the diastolic period is foreshortened to a greater degree than the systolic period, but the sinus tachycardia after exercise or during fever is distinct from the embryocardia type of rhythm noted in carditis. And this type of rhythm is not modified by cardiac rate, as long as carditis continues. Occasionally, a sinus bradycardia with a one-to-one rhythm is observed in active carditis.

The unstable character of the cardiac rate, the evanescent character of sounds and murmurs, and the disturbance in rhythm were noted in all of Taran's cases during the initial phase of the acute carditis. In one of every four cases, these auscultatory signs persisted after all laboratory evidence of rheumatic activity had subsided.

Taran concludes, "It is of great significance from the therapeutic standpoint, to note that the group of children showing only auscultatory evidence of carditis, did poorly when permitted to resume normal childhood activities. Some showed symptoms of cardiac insufficiency and a few presented unequivocal evidence of cardiac enlargement after a short period of observation. Many

children in this group began to show obvious signs of reactivation. The auscultatory signs of carditis increased and corroborative laboratory evidence became manifest."

In contrast to this, "When, however, all auscultatory signs of carditis had definitely subsided, a return to normal physical activity presented no untoward effects and signs of rheumatic reactivation were not observed."

Taran represents the extreme conservativism in the definition of active rheumatic activity. This report does, however, emphasize the importance of a careful clinical evaluation of the child with acute rheumatic carditis.

Levine (110) states that it is a common experience to see the heart rate continue around 120 for months with a fever of only one degree. Even if practically all the symptoms have disappeared and the patient feels fairly well, a slight fever and a rapid heart may persist. Levine has seen instances in which a temperature of about 100 degrees F. and a heart rate of about 110 lasted for several years. During this time the patients were feeling quite well, attending school, and undertaking ordinary activities. Finally, without any particular treatment, the slight fever and tachycardia gradually returned to normal.

These observations offer proof of the chronicity of this disease. This also throws light on how the rheumatic infection may lurk within the body, smolder in a comparatively inactive way, and suddenly, without any evidence of a reinfection, flare up and new symptoms appear. Reactivation is an excellent term describing these instances.

Jackson in his excellently controlled and reported series utilized the criteria of Taran in determining the state of rheumatic activity. It is desirable to have the patient remain in bed until the disease is inactive.

Levine states, "One would prefer to continue bed care until there are no symptoms and the temperature, pulse, white count, and sedimentation rate have been normal for at least one month."

Rosenblum (111) in a recent report states, "In other words if the sedimentation rate is becoming slower, even though it has not reached normal and all other signs point toward recovery, the patient may be permitted up and about." He does not define, however, the phrase "and all other signs point toward recovery." One has no concrete definition of his method of determining when the child should be permitted activity. The return of electrocardiographic changes to normal or its becoming static was also considered helpful by Rosenblum. Assuming, without just provocation, that Rosenblum refers to disturbance in auriculoventricular conduction time; we are faced with Taran's view that 75 per cent of his series showed clinical evidence of active rheumatic disease when the auriculoventricular conduction time had returned to normal. Certainly, the views of Rosenblum concerning sedimentation rate and indications for resumption of activity are not widely held.

Struthers (112) in a report of his management and prevention of rheumatic fever states, "In my experience, one of the striking evidences of reactivation of infection is the early and constant appearance of a severe anemia associated with this disease, which

should always forewarn the practitioner of the possible recurrence of activity."

Struthers also emphasizes one clinical observation. "It has been noticed that after the acute infection has begun to subside, emotional outburst become less frequent, and at the same time the physician has usually recorded improvement in the condition of the heart." The nurse in charge and her staff are instructed to watch for and report epistaxis, skin rashes, joint and abdominal pains: the appearance of nodules, signs of chorea, pallor, sweating and malnutrition.

The night nurse must carefully record the sleeping pulse at midnight and at 4 A.M. As a general rule, after the sedimentation rate has remained normal for four to six weeks, Struthers allows standard graded exercises to be undertaken by the department of physiotherapy. Bathroom privileges and allowing the child to sit up for meals are permitted only upon request of this department.

