The kidney in rheumatic heart disease

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SYNOPSIS Histological evidence of glomerulonephritis is reported in 95 (38.6%) of a series of 246 necropsies with concomitant rheumatic carditis. The details of these findings are given and their significance is discussed.

Although renal, and in particular glomerular, changes have long been recognized in the collagen diseases as a group, surprisingly little has been recorded of the kidney in rheumatic carditis. In 1932 Bell reported glomerulitis in 21% of a series of 104 cases with active rheumatic endocarditis, chronic changes being absent in 53. He described the glomerular lesion as diffuse, consisting of an increased number of endothelial cells, with occasional thickening of the basement membranes. In some examples the capillaries contained an excess of leucocytes. In three cases he found focal lesions of the tuft, described as being of embolic type; these, however, were unaccompanied by any terminal infection. On the other hand Baehr and Schifrin (1932) found only three examples of glomerulonephritis amongst 235 cases in which death was due to rheumatic heart disease. Active carditis was present in 118. They excluded patients over 31 years of age to avoid confusion with atherosclerotic valvular deformities. Not surprisingly, they concluded that glomerulonephritis was not associated with rheumatic carditis. This view seems to have been tacitly accepted thereafter, and Allen (1951) dismisses the subject with a brief but somewhat equivocal statement.

A few chance observations suggested that the matter merited further investigation. To this end a series of 246 cases was selected for examination from material available from 1911 to 1959. Cases were rejected where intercurrent infection, especially bacterial endocarditis, extensive infarction of the kidneys, gross post-mortem change, or other factors were prejudicial to the analysis. Chronic heart failure was the cause of death in most instances but some patients died from a variety of intercurrent diseases. Elderly subjects with slight degrees of mitral-cusp thickening were excluded on the grounds that the rheumatic basis of this condition is question-
were uraemic at the time of death. Microscopically a diffuse glomerulitis, suggestive of type I, was found in three cases (Fig. 1), associated with polyarteritis nodosa in one; in two cases the picture resembled that of type 2 glomerulitis, but the remaining six cases could not be assigned to either category (Fig. 2).

The kidneys represented by Fig. 2 were of normal size and finely flecked with lipoid. The principal glomerular change was an uneven proliferative glomerulitis. In a few glomeruli the capsular epithelium was heaped up, and occasionally fusion of the tuft to the capsule had led to disorganization through invasion by fibroblasts. The interstitial tissue was diffusely increased, sparsely cellular and oedematous. The lumina of the tubules contained many red corpuscles. The patient, aged 50 at death, was known to have rheumatic endocarditis at 45, his urine then being reported as normal. Ten weeks before death the urine became dark and three weeks later he was admitted to hospital with heart failure, albuminuria, and haematuria. Following this he had a phase of uraemia, but his blood urea returned to normal and death was ultimately due to heart failure.

2 PROLIFERATIVE GLOMERULITIS In 76 cases the glomeruli principally showed proliferative glomerulitis. This change, when advanced, caused enlargement of the tuft (Fig. 3) in excess of any that could be attributed to simple back-pressure congestion (Fig. 4). Both the endothelial proliferation and thickening of basement membranes varied in degree and distribution. Although widespread when present, a number of the glomeruli, or part of an affected tuft, might appear normal. Thickening of basement membranes can only be correctly assessed by special stains, the appearances in haematoxylin-and-eosin preparations being frequently deceptive. The P.A.S. method proved the most reliable, demonstrating that the thickening is due to an increase of fine, interwoven fibrils between the capillary loops and not of the 'wire-loop' character seen in disseminated lupus erythematosus. In one case only was this picture equivocal (Fig. 5). The centres of lobules were more affected than the periphery and, when the hilar region was involved, there was sometimes in continuity a peri-adventitial increase of fibrils and cells about the glomerular arterioles. Figs. 6 to 9 inclusive illustrate moderate or lesser degrees of proliferative

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**FIG. 1.** Proliferative glomerulitis and capsulitis with increase of adjacent interstitial tissue. From male aged 49 with severe mitral stenosis and rheumatic vegetations. P.A.S. × 290.

**FIG. 2.** Proliferative glomerulitis with increase of interstitial tissue. Details in text. P.A.S. × 290.
FIG. 3. Enlargement of tuft from proliferative glomerulitis. From male aged 52 with severe mitral stenosis; death due to mesenteric embolus. Haematoxylin and eosin × 290.


FIG. 5. Basement-membrane changes of 'wire loop' type, not fibrinoid. From male aged 56 with mitral stenosis; no evidence of active carditis. P.A.S. × 290.

