GLomerular Lesions of Subacute Bacterial Endocarditis.*

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Plates 48-51.

In the kidneys of nearly all individuals dying during the course of subacute bacterial endocarditis,1 there exists a pathological lesion which affects one or more loops of a variable proportion of the glomeruli. The uninvolved glomeruli and the uninvolved loops of affected glomeruli in these kidneys are apparently normal. This pathological picture has been almost universally overlooked, probably because few observers have had the opportunity of investigating a large number of cases during a relatively short space of time. The study that forms the subject of this report was possible only because of the large amount of material which Dr. Libman has carefully collected, especially during the past few years, from cases of this disease.

When the prominence of the lesions, or the symptoms referable to them, have attracted any attention, they have, as a rule, been called glomerulo-nephritis. Lenhartz,2 for example, has included four instances among his reported cases of “subacute and chronic infective endocarditis” in which microscopically a diagnosis of

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1 The term “subacute bacterial endocarditis” is here used in preference to chronic infective or chronic ulcerative endocarditis. This substitution was suggested by Dr. Libman and possesses some distinct advantages. The disease, with very few exceptions, runs a subacute course. The term “infective” is objectionable for it includes that large group of endocarditis due to syphilis, and it may eventually be shown to include that due to rheumatic fever. The term “ulcerative,” moreover, is a misnomer, the majority of the cardiac lesions presenting no evidences of an ulcerative process.

2 Lenhartz, Die septischen Erkrankungen, Vienna, 1903, 393.
nephritis hemorrhagica was made. Similarly, Heubner, Romberg, and Horder, among others, have noted the presence of hematuria during the course of infective or ulcerative endocarditis, but apparently they were not aware of its constancy in the chronic type of the disease. Only Harbitz, in a report of sixteen cases of chronic infective endocarditis, called attention to the fact that in this condition the renal symptoms are of special interest because of their frequency and intensity, these often being so marked that the clinical diagnosis of acute hemorrhagic nephritis is made.

Aschoff has included "ulcerative" endocarditis among the commonest causes of glomerulo-nephritis. And in considering the various types of glomerular changes that can occur in glomerulo-nephritis, he has included a very brief description of a lesion which, in some details, resembles the one to be described in this paper. He has not, however, noted any association between this type of glomerulo-nephritis and chronic "ulcerative" endocarditis.

In his monograph on the inflammatory changes in the glomeruli, Löhlein included among the thirty-five cases of primary glomerular disease two cases in which the lesions were identical with those that I shall describe. In both instances, the individuals died during the course of chronic "ulcerative" endocarditis. At that time, he believed that the lesion was one of the effects of the toxemia of this disease and that it was not of embolic origin. He therefore included it in his group of subacute glomerulo-nephritis. Subsequently, in March, 1910, he reported eight cases of chronic "ulcerative" endocarditis in all of which loops of some of the glomeruli showed this lesion. In three of these cases Streptococcus viridans was obtained in blood cultures taken during life, and in one other case the organism was not obtained. In both of these cases the lesion was of long standing, and in one other case it was of short duration. In all of these cases the lesion was of the chronic type, and in none of them did it lead to the development of acute hemorrhagic nephritis.

Aschoff, in his second edition of Pathologische Anatomie, which has appeared since the above was written, describes the relation of the lesion to endocarditis.

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Löhlein, Über die entzündlichen Veränderungen der Glomeruli der menschlichen Nieren und ihre Bedeutung für die Nephritis, Leipzig, 1907.

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it was cultivated from the vegetations post-mortem. Although a search was made, bacteria were not demonstrated in the glomeruli. But in one case, the lumen of an artery entering an infarcted area was occluded by an embolus which contained numbers of streptococci. Because of this finding, Löhlein presumed that the glomerular lesions might also be due to bacterial emboli.

