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A HITHERTO UNDESCRIBED FORM OF VALVULAR
AND MURAL ENDOCARDITIS*

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In previous communications¹ cases of endocarditis were classified as rheumatic, syphilitic, acute bacterial and subacute bacterial. We have introduced the designation "indeterminate" for an additional group of cases concerning which very little is known. The term is used to include (a) the cases of so-called "terminal" endocarditis and (b) cases of atypical verrucous endocarditis. The object of the present communication is to discuss the cases included in the latter group, which we believe represent a hitherto undescribed form of endocarditis.

In a study of the postmortem material of the Mount Sinai Hospital, two cases of endocarditis were encountered which showed valvular and mural lesions of a peculiar type. These lesions were free from bacteria when studied by the usual methods and differed in morphology and localization from those found in rheumatic and subacute bacterial endocarditis as well as other forms of endocarditis. Moreover, both cases showed fibrinous pericarditis, but there were no Ashoff bodies in the myocardium. Because of the unusual character of the endocardial lesions and their verrucous appearance, these cases were designated: "atypical verrucous" endocarditis. When this form of endocarditis is better understood a more appropriate nomenclature will doubtless be introduced.

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More recently we had the opportunity of studying two additional fatal cases, the clinical histories and postmortem examinations of which are recorded below. For purposes of brevity, the findings in the first two cases only will be presented in summarized form. At a later time, we shall publish the complete records of all our cases.

CASE I.—S. H., (Admission No. 216669), female, aged twenty-four years, married, was admitted to the Mount Sinai Hospital on January 21, 1922. The family history was negative. The only previous illness which she remembered was an attack of polyarthritis three years before. Her present illness began six weeks before admission with sticking precordial pain. Two weeks later her knees, ankles, wrists, elbows and shoulder-joints became swollen and painful. At the same time she developed a chill and fever. Her face became so swollen that her eyes were practically closed. Her urine was scanty, her blood-pressure was elevated and she experienced "drawing" pains in the left lumbar region. A week before admission she began to complain of sore throat. The edema of the face diminished, but the precordial and articular pain persisted.

Examination. The patient was poorly nourished, acutely ill and febrile (temperature, 103.6°). There was slight puffiness of the face. Petechiæ, some of which had white centers, were found in the conjunctival mucous membrane of both lower lids and on the anterior aspect of the thorax and both sides of the neck. The tonsils were moderately enlarged and congested. The lungs were negative. The heart was not enlarged and the action was accelerated but regular. The first sound at the apex was increased in intensity. A systolic murmur was audible over the entire precordium and left axilla. The second pulmonic sound was accentuated. The blood-pressure was 145 systolic and 90 diastolic. The abdomen was distended and held rigidly and there was pain and tenderness in the left hypochondrium, symptoms pointing to splenic infarction. The spleen was not palpable. The left elbow and both ankle-joints were swollen and tender. The metacarpophalangeal joints of the left hand were tender and painful, but although there was no swelling, the overlying skin had a peculiar red color. There was erythema and induration of the skin and cutaneous and muscular tenderness over the extensor surface of both forearms.

The blood count showed: Red blood cells, 5,400,000 per cu. mm.; hemoglobin, 84 per cent. White blood cells, 6500 per cu. mm.; polymorphonuclear neutrophilic leukocytes, 84 per cent; eosinophiles, 1 per cent; lymphocytes, 13 per cent; monocytes, 2 per cent. The Wassermann reaction was negative. The phenolsulphonephthalein output was 50 per cent in two hours.

Course. In the following week the joint pains improved and the dermatomyositis disappeared. The temperature continued to be elevated, reaching 101° to 103° daily. Albumin and hyaline and granular casts were present in the urine, and there was persistent oliguria. At first there were no erythrocytes in the urinary sediment and the blood showed normal nitrogen figures; later, microscopic hematuria appeared and the blood showed moderate nitrogen retention. Crops of white-centered petechiae recurred at frequent intervals. The articular pains returned from time to time. On February 8 a pericardial friction rub became audible and there was a return of the intense precordial pain from which the patient had suffered prior to her admission to the hospital. On February 17 the temperature rose to 104°. In the meantime signs of fluid in the chest had appeared, and on February 19, 250 cu. cm. of clear, yellowish fluid were withdrawn from the right pleural cavity and 20 cu. cm. of blood-tinged fluid from the left. The fluid from both sides was sterile. On the following day the temperature fell to 99.8°, and from this time on, with only occasional exceptions, the temperature remained below 101°. Ascites now appeared and the fluid in the chest reaccumulated.