FIG. 7. Proliferative glomerulitis with 'lobulation' of tuft. From female aged 52 with chronic pancarditis; no evidence of active lesions. P.A.S. × 290.


Proliferative glomerulitis in this group: all are from cases in which this was the sole change observed.

ADDITIONAL GLOMERULAR CHANGES In 39 examples of this group the glomeruli also showed adhesions of the tuft to the capsule (Figs. 10 to 12), often with localized degeneration ('focal necrosis') of the tuft. In 13 cases the altered tuft contained aggregates of foam cells. In eight cases the adhesions were associated with hyaline-droplet degeneration of the capsular epithelium, and in these it was remarkable that the proximal convoluted tubules were not similarly affected though the distal segment sometimes contained rather sparse droplets.

The tuft in the region of an adhesion sometimes had a smudged appearance resembling that often seen in disseminated lupus (Fig. 11), but the haematoxyphil deposits so characteristic of the latter were never observed. Slight degrees of proliferation of the capsular epithelium were found in nine examples, and an excess of leucocytes in the tufts in five.

INTERSTITIAL TISSUE In 12 cases this was increased, being generalized through the cortex in five and focal, mainly periglomerular, in seven. This change was not the collagenous sclerosis of the ischaemic kidney, but a finely fibrillated and sparsely cellular tissue, the cells being fibrocytes, occasional large mononuclear cells, and lymphocytes; polymorphonuclear leucocytes and plasma cells were rare.

3 In three cases there was no obvious proliferative glomerulitis, but scattered tufts showed adhesions and focal necroses. In one there was slight epithelial proliferation in a few other glomeruli. In addition two of these examples showed focal, periglomerular increase of interstitial tissue.
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chronic valvulitis found at necropsy was only slight or moderate. In one case there had been an attack of acute haemorrhagic nephritis seven years before death and the terminal picture resembled type 1 (Ellis). The question of coincidence might be clarified by estimating the natural incidence of chronic nephritis in adult necropsy material over the period of this investigation. This has not been attempted owing to the obvious inflation in the number of such cases at the London Hospital from the activity of the Nephritis Clinic.

The 11 cases classified as 1b fall into a different clinico-pathological category. Cardiac disease was dominant during life except in one case where polyarteritis nodosa posed a diagnostic problem. In this small group the nephritis was clinically submerged in nine cases and was not detected at necropsy except in the two instances in which the kidneys were lipid-flecked. Microscopically this group includes cases that so closely approximate to the more florid examples in group 2 that they may reasonably be regarded as transitional.

In this second and largest group (76 cases) the total number hinges on the identification of proliferative glomerulitis as objective evidence of disease when this was the sole change found. Minor degrees are obviously difficult to detect, even with the help of the P.A.S. stain. Therefore examples that appeared marginal were repeatedly examined, at intervals of weeks or months, and those that seemed doubtful were ultimately rejected. A different observer might increase or reduce the number of cases in this group; therefore the total assessed must be regarded as the fairest approximation that can be reached in the circumstances.

However, as already shown, solitary proliferative glomerulitis was restricted to 33 cases; in the remainder this finding was reinforced by other significant changes: focal necroses and adhesions, or an inflammatory increase of interstitial tissue, or both. If the 33 cases were totally removed from the series the percentage showing evidence of nephritis would be reduced to 25, still a considerable proportion of the whole.

It might also appropriately be asked whether the changes recorded could be interpreted as terminal; this applies particularly to examples in which no increase of interstitial tissue was found. This suggestion is poorly supported by the circumstances responsible for death. Although chronic heart failure was the principal cause of death, in five patients it was due to severe haemorrhage from different sources, two died as the direct result of valvulotomy, one from carcinoma of the stomach, and one during anaesthesia for appendicectomy (Fig. 12). Focal necroses in addition to proliferative glomerulitis were

**FIG. 12. Focal thickening of basement membranes and adhesion of tuft to capsule. From female aged 59 with chronic aortic and mitral endocarditis. Death under anaesthesia (appendicectomy). P.A.S. × 290.**

The findings in groups 2 and 3 (79 cases) are summarized:

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<tr>
<th>No. of Cases</th>
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<tr>
<td>Proliferative glomerulitis alone</td>
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<td>Proliferative glomerulitis with increase of interstitial tissue</td>
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<td>Proliferative glomerulitis with increase of interstitial tissue and focal necroses</td>
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<td>Proliferative glomerulitis with focal necroses</td>
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<td>Focal necroses alone</td>
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<td>Focal necroses with increase of interstitial tissue</td>
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**DISCUSSION**

**SIGNIFICANCE OF RESULTS** The incidence of glomerular disease in a total of 38·6% of this series suggests more than coincidence. It might, however, be agreed that coincidence accounts for the five examples of contracted kidney, for this small group seems to lie apart from the rest of the series. The ages of these five patients ranged from 24 to 52 years and in none could the duration of the rheumatic carditis be clinically assessed. In three, however, the degree of
found in three of these cases, and in two there was
an increase of interstitial tissue.