Bacteriology.—In the present work, the kidneys of thirty-four cases of chronic bacterial endocarditis were studied. Of this number, twenty-five cases were proven to be due to the organism which Schottmüller calls the *Streptococcus mitis* or *viridans*, but which Rosenow believes to be a modified pneumococcus. On the other hand, Libman and Celler have shown that this organism possesses some characteristics of the streptococcus and other characteristics of the pneumococcus. As Libman has recently pointed out, it has not been determined up to the present whether this organism is a streptococcus, or a pneumococcus that has been attenuated during its long residence in the body, its cultural characteristics becoming modified. Until this is determined, the possibility will exist that it belongs in a separate group intermediate between the streptococcus and pneumococcus. For the present, therefore, Libman has chosen to avoid the terms “attenuated streptococcus,” “modified pneumococcus,” or even “*Streptococcus viridans*,” and prefers to speak of it as the endocarditis coccus or the coccus of subacute bacterial endocarditis. This seems justified by the fact that of the large number of cases of subacute bacterial endocarditis which he has observed, in sixty-four, in which positive blood cultures were obtained, this distinctive organism was found in almost 94 per cent.

As will be seen in table II, the endocarditis coccus was found in twenty-two of the cases in this series in the blood cultures taken during life, once in the vegetations when repeated blood cultures were negative, and twice in the vegetations when no previous blood cultures had been taken. It was undoubtedly, therefore, the causative agent in twenty-five of these cases. Of the two other cases of

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the series in which positive blood cultures were obtained during life, in one the influenza bacillus was found, in the other the gonococcus was recovered.

Seven other cases have been included in the present series, although the blood cultures were negative in all, and microscopic examination of the vegetations demonstrated that they contained no bacteria. Libman has recently demonstrated these cases as examples of subacute bacterial endocarditis in a bacteria-free healing or healed stage. The reasons for this view will be presented when a consideration of the findings in the glomeruli of these bacteria-free cases is taken up.

**Technique.**—In all of the thirty-four cases that form the basis of this report, numerous sections were studied. In each instance, three to ten blocks of tissue taken from one or both kidneys were cut in paraffin, sometimes in serial sections. The sections from each block were studied with single hematoxylin stains, either Harris's or Delafield's, with hematoxylin and eosin, Van Gieson's stain, the Gram-Weigert method for demonstrating bacteria, with Weigert's elastica or the acid orcein method for staining elastic fibrils, and with the Weigert fibrin method. The previous fixation was in most cases formol-Mueller (Orth), although some of the material was fixed in a 10 per cent. solution of formalin, in Zenker's, Flemming's, or Kaiserling's fluid, or in alcohol. Bacteria were demonstrable only in tissue from five organs that had been fixed in alcohol.

**The Endocarditis Coccus.**—Before proceeding to a consideration of the glomerular lesion, it is necessary to understand a few of the cultural characteristics of the endocarditis coccus in order to be able to appreciate the mechanism by which the kidney lesions are produced. On the surface of agar, its growth is exceedingly dry and sometimes difficult to remove. When an attempt is made to emulsify this growth in normal salt solution, as in the preparation of vaccines, the bacteria show a very marked tendency to hang together in small firm clumps which usually cannot be broken up even by very vigor-

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9 I am indebted to Dr. Humphries, of the German Hospital, for the material from this case.

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The persistence of these clumps makes a satisfactory emulsion almost impossible. Similarly the growth of the organism in bouillon is characterized by the formation of small firm clumps which cannot be broken up by shaking.

In the superficial portions of the vegetations, microscopical sections demonstrate the presence of immense numbers of the cocci in chains which are similarly grouped into small clumps. Smears made from pieces of vegetation squeezed between slides and stained by Gram's method, show the presence of the typical cocci in numbers such as are seen only in smears made from pure cultures. It is quite conceivable, therefore, that large numbers of these clumps are constantly being washed off the vegetations by the blood current, and, being just small enough to pass the vasa afferentia in the kidney, become lodged in the capillary loops of the glomeruli. Here, because the organisms are non-pyogenic and possess little or no chemotactic power, they induce the lesions which will be considered later. The description that follows of the pathological process aims to give a composite picture of the lesions studied in many cases.

Glomerular Lesions in the Bacterial Cases.—In the microscopical sections of kidneys of individuals in this series dying during the active bacterial stage of subacute bacterial endocarditis due to the endocarditis coccus, there were seen, as a rule, all stages of the glomerular disease to be described. The number of involved loops of a glomerular tuft, and therefore the size of the glomerular lesion, varied in the different diseased Malpighian bodies. Furthermore, the relative number of glomeruli showing the lesion varied within narrow limits in sections from different portions of the kidneys in the same individual, and, as will be shown, sometimes varied very widely in the kidneys of different individuals with this disease.