There is a discouraging paucity of literature concerning the definition of cessation of rheumatic activity. Rest is the most universally accepted measure in the treatment of rheumatic fever. Rest has been advocated chiefly damaged heart, or to prevent or minimize its damage, either directly by decreasing the work of the heart, or indirectly in the belief that absolute bed confinement would shorten the illness and thereby reduce the incidence of cardiac involvement. Variable criteria are being used to determine the time when bed rest is to be discontinued, the amount of activity allowed, and the amount of time alloted for rest periods.

Robertson, Schmidt, and Feiring (113) have recently presented

an article advocating early physical activity in rheumatic fever. Reasoning that rest is a relative term, they state that rest and confinement to bed are by no means synonymous. Rest, in their opinion, means maximum ease and comfort, physically, mentally, and emotionally. They state, "Prolonged confinement defeats rest, produces restlessness, and thereby increased physical, mental and psychic activity."

In their series of more than 200 cases of rheumatic fever, it was their opinion that greater rest was obtained by permitting more freedom for activity, such as sitting in or out of bed, and walking to the latrine. Activities were permitted their patients during the acute phase of the disease, usually within the first 24 hours after admission, if their physical discomfort did not prohibit it.

They were impressed by the high incidence of anxiety neuroses in conventionally treated young male adults and second the fact that prolonged bed rest was not necessary for an uncomplicated recovery.

In evaluating reports of the above type one must return to pathology for certain fundamentals. Levine (110) presents a description of the development of rheumatic heart disease, which is classical.

Assuming that the patient was left with a systolic murmur of moderate intensity, Levine traces the possible changes which may take place. He may remain well, never have a return of rheumatic fever and always show a systolic murmur on examination. Occasionally, the systolic murmur may gradually diminish in

intensity. Rarely, it may disappear entirely. He may, therefore, live out his life as a normal individual and never be embarrassed by his heart. Levine feels that the latter is the exception, unless recovery with no murmurs occurs.

In a fair number of patients in whom all the findings on examination, including the systolic murmur, were considered benign, some years later, usually a decade or two, a fatal subacute bacterial endocarditis will develop. The remainder, either as a result of recurrent bouts of rheumatism and reinfections of the heart, or possibly because of the inherent nature of the original infection with its subsequent chronic progression and contraction without any recognized reinfection, will develop signs of mitral stenosis or aortic stenosis at some future date.

How soon the changes occuring in mitral stenosis will occur following the acute episode is variable. Upon rare occasions Levine states they begin within one year, although generally many years elapse between the original infection and the development of definite evidence of mitral stenosis. He further states, "During these years, the symptoms may be none or few, such as slight dyspnea and palpitation."

Thus, the report of Reobertson et al. with a follow-up period of six to twelve months are inadequate to evaluate results as regards cardiac residuals: that is, the prevention of organic heart disease; the most important problem in the treatment of acute rheumatic fever. Also one must remember that their series was composed of young adults in whom the incidence of cardiac sequelae is lower than that of young children. Thus, no conclusion can be

drawn regarding children.

It is always a matter of considerable moment for the clinician to decide how long to keep the patient in bed. Levine states the question very ably. "When the disease persists and smolders, showing only slight evidence of activity, the practical problem becomes extremely difficult. To obtain the desired result, one might have to confine the patient to bed for one or more years. At some point in the course of the illness, the question of diminishing returns comes in. In the average public clinic patient, if such a drastic procedure is carried out in the attempt to obtain a slight and somewhat questionable advantage by means of a time-consuming and troublesome plan of treatment, the child frequently loses years of schooling."

Realizing the importance of this problem the sanatorium method for the care of rheumatic has been evolved, to aid the practitioner in the treatment of rheumatic children. The sanatorium program attempts to provide complete bed rest for the type of patient described by Levine and the child with acute rheumatic carditis.

