Albuminuria in Congestive Heart Failure

By George A. Race, M.D., Charles H. Scheifley, M.D., and Jesse E. Edwards, M.D.

Albuminuria may be an integral part of the picture of congestive heart failure. Of 161 patients in whom the histologic renal findings were considered to be either normal or to be of such a nature as not to be responsible in themselves for albuminuria, and in whom clinically obvious causes for albuminuria had been eliminated, 141, or 88 per cent, had albuminuria. The incidence of albuminuria was about equal among the various types of heart disease when heart failure existed. A trend existed for the grade of albuminuria to parallel the grade of heart failure. Based on a study of 21 patients, there seemed to be a correlation between the grade of albuminuria and the group of hypertension, according to funduscopic examination. No correlation was found between the grade of albuminuria on one hand and the systolic or diastolic values for blood pressure, the known duration of elevated blood pressure, the grades of hematuria or the values for blood urea on the other hand. Among the 161 patients with heart failure in our group 1 (kidneys either normal or containing lesions not judged to be causes for albuminuria), there was no predominant renal lesion associated with any one cardiac lesion.

Albuminuria has been observed commonly in the presence of congestive heart failure. In a given case of congestive heart failure, the presence of albuminuria raises the question as to whether it is a reflection of independent renal disease or simply one aspect of the cardiac failure. A review of the literature from 1916 through 1954 failed to reveal any pertinent studies carried out with necropsy material that would resolve this question.

Material and Methods

In this study, basic data were extracted from clinical and necropsy material. The chief types of data were: (1) the various types of heart disease as determined at necropsy; (2) histologic renal findings, which revealed either a renal disorder or normal kidneys; (3) the presence and grades of albuminuria and (4) gradations of heart failure. These four sets of data were derived independently, and the comparisons were made from them after all data had been accumulated.

The study is based on the clinical records of all patients at the Mayo Clinic for whom a diagnosis of congestive heart failure had been made during the final illness in the period 1948 through 1953, and who had come to necropsy.

The clinical bases for the diagnosis of congestive heart failure were first verified by a review of the clinical records. Next, for a given case to be eligible for inclusion, it was necessary that urinalysis had been done at the same time as the examination at which a diagnosis of congestive heart failure had been made. Clinically, there was no obvious cause for albuminuria other than congestive heart failure at the time congestive heart failure was diagnosed.

In the present study, albuminuria was graded on the basis of 1 to 4. The Section of Clinical Pathology of the Mayo Clinic, in which these urinalyses were made, has determined grade 1 albuminuria to represent 5 to 20 mg. of albumin per 100 ml. of urine; grade 2: 30 to 50 mg. per 100 ml.; grade 3: 60 to 90 mg. per 100 ml.; and grade 4: more than 100 mg. per 100 ml.

On the basis of the above criteria, 212 cases of congestive heart failure in which necropsy had been done were studied. The clinical records were reviewed and pertinent information was extracted. The necropsy records were reviewed for the classification of the heart disease, the manifestations of congestive heart failure and evidence of gross abnormalities of the kidneys.

On the basis of the clinical and pathologic data, a system of gradation of heart failure was evolved. The heart failure of each patient was graded from 1 to 4. In addition, the heart disease of each patient was placed in one of the following six categories: (1) mitral-valve disease, with or without aortic stenosis; (2) coronary arterial disease, with or without hypertension; (3) isolated aortic-valve disease; (4) hypertensive heart disease; (5) myocardial hypertrophy of unknown cause and (6) miscellaneous.

A histologic examination of the kidneys of each patient was then made, independent of any knowledge of the clinical history or of the gross pathologic findings. The cases were divided into two groups, depending upon the renal histologic findings.

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Abridgement of thesis submitted by Dr. Race to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Medicine.
Group 1 was comprised of 161 cases in which the kidneys were considered either to be normal or to contain lesions not thought to be of such a nature or degree as to be obvious causes for albuminuria. Four different categories of renal findings were included in group 1: (1) a normal kidney; (2) benign nephrosclerosis; (3) benign nephrosclerosis associated with small scars of either healed infarcts or healed pyelonephritis and (4) only small scars of either infarcts or pyelonephritis.

Group 2, comprising 51 cases, included those in which the renal lesions were of such a nature or degree that they could have been considered responsible for albuminuria. Six different categories of renal conditions were included in group 2: (1) acute infarction; (2) malignant nephrosclerosis; (3) intercapillary glomerulosclerosis; (4) unilateral renal atrophy; (5) nephrosclerosis associated with hydropic tubules; and (6) a miscellaneous group.