At the outset, it must be understood that an essential part of the picture is the absence of any apparent changes in the uninvolved glomeruli and the uninvolved loops of affected glomeruli.

The very earliest stage of the process appears to consist of a swelling of the glomerular epithelium in the involved loops. If the lesion is small and affects only one or more loops, it may be situated at any portion of the glomerular tuft. In other words, it may
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involve loops at the periphery or even in the central portion of a glomerulus. If the lesion is larger, a segment of the glomerulus, or even the entire Malpighian body may be involved by the process. At first the outlines of the swollen epithelial cells in the diseased segment can be made out. The capillaries are compressed, contain no blood, and their lumina are obliterated. The swollen glomerular epithelium resembles at this stage the epithelium of the tubules, taking the various stains even more intensely.

Subsequently the outlines of the swollen cells become lost and the entire structure is fused into a homogeneous finely granular material (figure 1). In this mass, some of the nuclei are fading or undergoing karyorrhexis, although a few may still remain fairly well preserved. At this stage, by the Weigert method, the presence of a small amount of fibrin can often be demonstrated, though never in any considerable quantity. The homogeneous mass is fairly circumscribed. With the single hematoxylin stain, either Delafield's or Harris's, it takes an intense stain, causing it to stand out very prominently. For this reason, the single hematoxylin stains are most satisfactory for studying the early stages of the lesion. With Van Gieson's stain, it presents a reddish brown or golden brown color which also forms a sharp contrast with the examples of the later stages of the process usually observable in the same section.

If the deep staining, finely granular mass is situated at the periphery of the glomerulus, the epithelium of the visceral layer of Bowman's capsule over it is usually found to be swollen, proliferating, and desquamating into the capsular space. At this stage, as in figure 1, it can often be distinctly seen that the epithelial cells in the capsular space are being derived from the visceral layer of Bowman's capsule and not from the parietal layer. When the mass with its overlying epithelium comes into contact with the parietal layer of Bowman's capsule, the latter then probably also takes a share in the desquamation, and perhaps in the proliferation. The amount of epithelium in the capsular space varies in the different cases. Usually it is very slight, as in figures 1 and 2; but in a few cases, fairly large crescents are formed resembling those of sub-
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Acute glomerulo-nephritis. Occasionally these cells are seen to contain mitotic figures.

Eventually this epithelium undergoes necrosis, as did the previously swollen epithelium of the involved loops of the glomerulus. It also becomes part of the homogeneous, finely granular mass which now fuses with the parietal layer of Bowman's capsule. At this stage, if disintegration is well advanced, the mass may become flattened out over the area of fusion with Bowman's capsule in a crescentic fashion.

In many pictures like the latter, the homogeneous cellular material is seen, in Van Gieson's stain, to be traversed by a very delicate pink-staining network. The membrana propria of Bowman's capsule, if it is at all visible, is seen to be markedly swollen, as in figure 4. Usually by this time it has entirely disappeared at the site of the lesion. The circumcapsular connective tissue is usually at first slightly edematous; this accentuates its fibrillar character. Usually it is seen to be actively proliferating, or at least the site of a small collection of round cells. Occasionally fibroblasts can be seen invading the homogeneous cellular debris from this circumglomerular connective tissue, and to be actively taking part in the production of the delicate fibrillar meshwork just described.

Simultaneously with the replacement of the cellular debris by this connective tissue network, there occurs an active growth of the epithelial cells of the adjacent intact portions of the parietal layer of Bowman's capsule. They advance over the inner aspect of the necrotic mass which by this time has usually separated somewhat from the rest of the glomerulus. Eventually the entire lateral surfaces of the mass are covered by this invading epithelium (figure 4).