Taran (96) has an elaborate physical plant designed for sanatorium care. He describes his sanatorium method in an article in 1943. The average stay at the sanatorium was, at that time, ten months. The minimum period was seven months. The clinical course was the factor which decided when the children were discharged. No child was discharged until eight months had elapsed following complete subsidence of rheumatic activity. Children who were admitted with active carditis or signs of insufficiency remained a longer

period after reaching the ambulatory state. In general, all factors being equal, children 6 to 10 years of age are kept longer than those 10 to 16 years of age.

Before a child is considered for discharge, he must show:

(a) Definite and consistent nutritional improvement,
(b) Definite improvement in cardiac reserve,
(c) No evidence of infection on repeated complete examinations.

Complete bed rest was required until all criteria for activity had subsided. In many instances Taran based his final judgment upon the clinical impression irrespective of some of the adverse findings of the laboratory, and conversely he declared cases of many children active when all laboratory evidence was to the contrary.

He also emphasized the need for a psychologic approach in the patient-doctor relationship; bedside teaching; occupational therapy; and isolation of sick patients.

Taran interestingly states, "It is our conviction that 'quiescent' patients, whatever their general well-being may be, will do better if properly supervised at home."

Other authors report varied types of sanatorium care. The child may be discharged at the end of the acute episode from the sanatorium, and followed in the manner depicted by Jackson (62) et al. in their study of environmental factors in recurrence. Certainly Taran has an ideal type of program with unlimited resources. The type of program followed will certainly be limited by the wealth of the child's family and the amount of assistance offered by state, federal, or privately endowed agencies.

Under the above program the patient with quiescent rheumatic

fever may or may not have escaped heart disease. If he has developed heart disease, it may have taken him a little longer to reach the status of being up out of bed. The child is gradually allowed out of bed for six or eight hours daily. At first, he is allowed out of bed for one hour daily under most programs and the period of activity slowly lengthened to six or eight hours daily.

During this exercise period, he has schooling in a classroom if he is in a sanatorium. Competition among students is purposely de-emphasized in the sanatorium. If he is in his own home or in a foster home, a home teacher should be provided. In addition to this, his time has been spent in doing some occupational therapy or in recreation. He has probably been allowed to go to the bathroom at will, to sit at the table for meals, and to go for short walks. He may have a rest period before meals and a rest period in the afternoon for two to three hours.

If the child has been discharged during this period to his parents, specific instructions must be given the parents or the patient may be given a full day's privilege of overwork which may lead to trouble. His schedule during the first three months out of bed, if at home, should remain the same as if he were under constant medical supervision.

The literature fails to reveal many descriptions of the program during the convalescent stage as regards physical activity. Before lamenting thepaucity of reports on this subject, it must be remembered that any program must be individualized for the child and that a rigid program should not be adhered to indiscriminately.

Each family should be advised to have the child sleep in a room of his own whenever possible or at least to sleep alone, and to have about ten hours of rest each night. The importance of proper clothing is to be stressed, as well as control of temperature and humidity of the home.

With regard to the care of intercurrent infection, the family should be advised to have the child go to bed if there are any signs of infection, and to consult the physician as early as possible. If another member of the family has a cold, sore throat, or any other infectious disease, the child is to be kept away from that person, and the physician notified. Sieracki (114), in 1945, advised further that if the patient is discharged home during the season for hemolytic streptococcal infections, he is to be kept from school and a home teacher provided. Movies are also denied him under this program.

Certainly sulfonamide prophylaxis has reduced the hazard of intercurrent hemolytic streptococcal infections, yet I feel that simple precautions as regards upper respiratory infections should be followed.

Under the program of Sieracki the rule is, for the first year to prevent an individual who has recovered from a recent bout of rheumatic fever from partaking in most forms of strenuous exercise, especially that which involves competition. This is the instruction given to both cardiacs and to non-cardiacs since the latter may show evidence of heart disease at a future date. The patient is allowed to increase his time out of bed to eight or ten hours daily. During his time up, he is allowed to walk up and down stairs, to

walk to and from the store if it is not over half a mile, to go to school, to go to the beach but to keep out of water above the knees, to bat a baseball, and even to run a short distance after one, but not to play a real game, and to go for auto rides.