ACTIVITY OF THE RHEUMATIC CARDITIS Evidence of
activity was provided by the macroscopic description
of the characteristic vegetations and, when available,
the examination of histological preparations. The
latter were not always satisfactory and, indeed, an
exhaustive examination of the heart would be
necessary if evidence of rheumatic activity were to
be positively excluded. But such an examination has
not been feasible in an enquiry of this kind. Subject
to these limitations it can only be stated that 30%
of the group with glomerular changes had positive
evidence of active inflammation in the heart, whereas
activity was found in 19% in the group with no
renal inflammation.

AGE INCIDENCE All decades, from the first to the
eighth, are represented in both the nephritic and
non-nephritic groups. On analysis there appears to
be little difference between them: the second and
third decades are better represented in the former
than in the latter, but in both the greatest number of
cases falls in the fourth to sixth decades. The actual
figures for consecutive decades are: (a) nephritic,
1, 12, 15, 21, 16, 22, 6, 1, 1; (b) non-nephritic, 5, 8,
9, 22, 41, 39, 21, 6.

EVIDENCE OF NEPHRITIS The renal implications of
rheumatic carditis were not detected clinically, with
the exception of those patients, already mentioned,
who died in uraemia. Cardiac failure dominated the
picture; albuminuria and oedema were naturally
attributed to this and haematuria, if present, could
be explained by infarction. Blood-urea estimations
were available in only 14 cases, seven of these being
in group 1. In the seven of group 2 the figures ranged
from normal to 78 mg. % except in one case where
300 mg. was recorded two months before death.

This man, aged 45, was admitted with chronic
mitral and aortic endocarditis. The urine contained
9/10 albumin and a deposit of leucocytes, red
corpuscles, granular and hyaline casts. He was
discharged, one month before death, with gross
anaasarca and pleural effusions. At necropsy death
was attributed to serofibrinous pericarditis. There
was chronic endocarditis of the aortic and mitral
valves, with slight stenosis of the latter and micro-
scopic evidence of active inflammation. In the
kidneys a uniform diffuse fibrosis pervaded the
cortex and extended into the upper medulla. The
tissue appeared oedematous and contained scanty
fibroblasts mixed with an uneven, rather sparse
infiltration of lymphocytes, plasma cells, occasional
large mononuclear cells and neutrophil leucocytes.
Proliferative glomerulitis was slight and focal. Hyaline-droplet degeneration of the capsular
epithelium was associated with slight focal cellular
proliferation, adhesions, and focal necroses. Isotrope fatty droplets occupied the epithelium of the
convoluted tubules and hyaline droplets were found
in the ascending loops of Henle. Bulky eosinophilic
hyaline casts were numerous.

These details illustrate the kind of case in which
nephritis might well be suspected clinically. In this
instance a nephrotic syndrome (though information
about the plasma proteins is lacking) was associated
with raising of the blood urea and renal changes that
have points in common with Bright's disease but do
not lend themselves to any existing classification.
The case also demonstrates the artificiality of
separating the small group of 11 cases (1b) from
group 2: it is clearly transitional.

In conclusion, the findings in the present investi-
gation support those of Bell (1932), and suggest the
desirability of further investigation of this problem
both clinically and in the laboratory. The surprising
negative results reported by Baehr and Schifrin (1932)
may be partly accounted for by their exclusion of
cases over 31 years old for, in the present series, most
of the glomerular changes were found in older sub-
jects. This in itself suggests that successive attacks of
carditis may generate an immunological state in
which the kidneys become vulnerable, by analogy
with disseminated lupus. On the other hand, the
incidence of glomerulonephritis in any series investigated might depend in its turn upon the
incidence of infection with nephritogenic strains of
group A streptococci (Rammelkamp and Weaver,
1953). Further speculation is unprofitable until the
background of combined renal and cardiac disease
in rheumatism is more fully investigated.

REFERENCES
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