Finally, the fibrillar network, as seen with Van Gieson's stain, becomes gradually thicker until it has entirely replaced the cellular debris. The end stage is reached when the material consists of an almost solid mass of dense fibrous material staining a uniform deep red with Van Gieson's stain, and showing clefts here and there in which spindle-shaped nuclei are present (figure 6). With the single hematoxylin stain, the mass assumes a very pale homo-
geneous blue and presents the characteristic appearance of hyaline tissue (figure 5). This represents the healed stage of the lesion: a hyaline mass having roughly the shape of a truncated pyramid; its base fused with the adjacent interstitial tissue; its mesial aspect adherent to the remainder of the glomerulus; its sides clothed by a reflection from the adjacent epithelium of Bowman's capsule.

When the whole or a large part of the glomerulus is involved by the process, the last picture is slightly different, but the process is essentially the same. The invasion of the disintegrating cellular material by the connective tissue is always seen to take place from without inward. The invading fibrillar material, as seen with Van Gieson's stain will, however, tend to assume a concentric arrangement. If the entire glomerulus is involved, its peripheral portion may be seen to be replaced by concentric fibrils of connective tissue origin staining an intense red, whereas the central portion still consists of a homogeneous reddish brown or golden brown material. In the same section, however, examples of even later stages are frequently seen, the glomerulus being entirely replaced by a mass of hyaline fibrous tissue.¹⁶

Practically every stage of the process described above, from the early one shown in figure 1 to the later, or healed stage, as seen in figure 5, and even the hyalinization of an entire glomerulus, is to be seen in nearly every microscopical section of the kidney cortex from most of the cases of subacute bacterial endocarditis due to the typical endocarditis coccus. And this association of the various stages is an important part of the pathological picture.

Of the twenty-five cases in this series which were proven to be of this origin, in twenty-three the glomeruli were diseased, and in twenty-one the typical lesions just described were present. To a consideration of the two cases which did not show glomerular disease, and to the two cases in which the glomerular lesions could not be called typical, I shall subsequently return.

Contrary to Löhlein's views, I believe that when one or more loops of a glomerulus have reached this end stage and have been converted into a hyaline mass, the process does not spread by extension to the remainder of the glomerulus. These other loops can only be involved if they in turn are struck by other emboli.
I desire to emphasize the fact that in the twenty-one cases just referred to, usually only a minority of the glomeruli were affected. As a rule, the majority of the glomeruli, and even the portions of diseased glomeruli unaffected by the process, were, as has been said, for the most part normal. The percentage of glomeruli involved varied from 2 to 75 per cent. In the cases that showed a small number of lesions, sometimes several sections from some portions of the kidney showed none whatever. Other cases also varied widely, some portions of a kidney having an involvement as low as 5 per cent., other portions from the same organ having 30 per cent.

**TABLE I.**

**AVERAGE NUMBER OF GLOMERULI INVOLVED.**

<table>
<thead>
<tr>
<th>Percentage Involved</th>
<th>Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 to 10 per cent.</td>
<td>4 cases</td>
</tr>
<tr>
<td>10 to 20 per cent.</td>
<td>5 cases</td>
</tr>
<tr>
<td>20 to 30 per cent.</td>
<td>4 cases</td>
</tr>
<tr>
<td>30 to 40 per cent.</td>
<td>6 cases</td>
</tr>
<tr>
<td>50 to 75 per cent.</td>
<td>2 cases</td>
</tr>
</tbody>
</table>

In these twenty-one cases, the average number of glomeruli showing the typical disease was about 26 per cent. The variations in the proportionate number of glomeruli involved probably depend in great part upon the previous duration of the disease,—a point which can seldom be accurately determined. The extent of the cardiac vegetations, the number of bacteria in the blood, variations in some characteristics of the infecting organism, etc., may also be influential factors.17

Of these twenty-one cases of subacute bacterial endocarditis which were due to the typical coccus, and in which the glomerular lesions described above were found, the relative proportion of the early to the late or healed stage of the lesion varied as follows:

**TABLE II.**

<table>
<thead>
<tr>
<th>Type of Lesion</th>
<th>Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early lesion only</td>
<td>2 cases</td>
</tr>
<tr>
<td>Healed lesion only</td>
<td>1 case</td>
</tr>
<tr>
<td>Both varieties:</td>
<td></td>
</tr>
<tr>
<td>Majority of lesions in early stage</td>
<td>5 cases</td>
</tr>
<tr>
<td>Equal proportion of early and healed</td>
<td>3 cases</td>
</tr>
<tr>
<td>Majority of lesions healing or healed</td>
<td>10 cases</td>
</tr>
</tbody>
</table>

17 Further data concerning these factors are at present being collected by Dr. Libman and me, and will shortly be published by us.
These variations are also probably due to different factors, chief among which is probably the period of the duration of the disease before death occurred.