During this first year he is forbidden to swim, ride a bicycle, and jump rope. In other words, without making him conscious of it, he is still a semi-invalid. Sieracki states that most of his patients with carditis will be able to tolerate this form of exercise; those who cannot are allowed as much activity as is possible within the limit of dyspnea.

The patient is seen in the clinic or office fairly frequently so that he may be evaluated for further recurrence of infection. At first, the period of observation may be monthly, then every six to eight weeks. After the first year, visits may be made every three to six months, depending on the amount of heart disease and the presence or absence of intercurrent infection.

A full year after the active stage of rheumatic fever, the non-cardiac is given full freedom in the amount of exercise. Only one minor restirction is put on him--he is asked to take a rest at noon. He does not usually heed this advice in the group's experience, which is given because it is felt that this noon rest helps to increase his physical reserve in combating possible infection.

The patient with murmurs, with slight or no cardiac enlargement, is also given the same freedom since his physical effort will have no effect on the amount of heart damage once the infection has become definitely quiescent.

It is unfortunate that the activities of many children who have minimal heart damage are restricted. Some of these restrictions are based on the fact that a murmur is present which does not necessarily preclude the diagnosis of heart disease. Those cases are usually picked up in a school examination, and unless a full evaluation is made, certain restrictions are placed which lead to "heart consciousness" and neurocirculatory asthenia.

Thus, the child's activities may be planned to avoid fatigue. Sieracki presents definite recommendations; one of the few authors to do so, rather than the vague recommendation to avoid fatigue.

Hiss (115) also feels that children are not to be restricted if they have merely a tachycardia or a soft blowing mitral murmur even if considered organic in origin if there is no cardiac enlargement or history of recent rheumatic activity. Children with other murmurs but without enlargements are only slightly restricted. Frequently only permission to engage in competitive interscholastic athletics is denied. He should not be made to climb too many stairs; should be excused from strenuous gymnastics when there is slight cardiac enlargement.

When there is marked enlargement he is excused from all physical activities. He may be given rest periods in school and be restricted from recess activities. Hiss feels that most children may be kept in regular classes in their nearest school. However, with some children, recommendations may be given for a school for the handicapped, with transportation to and from school provided or a home teacher or a convalescent home.

These are the recommendations offered by various authors

dependent upon the facilities available to them in their therapeutic program. The treatment of rheumatic fever in the "quiescent" stage is dependent upon adequate follow-up.

Taran has presented criteria to establish that the disease has become inactive. During the acute stage, the child is hospitalized or given sanatorial care, unless a high level of home care can be provided or the family refuses to accept institutional care. During the convalescent stage continued rest should be observed. I have presented the recommendations of Taran as regards sanatorial care and those of other authors whos patients are returned to their homes. I also have attempted to present the implications of recommendation of "avoidance of fatigue". The importance of perservering with a high level of care day after day and year after year must be emphasized and re-emphasized to the parents and overprotection prevented.

CLINICAL REVIEW

A series of 37 rheumatic children who have received convalescent home care at Hattie B. Munroe Home, Omaha, Nebraska were reviewed in attempt to evaluate the factors previously discussed in the treatment and follow-up of rheumatic fever patients. These children were under the care of the Nebraska State rheumatic fever program. This series of patients received varying periods of convalescent home care during the years from March, 1944 to October, 1947.

When first seen under the above program the distribution as regards type of rheumatic involvement was as follows: 12 gave a history of recurrent attacks and evidence of mitral insufficiency or stenosis or both; 4 with recurrent attacks showed no evidence of cardiac involvement; 6 were seen following their initial attack without showing evidence of carditis; 4 seen following what apparently was their initial attack had an organic systolic mitral murmur; 3 following their initial had buzzing systolic murmurs which were considered functional in character; 2 had polycyclic attacks with a functional systolic murmur when first seen; 2 were seen initially in recurrences with congestive heart failure; 3 gave a history of recurrent episodes, chorea and had mitral valvular involvement; and one with ahistory of polycyclic attacks, chorea, without evidence of carditis. The murmurs regarded as functional and therefore not indicative of rheumatic heart disease were buzzing in nature, systolic in rhythm, usually heard best to the left of the sternum in the fourth interspace and disappeared on sitting up.