The patient had become progressively more anemic, and on March 6, the erythrocyte count had fallen to 2,088,000 per cu. mm. and the hemoglobin percentage to 34. The leukocytes now numbered 13,400 per cu. mm., 79 per cent of which were polymorphonuclear neutrophils. On March 10 a bed-sore appeared over the sacrum and later others developed. From time to time the patient complained of severe pain in the epigastrium and left hypochondrium and over the precordium. Vomiting set in and occasionally the vomitus contained blood. On March 20 the patient became dyspneic, the albuminuria increased and the breath became uremic. The ascitic effusion had increased to such an extent that it was necessary to tap the patient. Accordingly, on March 22, 1500 cu. cm. of clear, straw-colored fluid were removed from the peritoneal cavity. On April 3 the phenolsulphonephthalein output was 5 per cent in two hours. The following day the patient had a convulsion, following which she complained of severe precordial pain. Two days later she had a second convulsion, following which she developed an attack of pulmonary edema. One week later a second abdominal paracentesis was performed and 5000 cu. cm. of fluid were withdrawn. On May 3 a diffuse herpetic eruption appeared below the left breast and scapula. The subcutaneous edema had now become generalized and the pericardial friction rub could again be heard. The temperature no longer rose above 99° and was often subnormal. In the last three weeks of the patient's life she frequently complained of severe epigastric and precordial pain. The daily urinary output fell below 500 cu. cm. On May 31 she suddenly developed dyspnea and cyanosis. The pulse became very rapid and irregular and she became stuporous and died.

Four blood cultures were made, all with negative results. The methods employed were those which generally gave positive results in cases of subacute bacterial endocarditis.

It was evident that the patient was suffering from a subacute febrile illness which began with renal manifestations and that some form of endocarditis was present. The main features were the onset with acute nephritis, the protracted course with long-continued fever and progressive anemia, acute pericarditis, mitral insufficiency, recurrent crops of white-centered petechiæ, articular symptoms, nitrogen retention, abdominal pain and hematemesis, symptoms of splenic infarction, dermatomyositis, herpes zoster and negative blood cultures.

The clinical picture was unique and it was difficult to arrive at a diagnosis which satisfactorily explained all the symptoms. The differential diagnosis was apparently between rheumatic and subacute bacterial endocarditis. The pericarditis, arthritis and negative blood cultures spoke for the former diagnosis, whereas the white-centered petechiæ, splenic infarction and glomerulonephritis pointed to the latter. Accordingly, the most probable diagnosis appeared to be a combined infection caused by the etiologic agents of both diseases. Assuming the diagnosis to be correct, it was difficult to explain the occurrence of acute nephritis at the onset of the disease, inasmuch as acute nephritis occurring in subacute bacterial endocarditis develops only when the latter disease is well established. The postmortem examination showed that neither rheumatic nor subacute bacterial endocarditis was present, but revealed instead the lesions which we believe are characteristic of the atypical form of verrucous endocarditis.

Summary of Autopsy Findings. Heart: Weight, 360 grams. There was an organizing fibrinous pericarditis, with partial obliteration of the pericardial sac. The tricuspid valve showed a discontinuous, fibrous thickening, representing a healed organic lesion. There were several minute vegetations along the line of closure. The mitral valve showed a fairly continuous thickening involving the closure line and free edge, pointing to a previous attack of endocarditis. Along the line of closure, extending in places to the free edge, there was a row of slightly polypoid, verrucous vegetations, varying in diameter from 0.5 to 2 mm. Their

consistence was fairly firm, and their appearance for the most part slightly translucent and the color grayish. A part of some of the vegetations was opaque and yellowish-gray in color. In addition, the endocardium over the upper part of both papillary muscles of the left ventricle and the intervening mural endocardium was the seat of an inflammatory process. There had also been extension of the endocarditic process from the ventricular aspect of the posterior cusp of the mitral valve near the line of attachment downward for a short distance along the endocardium of the posterior wall of the ventricle. The surface in these areas was apparently denuded of its endothelium and covered by extensive flat patches of thrombus deposit, the deeper layers of which were firmly attached to the underlying myocardium. Near the apex of the ventricle there was a similar patch of mural endocarditis, measuring 2.5 x 3.0 cm. The mural vegetations for the most part had a grayish or reddish-brown color, with here and there a yellowish area. The lesions were irregular in outline and flat and had an opaque, roughened, irregularly fissured surface. On cut section the deeper layers had a grayish, translucent appearance, indicating fibrosis, with irregular extension into the subjacent myocardium. The aortic valve showed a few small, firm, healing vegetations. The heart muscle was pale and brownish in color and showed fine grayish streaking. The coronary arteries showed an inappreciable degree of sclerosis.