Bacterial Emboli.—In sections of five cases in which portions of the kidneys were fixed in alcohol, Gram-Weigert stains demonstrated bacterial emboli in the capillaries of the glomeruli. These consisted of small masses made up of cocci arranged in chains and presenting the typical morphology. Occasionally the clumps were quite large, filling up one or more of the capillary loops. The individual organisms were usually lancet-shaped, and often bacillary, as in figure 3. The bacterial plugs were found in the very early glomerular lesions, though some were demonstrable in glomerular capillaries which showed little or no lesion. The latter probably represented bacterial masses which were thrown off the vegetations just before death. In the later stages of the lesions, bacteria were never found; apparently they underwent destruction during the early stages when the glomerular structure was disintegrating.

In two cases, these glomerular emboli were quite numerous, and in the three remaining cases they were discovered after a brief search. In the two former cases, bacterial clumps were also found in capillaries in the interstitium, some in the midst of small areas of round cell infiltration.

The Tubules and Interstitium.—In all of these twenty-one cases, blood was found in the tubules, and in the serial sections it was possible to trace this up to glomeruli which were in the earliest stages of the process. This is the explanation of the almost constant hematuria that is observed in individuals with this disease, if the urine is examined microscopically. The hemorrhage occurs very early in the glomerular disease, probably even before the stage depicted in figure 1. The red blood cells also disappear very early from the capsular space, probably because the greater part of the glomerulus being usually undamaged, the continued secretion of urine from the intact portions of the glomerulus washes them away.

In these kidneys, the effect of a damaged glomerulus upon the tubules in relation to it,—the so-called "inactivity atrophy,"—can be easily studied. In addition to relatively insignificant diffuse paren-
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Chymatous changes throughout the organ, the tubules in intimate relation with the badly diseased glomeruli undergo a marked atrophy. Their epithelium becomes small and shrunken, just a rim of cytoplasm remaining about the nucleus; their lumina disappear. Around these cords of atrophic cells, a round cell infiltration occurs, a replacement fibrosis. Eventually the picture in these places is that of a very cellular connective tissue in which, here and there, are irregular strands consisting almost wholly of nuclei representing what was once tubular epithelium.

Areas of round cell infiltration can also occur in the interstitium without any relation to atrophic tubules. They occur in the vicinity of diseased glomeruli, and in other portions of the interstitium around capillaries which have been closed by bacterial emboli.

If the glomerular disease is very marked and the so-called "inactivity atrophy" of the tubules with its resultant replacement fibrosis in the interstitium very advanced, a picture will eventually be produced that is identical with that of the usual secondary contracted kidney. Strands of a cellular fibrous tissue in which are buried irregular cords of atrophic tubules alternate with areas in which the tubules are widely dilated, their epithelium flattened to a low cuboidal type, and the interstitial tissue little or not at all increased. A picture like this was seen in two of the twenty-one active cases of subacute bacterial endocarditis showing typical glomerular lesions, and in two of the seven cases in the healed or bacteria-free stage which will be described later.

Cases with No Glomerular Lesions.—Of the twenty-seven cases in the active bacterial stage of this disease, all but two were due to the endocarditis coccus. Of these two, in one, the infecting agent was Bacillus influenzae, in the other, the gonococcus. In none of the sections from either of these two cases was a single glomerulus found that showed any pathological lesions.

Similarly, in two of the cases due to the typical coccus of subacute bacterial endocarditis, no glomerular lesions were found, although in one case seven, and in the other nine blocks taken from various parts of the kidneys were examined.

The first case was that of a girl of twelve years whose entire
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TABLE III.

Thirty-Four Cases of Subacute Bacterial Endocarditis.