The major comparisons of this study were made only on the cases in group 1.

RESULTS

The 61 female patients in group 1 were from 5 days to 89 years old, the mean being 64 years. Of the 100 male patients, the youngest was 17 and the oldest was 89 years old, with a mean of 62 years.

The incidence of albuminuria, as well as the distribution according to the grades of albuminuria, was almost identical between the two sexes. Albuminuria occurred in 86 per cent of the males and in 90 per cent of the females of group 1.

The types of renal conditions among the 161 patients of group 1 were as follows: 34 had normal kidneys, 68 showed the lesions of benign nephrosclerosis alone, 48 had benign nephrosclerotic lesions associated with small healed infarcts or pyelonephritic scars and 11 showed evidences of small scars only.

Twenty patients, or 12 per cent, of the 161 forming group 1 had no albuminuria, as compared to 141, or 88 per cent, with albuminuria. Albuminuria of grade 1 or 2 was found most frequently in the patients with congestive heart failure. One hundred and fifteen of the 161 patients in group 1, or 71 per cent, had such a degree of albuminuria. None of the patients with scars of healed pyelonephritis or infarction had albuminuria of grade 3 or grade 4, whereas the patients in each of the other categories of group 1 including that of normal kidneys had albuminuria ranging from grade 1 through grade 4.

All but two of the 51 patients (96 per cent) in group 2 had albuminuria. The only two patients in group 2 who did not have albuminuria were among the 17 with acute infarction of the kidney.

The findings in this study also showed that there was no predominant renal lesion associated with any one cardiac lesion. Normal renal findings as well as the histologic evidence of nephrosclerosis and the small healed scars of pyelonephritis and renal infarction were found in each of the six categories of heart disease.

In group 1, the types of heart disease, together with the numbers of cases in each category, are seen in table 1. It is readily apparent that the incidence as well as the distribution of the grades of albuminuria in the various categories of heart disease was roughly equal. Among the four largest categories of heart disease in this study (mitral valvular disease with or without aortic stenosis, coronary arterial disease, isolated aortic valvular disease and hypertensive heart disease), representing 90 per cent of the total number of cases, there was a spread of only 9 per cent—

<table>
<thead>
<tr>
<th>Type of heart disease</th>
<th>Patients with albuminuria</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cases</td>
<td>Grade</td>
</tr>
<tr>
<td>Mitral-valve disease with or without aortic stenosis</td>
<td>26</td>
</tr>
<tr>
<td>Coronary-artery disease with or without hypertension</td>
<td>76</td>
</tr>
<tr>
<td>Isolated aortic-valve disease</td>
<td>26</td>
</tr>
<tr>
<td>Hypertensive heart disease</td>
<td>17</td>
</tr>
<tr>
<td>Myocardial hypertrophy; etiology unknown</td>
<td>11</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>161</td>
</tr>
</tbody>
</table>
from 85 to 94 per cent—in the occurrence of albuminuria. Likewise, in the foregoing four categories, all four grades of albuminuria were represented.

In the literature, considerable emphasis is laid on the relatively higher incidence of albuminuria in congestive heart failure associated with hypertensive heart disease as compared with the prevalence of albuminuria in the presence of heart failure on the basis of other cardiac classifications. Among others, Ehrström\(^2,3\) and Bruce and Robinson\(^4\) have made this point.

The figures reflected in table 1 show that there is no preponderance of albuminuria in any one category of heart disease.

On the basis of clinical and necropsy findings, the conditions represented in the study were divided into four grades of heart failure. This gradation was established independently of urinary and histologic renal findings.

In appraisal of this correlation between the grade of albuminuria and the grade of heart failure, it must be emphasized that many of the factors involved are dependent upon individual interpretations. Thus, the original descriptions of the physical examination depended on the astuteness of the observer. On occasions, the findings of one clinician varied from those of another examiner, and the choice of the finding to be quoted was subject to the discretion of the person abstracting the clinical history. Accurate necropsy reports required comparable levels of recording. Moreover, the balancing of clinical and postmortem findings again permitted the intrusion of the human factor. It is also reasonable to assume that the grading of albuminuria in the laboratory is subject to human error. Thus, each of the two components in this correlation is liable to probable error of one grade, plus or minus.