The remainder of the findings will be given briefly. There was bilateral, organizing, fibrinous pleurisy with effusion into the left pleural sac, edema and congestion of the lungs, ascites, edema of the lower extremities and decubitus ulcers over the sacrum. The kidneys showed subacute diffuse glomerulonephritis, and in the left kidney there were also a few small abscesses, from which the *Staphylococcus aureus* was grown. The spleen was small and showed a small healed infarct.

Microscopic examination of the mitral valve showed lesions which were larger than those encountered in rheumatic endocarditis. The greater part of the vegetations consisted of a mass of hyaline thrombus on which was deposited a fresher blood platelet thrombus, the surface of which was only partially covered by endothelium. The patches of mural endocarditis showed extensive deposition of hyalinized blood platelet thrombus, the greater part of which was not covered by endothelium. The endocarditic process had invaded the underlying myocardium rather deeply, with resulting destruction and replacement of many of the muscle fibers. The deeper layers of both the valvular and the mural lesions were diffusely infiltrated with round cells and showed extensive fibrosis, indicating advanced healing. No bacteria were found in any of the vegetations. The heart muscle showed neither Aschoff bodies nor Bracht-Waechter lesions.

A glance at the heart suffices to convince one that the lesions do not correspond to any of the recognized forms of endocarditis. The individual points of difference from the forms of endocarditis which it resembled most are outlined below. That the endocarditis was not a terminal phenomenon is indicated clinically by the appearance of petechiæ early in the disease and pathologically by the presence of extensive fibrosis in the deeper layers of all the endocardial lesions. The abscesses in the left kidney in all probability developed independently of the underlying disease. No purulent foci were found in any of the other internal organs and no staphylococci were found in the vegetations. We interpret the kidney abscesses as metastatic lesions, occasioned by the presence of suppuration in the decubitus ulcers.

The clinical history and postmortem findings of another case belonging to the atypical group will be given briefly to illustrate certain additional manifestations of the disease:

CASE II.—E. E. (admission No. 266822), female, aged thirty-seven years, married, was admitted to the Mount Sinai Hospital on January 25, 1923, in the service of Dr. N. E. Brill, to whose kindness we are indebted for the privilege of making this report. Her present illness began nine months before admission with pain, tenderness and swelling of both feet. She was febrile at the time and was obliged to remain in bed for a while. Later, the joint pains became universally distributed and persisted throughout the remainder of her illness. Three weeks before admission she developed chilly sensations, fever, night sweats and cough. She was admitted to the hospital complaining of dyspnea, dysphagia and pain in the throat, all of which had developed during the previous night.

On examination the important findings were fever (temperature, 104.8°) tachycardia, intense dyspnea, an erythematous eruption of butterfly outline over the bridge and sides of the nose extending to the cheeks, resembling acute lupus erythematosus, ulcerative lesions on the lower lip and tongue, purpuric laryngitis, bilateral neuroretinitis, signs of fluid at the left base and enlargement of the liver. The heart was not enlarged; the action was rapid but regular; the sounds were not altered in quality and there were no murmurs. Several days after admission, petechiæ, some of which had white centers, appeared in the conjunctival mucous membrane of both lower lids. The signs of fluid at the left base persisted and signs of consolidation appeared over the right lower lobe. The temperature was constantly elevated, fluctuating between 102° and 104°. The patient grew progressively worse and finally became stuporous and cyanotic, and

died ten days after admission to the hospital. Two days before exitus a friction rub was heard over the left fourth interspace. The blood culture was negative.