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Diseased</th>
<th>Typical</th>
</tr>
</thead>
<tbody>
<tr>
<td>27 cases in the bacterial stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25 due to endocarditis coccus (Streptococcus viridans)</td>
<td>2</td>
<td>23</td>
<td>21</td>
</tr>
<tr>
<td>22 in which blood cultures during life were positive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 in which blood cultures were negative but vegetations contained the bacteria</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 in which blood cultures were not taken but vegetations contained the bacteria</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2 not due to the endocarditis coccus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 in which B. influenzae was found in blood cultures during life</td>
<td>0</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>1 in which gonococcus was found in blood cultures during life [\text{\textsuperscript{34}}]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 cases in the bacteria-free stage [\text{(4) had negative blood cultures; (3) none were taken. In all, vegetations were bacteria-free}]</td>
<td>0</td>
<td>7</td>
<td>6</td>
</tr>
</tbody>
</table>

\[\text{\textsuperscript{34}}\] This case is included although the clinical course was relatively acute, because the lesions found in the heart were characteristic of subacute bacterial endocarditis.

illness previous to her admission to the hospital was less than three weeks. After entering the hospital, her condition was critical, and during the eight days that she was under observation, two blood cultures showed the association of the endocarditis coccus with *Staphylococcus albus*. At autopsy, the vegetations were found to be filled with polymuclear leucocytes, and extensive purulent infiltrations were present in the kidneys and other organs. This was unlike the process seen in any other case for, as was previously mentioned, the endocarditis coccus possesses no chemotactic power. Here was evidently an intercurrent infection with a staphylococcus that cut the disease prematurely short. It is possible that the duration of the disease was not long enough for the production of any extensive glomerular injury.

The second instance in which no glomerular lesions were found occurred in a man of thirty-four years who, during his stay in the hospital, had five blood cultures taken. The first three were negative, the fourth showed the presence of two colonies of the typical organisms in one plate, and the fifth blood culture was
negative. At autopsy, the greater part of the vegetations was found to be healed and bacteria-free. The explanation for the absence of glomerular lesions might be that the duration of the disease was cut short by the vegetations becoming free of bacteria very early during the course of the disease, the lesions then going on toward healing. On the other hand, the characteristics of the infecting organisms in these two cases may have been different, so that clumps were not formed in the usual fashion. This point cannot now be determined.

Cases with Atypical Lesions.—In two other cases in the active bacterial stage, the glomerular lesions were exceedingly severe, very extensive, and resembled a subacute glomerulo-nephritis. Nearly all the glomeruli were affected, and usually the entire glomerulus was involved. As seen in figure 8, all the epithelial cells within the Malpighian tufts were markedly swollen, more or less destroying the capillary structure. One side of the capsular space was usually filled with a crescent of desquamated and compressed epithelial cells mixed with a few leucocytes and sometimes with red blood cells.

One of these cases manifested symptoms of renal insufficiency before death which was due to uremia. Clinically and pathologically, therefore, these two cases resembled a subacute glomerulo-nephritis. Yet the possibility that the glomerular lesions could be embolic in origin must be considered.

In Löhlein's experience, kidneys in cases of glomerulo-nephritis having glomerular lesions of this type and of this severity show involvement of every glomerulus. Some glomeruli may show more severe lesions than others, yet all will present some disease. In these cases, although some portions of the kidneys showed such a universal involvement, other portions contained an admixture of glomeruli that were absolutely normal. Furthermore, in almost every involved glomerulus, serial sections demonstrated that a number of loops at some part presented a much more advanced stage of disintegration than did the remainder of the glomerulus. In other words, the usual picture was that seen in figure 8, but with a number of loops showing a lesion resembling that depicted in
figure 1. As Aschoff and others have pointed out, such a picture is sometimes seen in glomerulo-nephritis. But in these two cases it was present in almost every involved glomerulus. It strongly suggests the possibility that the lesions were of embolic origin but that, unlike the process in the typical cases, the adjacent epithelium both within the glomerulus and in Bowman's capsule have undergone a reactive swelling and proliferation, probably because of some difference in the infecting organism or the reaction of the host.