These were not considered significant and according to most authorities disappear with the advent of adolescence.

In reviewing the dietary histories of these 37 children one is impressed with the parents' statements concerning the child's eating habits. These children have been "finiky eaters", "finiky about foods other than milk", etc. Also, due to the low socio-economic status of the families, these children have been unable to secure an adequate diet. Dietary histories were rather scanty in numerous instances, yet the impression received substantiates the work of Coburn and Moore, etc., as regards dietary deficiencies as a conditioning factor in the development of the rheumatic state. Few, if any, of the children were receiving adequate diets.

Even more striking, however, in reviewing the histories of the children with recurrent episodes is the paucity of adequate follow-up by the clinicians making the initial diagnosis of rheumatic fever. Parents have repeatedly stated that the need of a follow-up program has never been impressed upon them. The recurrent nature of the disease has not been emphasized. The relationship of poly-cyclic attacks of rheumatic fever to the development of rheumatic carditis has not been impressed upon the parents. The question of initial treatment cannot be evaluated accurately as numerous parents either cannot remember what treatment was employed or are uncertain of the drugs used.

Contrasting with the group of 24 patients with histories of recurrent episodes of rheumatic polyarthritis or chorea or both, 18 of whom subsequently developed organic mitral valve involvement; is the group of 13 patients seen following the initial attack, 4

of whom have developed organic mitral disease under the program. These observations seem to support the belief that if rheumatic attacks were always monocyclic and short-lived, severe cardiac damage would rarely occur.

Diets in these children were reenforced with Brewer's Yeast and Cod Liver Oil. The parents were given dietary instruction by the dietetian. Adequate rest following evaluation of the child's reserve was under the physicians' direction. Attendance at school was limited as deemed necessary. Home teachers were provided when the child was not allowed to attend school. The parents were instructed to keep the child in bed if he developed an upper respiratory infection and to administer aspirin. Sulfadiazine prophylaxsis was utilized in alternation with aspirin prophylaxsis. Children were sent to the convalescent home following acute episodes when deemed advisable or during periods when home care was not satisfactory and the child was not doing well. The standards for determining the quiescent state have been similar to those advocated by Taran.

The series is too small to offer any true evaluation of the recurrence rate or the ultimate result in those patients having rheumatic heart disease. The greatest factor in determing the effectiveness of the program in the series was the parents' and child's adherence to the program.

A 13 year old female first seen on 5-27-46 gave a history of frequent colds during the past 2 years, many attacks of fever, and pain in the joints. For one period during the past winter she was in bed several weeks with general malaise, fever, pain in legs and joints. Appetite has been quite good but diet has been inadequate

most of the time, because of the low income and the family's inability to buy proper foods all of the time. The child was hospitalized at University Hospital from May 27, 1946 to September 20, 1946.

Treatment in the hospital included barbitals, salicylates, and feosol; the latter for a hypochromic anemia. The diagnosis of acute rheumatic fever and a typical Sydenham's Chorea was made.

The child was dismissed to the convalescent home with recommendations for limited activity, bathroom privileges, walk to meals, no stair climbing, etc. On dismissal the chest film showed a slight enlargement with prominence at the left border.

The child was dismissed for the convalescent home on 11-18-46 with complete bed rest orders. The child, however, was up and about during December, 1946. In January, 1947, the patient showed a 4 lb. weight loss and an elevated sed rate. The child continued to show signs of rheumatic activity. Finally, the parents consented to hospitalization again in October, 1947 despite early attempts to secure their permission for doing so. At the time of her second admission this chold had demonstrable cardiac enlargement with a double mitral murmur.