At necropsy the heart was found to be somewhat enlarged and there was a patch of pleuropericarditis over the anterior aspect. There were small vegetations on the tricuspid and pulmonary valves. The mitral valve showed diffuse thickening. In the region of the junction of the two cusps, posteriorly, there was a mass of grayish and grayish-pink verrucous vegetations which extended from a point 2 mm. above the closure line to the free edge. There was another group of vegetations on the valve in the region of the junction of the two cusps, anteriorly, where the lesions were flatter. The endocarditic process, which also involved the ventricular aspect of the posterior cusp and the line of attachment of the latter, had spread downward for a short distance along the mural endocardium of the posterior wall of the ventricle. In addition, there were a number of discrete, small areas of mural endocarditis in the right auricle and both ventricles. No bacteria were found in the vegetations.

The right lung was the seat of bronchopneumonia and there was fluid in the left pleural sac. Both lungs showed edema and congestion. The spleen was enlarged, weighing 600 grams.

In this case the pulmonary symptoms dominated the clinical picture and distracted one's attention from the presence of endocarditis. The diagnosis was particularly difficult because of the absence of murmurs and cardiac enlargement. The only definite finding which pointed to infection of the heart valves was the presence of white-centered petechiæ in the conjunctival mucous membrane. The friction rub, which was shown to be due to pleuropericarditis, might have occurred in the absence of endocarditis. The eruption on the face was of the greatest interest, as a similar finding was noted in one other case in our series. The dermatologists were unwilling to identify these lesions as acute lupus erythematosus, but stated that there was a close resemblance. On one occasion we observed similar lesions on the face of a patient who appeared to be suffering from subacute bacterial endocarditis. The patient was being treated in the open air in a cold atmosphere, and it was not possible to state whether or not exposure to the cold and sunlight was responsible for the development of the cutaneous eruption. On the other hand we have never encountered such an eruption in a case of rheumatic endocarditis.

We have had postmortem examinations in 4 cases belonging to the atypical group. The lesions in 2 of the cases have already been described. In all there was involvement of the mitral valve. In 1 instance the vegetations were particularly flat and had a very broad attachment to the valves. The mode of extension of the vegetative process from the mitral valve to the mural endocardium was uniform. In each instance there was involvement of the ventricular aspect of the posterior cusp of the mitral valve as well as of the endocardium at the line of attachment, and from the latter point the vegetations spread downward along the mural endocardium of the posterior wall of the ventricle for a variable distance. In 1 case the vegetative mass extended not only downward toward the posterior papillary muscle, but also forward for a short distance along the interventricular septum. The additional occurrence of isolated patches of mural endocarditis in the right auricle and both ventricles has already been mentioned. Vegetations were found on the tricuspid valve in all the cases. Here the lesions were smaller and flatter and more irregularly distributed than on the mitral valve. In 1 case there was involvement of the endocardium along the line of attachment of one of the cusps. In 2 of the cases the pulmonary valve was involved. In both there were small, irregular, flat vegetations on the ventricular aspect of the valve and, what was more striking, there were also lesions along the line of attachment of two of the cusps. In 2 instances there were small vegetations on the aortic valve. An organizing fibrinous pericarditis was present in all but 1 case. In no instance was the heart greatly enlarged. The spleen showed small infarcts in 3 of the cases and diffuse glomerulonephritis was present in 2.

The microscopic appearance of the endocardial lesions of 1 of the cases was described briefly above. The lesions in the remaining cases were very similar. In all there was endothelial denudation over the greater part of the vegetations. The cellular accumulations in the subendothelial structures consisted chiefly of round cells; in 1 instance, however, the cells were predominately polynuclear leukocytes. Evidences of healing were present in all. In each instance the vegetations were free of demonstrable bacteria and the myocardium showed neither Aschoff bodies nor Bracht-Waechter lesions.

The clinical findings in the 4 cases may be summarized as follows: Three of the patients were females and one a male, their ages being ten and a half, nineteen, twenty-four and thirty-seven years respectively. None of the patients complained of any symptoms referable to the heart prior to the onset of the fatal illness. The disease ran a subacute course, lasting from four and a half to nine months. All had fever of irregular type throughout the greater part of the period of observation. Anemia of varying degree was present in all. Blood cultures were uniformly negative. The heart was either normal in size or showed but slight enlargement. All showed tachycardia, and murmurs were heard in all but 1 case (Case II). Three of the patients complained of precordial pain, and in each instance a pericardial friction rub was heard. In Case II the friction rub which was heard was proved at the postmortem examination to be pleuropericardial in origin.