Unfortunately these kidneys were fixed in formol-Mueller, which made a demonstration of the presence of such bacterial emboli impossible. Without this demonstration, such an hypothesis cannot be entertained. We must, therefore, continue to consider the pictures in these two cases as examples of subacute glomerulo-nephritis. Furthermore, the coccus, which is the causative agent in this type of bacterial endocarditis, is closely related to the ordinary streptococcus, the association of which with the occurrence of glomerulo-nephritis has been noted by nearly every pathologist and clinician.

*Acute Endocarditis.*—Sections were studied of the kidneys of fifty-four cases of acute endocarditis, about one half of which were proven by blood cultures or by cultural and microscopical examinations of the vegetations to be of bacterial origin. In not a single glomerulus, in all the cases studied, was any lesion discovered that might in any respect be said to resemble those of subacute bacterial endocarditis due to the endocarditis coccus. The reason is, that when, in cases of acute bacterial endocarditis, bacterial emboli lodge in the glomeruli, suppurative lesions are produced. The endocarditis coccus, on the contrary, is non-pyogenic, and, as is well known, possesses little or no chemotactic power.

*Healed Cases of Subacute Bacterial Endocarditis.*—In his large collection, Dr. Libman possesses seven hearts that present vegetative lesions of the endocardium, which he has considered as examples of a healed or bacteria-free stage of subacute bacterial endocarditis.\(^9\) This view was based in part upon the clinical

\(^9\) Libman, *loc. cit.*
course, the character of the vegetations, and their location upon sites which Libman at that time pointed out as characteristic of subacute bacterial endocarditis. Blood cultures taken on four of these cases were negative. Also the vegetations were, for the most part, completely healed and free from bacteria. None of these cases were under observation when in a bacterial stage, but Libman has seen several other cases pass from the bacterial to the bacteria-free stage during their clinical course.

This view of Libman's was considerably strengthened by the finding of the typical glomerular lesions of subacute bacterial endocarditis in six of these seven cases. In view of the absence of any such pathological lesion in the fifty-four cases of acute endocarditis studied, this finding seems to indicate definitely that the six cases were examples of healed subacute bacterial endocarditis due to the endocarditis coccus. In the seventh case, the patient suffered from general anasarca. At autopsy, his kidneys presented the picture of a most advanced degree of secondary contracted kidney. The glomeruli were identical with those described by Löhlein in some of his cases of secondary contracted kidney in which there was an antecedent glomerulo-nephritis; that is, a hyaline thickening of the walls of the glomerular capillaries and an enormous hypertrophy, some of the Malpighian tufts measuring over 400 micra in diameter.

As was to be expected, only the healed stage of the typical lesion was present in the six cases (figure 7). But a point of interest was that distinctly fewer glomeruli were involved than in most of the cases in the bacterial stage. As was previously noted, the average number of glomeruli affected in the twenty cases dying during the bacterial stage (excluding the atypical cases), was about 26 per cent. In these six bacteria-free cases, the average number was 17 per cent.; and if one case was excluded, in which 80 per cent. of the glomeruli were diseased and the kidney was a typical example of secondary contracted kidney, the average would fall to 5 per cent.

To explain this, the only plausible hypothesis is that complete healing of the endocardial process, should it occur, must take place within a relatively short time after the inception of the disease.
Otherwise the patient will die during the bacterial stage because of cerebral embolism, cardiac insufficiency, intercurrent infections, etc., or from the disease itself. Therefore the only healed cases that come to autopsy will, as a rule, be those cases in which complete healing has occurred very early and before there was much chance for death from any one of the many factors that threaten the life of these patients during the bacterial stage.

Clinical observations support this view. Cases are most frequently seen clinically during the bacterial stage, less frequently during the bacteria-free stage. But it is the rarest thing to see a case during the transition from one to the other. Libman, for example, has seen only two cases in which, after the blood cultures have been repeatedly positive, the patients have improved clinically, the blood cultures have become negative, and the patients have passed into the bacteria-free stage. In other words, the active bacterial stage in those cases that healed must be very short. Most patients with subacute bacterial endocarditis have had many previous attacks of articular rheumatism, and an active bacterial stage of brief course, with its joint symptoms, etc., would be almost impossible to distinguish clinically from a new attack of articular rheumatism or rheumatic endocarditis.