Contrast this with the history of an 11 year old male whose onset of rheumatic fever occurred at 4 years of age. He was hospitalized at University Hospital from 5-22-41 to 6-16-41 for treatment of Sydenham's Chorea and again from 2-18-43 to 3-12-43 with a diagnosis of right hemi-chorea. At the time of the second dismissal the recommendations of rest from lunch to 3 p.m., dietary reenforcement and sulfadiazine prophylaxsis.

Despite the family's cooperation, the child was rehospitalized

from 4-29-44 to 8-4-44 with a diagnosis of acute rheumatic fever, mitral insufficiency, and a systolic mitral murmur. Despite the recurrence this child has adhered to the program and when last seen in University Dispensary on June 11, 1947 showed no evidence of cardiac enlargement and disappearance of the heart murmur.

I believe that little need be added to the above. The second case history is illustrative of the results which may be achieved with an adequate program and the patient's compliance with the physician's recommendations.

The following case history represents in my mind what may be termed a smoldering rheumatic infection with acute exacerbations or sub-acute rheumatic fever: The five year old white male entered University Hospital for the first time on October 20, 1947. The present illness started in the fall of 1946 with complaints of chills, intermittent fever, vomiting, epistaxis, diffuse pain across the frontal bone below the hair line. The epistaxis would occur during fever episodes. Episodes continued throughout the winter occurring on an average of one per month--varying from 0 to 3 months. In May, 1947, the patient suddenly had a high fever, painful bilateral swelling of joints, especially knees, but involving elbows, wrists, shoulders, and ankles. Joint pains were generalized with shifting intensities.

Other complaints at that time were severe nose bleeds, nausea and vomiting. The child was put to bed during this attack which had been under way for a week without medication, before the mother took him to the LMD who diagnosed the child as having rheumatic fever and prescribed liquid medicine, believed to be green in color.

The acute phase continued with some remission of painful symptoms.

On June 12, 1947 the child was first brought to the hospital clinic. The clinical diagnosis at that time was sub-acute Rheumatic Fever.

Fever has reduced since then and is more intermittent as are joint pains. The patient has complained of dull pain across forehead at irregular intervals.

The child's behavior history showed that the boy was easily fatigued and became very irritable when fatigued. He ate well, but didn't like meat very much.

The child entered for removal of infected tonsils. Examination on admission revealed a heart with a soft, buzzing systolic murmur heard both sitting up and lying down over the left apex and fourth interspace to the left of the sternum. A sinus arrythmia was also noted on admission. T---99.4. P---90. R---24.

Laboratory on admission:

Hb.	14.4		
RBC	4.45		
WBC	17,650	Segs.	30
		Eos.	13
		Lympho.	52
		Mono.	5

Sedimentation rate---5 mm. hr.

The child's admission was characterized by a low grade fever until 11-4-47 when his temperature began to spike to 100 degrees. On the evening of 11-6-47 his temperature rose to 102.8 degrees. It is striking that with the onset of the rise in temperatures the patient became more irritable, complained of nausea and soon had episodes of vomiting.

Tonsillectomy was performed on 11-14-47. Despite sulfadiazine

given prophylactically previous to operation the leukocytosis remained high at 17,000 indicationg rheumatic activity. Sedimentation rates remained high and on dismissal the leukocytosis remained at 14,000 on 12-1-47.

To me this illustrates the difficulties encountered in the treatment of the smoldering or sub-acute phase of the syndrome. It illustrates Taran's view that therapy instituted late in these cases will have diminished effectiveness. Aspirin therapy had been given since June, 1947.

This short series was reviewed to gain an insight into some of the problems encountered in the application of principles discussed. No attempt has been made to evaluate the recurrence rate but my distinct impression is that the recurrence rate has been effectively reduced under the present, rather inelaborate program. Certainly rheumatic heart disease can be modified so that these children can live their lives comfortably within certain limitations. Cardiac damage will not show rapid progression with depletion of cardiac reserve; but will, as in the second case presented show apparent regression. Still the test of any of these rheumatic programs will be the results achieved in these children as regards their span of life and the ultimate complete depletion of cardiac reserve now seen to appear in the rheumatic subject during the third and fourth decades of life.

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