Pulmonary symptoms were present in all. Three of the patients had pleurisy with effusion, and one of these showed in addition outspoken signs of pneumonia. In a fourth patient there were signs of fluid at both bases. She was tapped with negative result, and at autopsy no fluid was found, but the method of examination was inadequate to determine its absence with certainty. Microscopic examination of the lungs, in this case, showed areas of bronchopneumonia.

All the patients showed arthritic symptoms. The joints were not swollen and red as in typical rheumatic arthritis, and presented certain peculiarities which are worthy of mention. It will be recalled that in Case I there was a peculiar discoloration over the metacarpophalangeal joints of the left hand, associated with tenderness but with practically no swelling. In another case some of the joints were swollen and the overlying skin was bluish in color, but there was no pain or tenderness.

Two of the patients had glomerulonephritis. Both had convulsions and died in uremia. A third patient also had convulsions, but no nephritis was found. In all, the urine showed albumin and casts, and in all but one erythrocytes were also present. Apparently there is little or no tendency to leukocytosis in the disease. Repeated examinations showed a leukopenia in 1 of the cases (Case II).

In another case the leukocyte count varied between 6000 and 8400 per cu. mm. The highest count observed was 21,600 (Case I).

The cutaneous manifestations were particularly noteworthy. All the patients showed petechiæ in the skin or conjunctival mucous membrane or both, generally occurring in crops. Many of these petechiæ had white centers. It has already been stated that 2 of the patients showed an erythematous eruption of butterfly distribution on the face which reminded one of acute lupus erythematosus. Erythematous lesions in other parts of the body also occurred. A generalized purpuric eruption associated with erythematous lesions was present in another case. It will be recalled that one of the patients (Case I) developed a localized dermatomyositis early in the disease and later herpes zoster, and that a second patient (Case II) showed ulcerative lesions of the lip and tongue and purpuric laryngitis. Reference has already been made to the occurrence of splenic infarction. In 1 case lesions resembling tender erythematous (Osler) nodes are mentioned in the clinical notes.

Certain of the clinical manifestations, it will be observed, bear a striking resemblance to the symptoms included by Osler in the erythema group. Under the latter designation Osler included a large number of ill-defined and poorly understood cutaneous and visceral manifestations, including certain forms of purpura, angioneurotic edema, erythemas of various sorts, joint symptoms, ulcerative lesions of the skin and mucous membranes, abdominal colic, pericarditis and acute nephritis. Although these varied symptoms were grouped under a single designation a unitary etiology was not hypothesized. It is of interest that Case XXVI of Osler's series² showed lesions in the face which resembled acute lupus erythematosus. It is not improbable that a definite relationship exists between the atypical form of endocarditis and certain of the cases included in the erythema group.

For the purposes of differentiation from other types only the rheumatic and subacute bacterial cases need be considered. With these, the disease has certain resemblances, but the dissimilarities are quite striking. The differences in the cardiac lesions, when comparison is made with the rheumatic cases, relate especially to the morphology and localization of the vegetations and to the pres-

ence of Aschoff bodies in the myocardium. In the atypical cases the vegetations have a verrucous character, but tend to be larger and less uniform in size and somewhat more friable than the typical rheumatic lesions, and are attached to the valve by a broader base. Unlike the rheumatic cases the lesions involve the line of attachment of the valves and attack the ventricular and auricular endocardium both by extension from the valves and also in isolated patches. Microscopically the vegetations show more massive superficial thrombus deposit, the cellular reaction is more extensive and more intense and larger areas are denuded of endothelium.

It is significant that none of the 4 cases showed Aschoff bodies in the myocardium. The failure to find these bodies is not conclusive, however, inasmuch as they are frequently absent in rheumatic cases. On the other hand, had Aschoff bodies been found we should have been compelled to classify our cases as rheumatic unless a combined infection could have been demonstrated.

Clinically the differences relate particularly to the manifestations in the skin and mucous membranes and to the occurrence of splenic infarction. We have never seen petechiæ with white centers in a proved case of rheumatic fever. On the other hand, petechiæ both with and without white centers were present in each of our 4 cases. Similarly, erythematous lesions on the face resembling acute lupus erythematosus do not occur in rheumatic fever. Infarction of the spleen is very unusual in rheumatic endocarditis, and when it occurs, generally has its origin not from the vegetations on the heart valves but from a thrombus in the left auricle occurring in association with mitral stenosis.