The finding of a much lower percentage of involved glomeruli in the bacteria-free cases than in the bacterial cases is, therefore, in accord with the clinical facts in indicating that those cases in which complete healing of the cardiac vegetations occur before death, have had a very short bacterial stage.

CONCLUSIONS.

1. In most cases of chronic or subacute bacterial endocarditis due to the endocarditis coccus (Streptococcus viridans), there exists a distinctive pathological lesion in some of the glomeruli due to bacterial emboli.

2. The salient features of the pathological picture are first, the involvement of one or more loops of a variable number of glomeruli; secondly, the absence of any visible disease in the uninvolved glomeruli and in the uninvolved portions of affected glomeruli; and
thirdly, the association in most of the bacterial cases of all the various stages of the glomerular process often seen in a single microscopical section.

3. The lesion does not occur in cases of acute endocarditis, and up to the present time it has been absent in cases of subacute bacterial endocarditis due to organisms other than the endocarditis coccus.

4. In a group of cases having vegetations that are typical of those in the active stage of subacute endocarditis (except that they are free from bacteria and healing or healed), the healed stage of this distinctive glomerular lesion is present, although it is less extensive than in the active bacterial cases.

5. These cases, therefore, are most probably examples of subacute bacterial endocarditis due originally to the endocarditis coccus, but in which the endocardial vegetations have become free from bacteria rather early in their course and are now healing or healed, as claimed by Harbitz and Libman.

6. During the active bacterial stage of the disease, if the glomerular lesions are not too numerous, the only symptoms produced will be an almost constant hematuria, usually demonstrable only microscopically. If the glomerular lesions are very numerous, symptoms resembling those of subacute hemorrhagic nephritis may occur and may even cause a fatal issue. If the glomerular lesions are very numerous but not sufficient to cause death, and the cardiac lesion should go on to healing, a contracted kidney, secondary to the glomerular lesion, may subsequently ensue and produce the typical symptoms and death. In such a case, the finding of the healed or healing lesion of subacute bacterial endocarditis will be accidental.

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George Baehr.

EXPLANATION OF PLATES.

PLATE 48.

Fig. 1. Early stage. The epithelial cells of the involved tuft are swollen and degenerating. In the capsular space are a few cells which represent the proliferated and desquamated epithelium of the glomerular layer of Bowman's capsule. The parietal layer is still intact. Stained with hematoxylin. X 315.

Fig. 2. Early stage showing destruction of a large segment. In the capsular space at the site of the lesion is seen the swollen epithelium which has proliferated and desquamated from Bowman's capsule. Stained with hematoxylin. X 315.

PLATE 49.

Fig. 3. A bacterial clump filling up a capillary loop in a glomerulus. Gram-Weigert's stain. X 1,000.

Fig. 4. Old lesion. The delicate fibrillar meshwork is replacing the necrotic debris. On the periphery of the mass, portions of the membrana propria of Bowman's capsule are seen to be still intact. Epithelium from the adjacent portions of Bowman's capsule has grown inward and now covers the inner aspect of the mass. Van Gieson's stain. X 315.

PLATE 50.

Fig. 5. Old lesion. The typical picture after organization has occurred. The hyaline wedge is covered on its inner aspect by epithelium which is continuous with the peripheral layer of Bowman's capsule. In the adjacent interstitium is a small collection of round cells. Stained with hematoxylin. X 315.

Fig. 6. Old lesion. The same glomerulus as in figure 4, but at a different level. With Van Gieson's stain, the dense fibrillar meshwork that occupies the hyaline mass is seen. X 315.

PLATE 51.

Fig. 7. From a case of healed subacute bacterial endocarditis. The typical wedge is shown with epithelium reflected over it from the peripheral layer of Bowman's capsule. Note the absence of any change within the glomerulus or in other portions of the capsule. Stained with hematoxylin. X 315.

Fig. 8. Early stage resembling the process in subacute glomerular nephritis. The entire glomerulus is involved and all its cells are swollen and degenerating. In Bowman's capsule is a crescent of proliferated and desquamated epithelial cells with a few round and polymorphonuclear cells. Stained with hematoxylin. X 315.