Positive statements cannot be made at present concerning the significance of the purpura and the glomerulonephritis which occurred several times in the atypical group. Thus far we have not encountered a single instance of generalized purpura or acute nephritis in a case of proved rheumatic endocarditis. The two forms of endocarditis resemble each other in the occurrence of fibrinous pericarditis, the frequency of involvement of the tricuspid valve and the absence of demonstrable organisms from both the vegetations and the blood.

In subacute bacterial endocarditis the vegetations are larger and

more friable than in the atypical cases, and when situated on the mitral valve characteristically spread upward along the posterolateral wall of the auricle and downward along the chordæ tendineæ. Moreover, involvement of the tricuspid and pulmonary valves is exceedingly uncommon in subacute bacterial endocarditis in the absence of a congenital lesion. Fibrinous pericarditis does not occur except in the presence of some complication or as a terminal event with uremia. Lesions resembling the Osler nodes (tender erythematous nodules) which have hitherto been described only in connection with subacute bacterial endocarditis occurred in one of the cases in the atypical group. In contrast to the latter the vegetations in the active cases of subacute bacterial endocarditis contain large numbers of the characteristic organisms, and the blood cultures are generally positive.

In both forms of endocarditis white-centered petechiæ are found. Whether the lesion on the face in the case of subacute bacterial endocarditis referred to above were identical with those seen in the atypical group cannot be decided definitely. Acute nephritis occurs in both diseases, and in both the spleen may be enlarged. In subacute bacterial endocarditis the so-called Bracht-Waechter lesions are found in the myocardium. These lesions are not specific, however, and cannot be used for differential studies. We have hitherto regarded the focal embolic glomerular lesions described by Loehlein³ and studied by Baehr⁴ as pathognomonic of the subacute cases. Although they were not found in any of the cases in the atypical group, it is conceivable, from a consideration of the character of the vegetations, that the latter may be capable of giving rise to these lesions.

NOTES ON ETIOLOGY, DIAGNOSIS AND PROGNOSIS. We have no clue at present concerning the etiologic agent of the disease. It has already been stated that the blood cultures in each instance were negative and that there were no demonstrable organisms in the vegetations. Should the anhemolytic streptococcus be isolated from the blood of an occasional case of the disease it will be necessary to determine whether it is to be regarded as a secondary invader or as indicative of a mixed infection. That the anhemolytic streptococcus is found in the blood of cases of endocarditis in which it is not the

causative agent is borne out by the findings of Swift and Kinsella,⁵ who were able to grow the organisms in 8.3 per cent of a series of cases of rheumatic fever. Inasmuch as we do not know the causative agent it cannot be stated with certainty that a unitary etiology obtain for all our cases. It must be left to future studies to determine whether the lesions are due to an undescribed virus or are the extraordinary results of a known etiologic agent.

In view of the limited number of instances of the disease which have been observed, it is obviously unwise to make dogmatic statements concerning the diagnostic value of any one symptom or group of symptoms. The ensuing remarks concerning the diagnosis are based on the assumption that the clinical findings in our cases are the typical manifestations of the disease. The simultaneous occurrence of white-centered petechiæ and fibrinous pericarditis seems to be the most valuable diagnostic finding. This combination of symptoms might be encountered (*a*) in cases of subacute bacterial endocarditis with marked nitrogen retention, where the pericarditis is a terminal event; (*b*) in cases of combined rheumatic and subacute bacterial endocarditis, and (*c*) in the atypical form of verrucous endocarditis. The first of these possibilities is generally easy to determine, for here the nitrogen retention is marked and the pericarditis is a terminal phenomenon. Furthermore, the blood cultures may be positive and the Osler nodes may be found. As for the second possibility, positive blood cultures and the occurrence of the Osler nodes would again indicate the correct diagnosis. In each of the 3 cases of combined rheumatic and active subacute bacterial endocarditis which we have observed the anhemolytic streptococcus was grown from the blood. There remains the third possibility, namely, the atypical form of verrucous endocarditis. It is our impression that the latter form of endocarditis will be found in the great majority of patients showing the combination of white-centered petechiæ, acute pericarditis and negative blood cultures.

The presence of lesions on the face and elsewhere resembling acute lupus erythematosus may prove to have some value for the diagnosis. It is not possible to decide at the present time what significance is to be attached to the occurrence of generalized

purpura, unusual erythematous eruptions, ulcerative lesions on the skin and mucous membranes and dermatomyositis. Acute nephritis seems to be an important finding, but apparently cannot be used for the diagnosis unless it occurs very early in the disease.

In all probability certain cases will be encountered in which the endocarditic manifestations will be masked by other symptoms. Case II is an illustration in point. It will be particularly important in cases of unusual erythematous or purpuric eruptions to search carefully for symptoms pointing to the atypical form of endocarditis.

The ultimate outcome of these cases is a matter of conjecture. The immediate cause of death in our cases was uremia in 2, and pneumonia in the other 2. It is highly probable that mild instances of the disease will be observed, and from a study of such cases it may be possible to determine whether this form of endocarditis is capable of producing chronic valvular defects. Inasmuch as sub-acute bacterial endocarditis is generally engrafted on diseased valves, it will be important to determine how often the latter disease attacks the valves in cases of atypical verrucous endocarditis. It is quite conceivable that such a superinfection can occur. There is some evidence, both clinically and pathologically, that recurrences develop in the atypical cases. In 3 of the 4 cases there were organic changes in the valves indicative of a previous attack of endocarditis. We have recently had under observation a patient who we believe developed the disease. He had fever, white-centered petechiæ, acute pericarditis, a valvular defect and negative blood cultures. Several weeks after the temperature fell to normal he developed a recurrence of the fever and a fresh crop of white-centered petechiæ appeared. He recovered and now shows only the manifestations of chronic valvular disease. How often a recurrent form and other forms of the disease will be encountered must be left for the future to decide.

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DISCUSSION

DR. GEORGE BLUMER, New Haven: Reports of a considerable number of cases of disseminated lupus erythematosus have been published in dermatological literature. In these the disease has frequently terminated in death, with a picture of sepsis. I wondered whether Dr. Libman had looked into these cases reported by the dermatologists to see whether any of them showed the endocardial lesions which he has described.

DR. L. A. CONNER, New York: Is there any clinical picture of cases of this type which have recovered? Did all cases of this kind prove fatal?

DR. L. F. BARKER, Baltimore: I am very much interested in these cases of acute generalized lupus erythematoses. In Baltimore, in Dr. Longcope's Clinic, we have recently had one such case, and Goeckermann in the Mayo Clinic has reported several cases. In some instances, lesions of tuberculosis have been found at autopsy, and it has been thought by some that the whole condition was due to a tuberculous infection; but really only about half the cases have shown tuberculous lesions. I would like to ask Dr. Libman if he thinks that tuberculosis can be regarded as a predisposing factor in some of these cases. It has seemed to me that in acute generalized lupus erythematoses, we must be dealing with some form of general infection (with distribution of the virus through the blood stream) of which the etiological agent is as yet entirely unknown.

DR. EMANUEL LIBMAN (closing): In regard to the questions of Drs. Blumer and Barker regarding acute lupus erythematosus, I do not think that this condition represents as yet a sharply delineated clinical picture. In a number of cases dermatologists will differ, some making a diagnoses of lupus erythematosus and others of some form of erythema. Some of the cases of lupus erythematosus have arthritis involvement, and there are cases of arthritis accompanied by a cutaneous lesion which is clearly not true lupus erythematosus. I have been interested in cases of erythema for over twenty years. There are cases of erythema, resembling lupus erythematosus, accompanied by remarkable visceral and other cutaneous manifestations. At autopsy a verrucous endocarditis was occasionally found. It had, however, the appearance of a terminal endocarditis. The same holds true of postmortem findings in cases of lupus erythematosus. Recently, I carefully studied a paper by Ehrmann, published in the *Archives f. Dermatologie*. It is a most exhaustive study of the subject of lupus erythematosus. I found no record of the occurrence of the type of endocarditis which Dr. Sachs and I have been studying. As regards the relationship of tuberculosis to lupus erythematosus, we have

not found it to be etiological in the cases in which we have had an opportunity of making pathological studies. Tuberculosis may be regarded as one of a number of etiological agents in the disease. It played no role in the causation of the lesions which we have demonstrated today.

In regard to Dr. Conner's question as to the clinical course, one case that probably belongs in the group is alive and doing well. There were two attacks of fever, with pericarditis, white-centered petechiæ and repeatedly negative blood cultures. I believe that the infection can recur, and there is some pathological evidence in support of such a view.