Theoretically, if this correlation were perfect, all patients with grade 1 albuminuria would have grade 1 heart failure, all patients with grade 2 albuminuria would have grade 2 heart failure and so on.

Thirty-one patients were classified as having grade 1 heart failure; 66 patients as having grade 2; 51 patients as having grade 3; and 13 patients showed evidences of grade 4 heart failure. Hence, the heart failure of the large majority of patients was of grade 2 and grade 3.

Of the 31 patients with grade 1 heart failure, 23, or 74 per cent, had albuminuria of grade 1 or 2. None with grade 1 heart failure had albuminuria of grade 3 or 4. Among those patients with grade 2 and grade 3 heart failure, a preponderance had albuminuria of grade 1 or 2, less of 3, and still less of 4. None of the 11 patients with grade 4 heart failure had albuminuria of grade 1. Seven of these 11 had albuminuria of grade 2, 3 had albuminuria of grade 3 and 1 had grade 4 albuminuria.

Volhard,\(^5\) Ehrström\(^2,3\) and others have stated that the degree of albuminuria is not in proportion to the degree of cardiac insufficiency. Our data do not support this contention. There seemed to be a fairly positive correlation between the degree of heart failure and the degree of albuminuria.

A fairly close correlation was also found to exist between the grade of albuminuria and the group of hypertension as determined by funduscopic examination in the 21 hypertensive patients who had undergone funduscopic examination. Thus, in these patients, all who did not have albuminuria had group 1 hypertension. Among the patients with grade 1 albuminuria, none had hypertension graded higher than 2. Six of the 12 patients with grade 2 albuminuria had group 2 hypertension, and the other six of these 12 had hypertension of group 1 or group 3.

There was no correlation between the grades of albuminuria and the values for either systolic or diastolic blood pressure.

Among the 161 patients in group 1, 216 urinalyses were recorded, with 59 instances of hematuria. It was found that there was no consistent relationship between the grade of albuminuria and the grade of hematuria.

For 144 patients a total of 157 determinations of blood urea were done, and it was likewise found that no relationship existed between the value for blood urea and the grade of albuminuria.

**Comment**

Much experimental work has been done to elucidate the mechanisms in the production of
albuminuria. The following are brief references to some of these investigations.

Hayman and Bender injected citrated plasma from three nephritic patients with heavy albuminuria into persons with normal kidneys. No albuminuria resulted in the healthy recipients. Rusznýák and Németh perfused a dog's kidneys with Ringer's solution to which human blood from a patient with nephrosis had been added. No albumin appeared in the urine, but when they added sodium oleate to lower the surface tension, albumin did appear. Upon the addition of calcium chloride, the membrane no longer allowed albumin to pass through.

Richards injected epinephrine intravenously into normal healthy rabbits in such a way that its action was maintained for several minutes. Transient albuminuria resulted. In healthy cats, subjected to stimuli which excited fear or rage, albuminuria subsequently developed. In like manner, Starr conducted four groups of experiments. He gave epinephrine intravenously to rabbits and to anesthetized dogs, aroused cats to fright or anger, and injected ephedrine into men. In all these experiments the common renal feature of vasoconstriction was recorded. Transient albuminuria developed in each case.

Bolton achieved temporary complete constriction of the inferior vena cava by means of a ligation and temporary partial constriction by means of a snarelike device, the manipulation of which determined the changes in the caval pressure. He noted an albuminuria which disappeared rapidly after the resumption of normal circulation. He explained this finding by the remarkable degree of reversibility observed in the asphyxial changes in the mesenteric capillaries. Within limits, it appears that recovery to normal is almost complete; certainly it is entirely complete so far as permeability to protein is concerned. Apparently, therefore, the plasma proteins can pass through the temporarily asphyxiated capillary wall, although the same wall, under conditions of sufficient blood flow and ample oxygenation, will still retain its normal impermeability to proteins.

The consensus of these and most other investigators in this field is that the albuminuria probably is due to an increased capillary permeability of the glomeruli as a result of stagnation of blood and of anoxemia from the inefficient circulation through the kidneys, due to failure of the heart.

With reference to the quantitative values of albuminuria, the information in the literature is scanty. Most of the textbooks state that albuminuria in cardiac insufficiency is a fairly common phenomenon but that the protein content is rather small—less than 5 mg. per 100 ml. of urine. As mentioned earlier, grade 1 albuminuria in this study represented 5 to 20 mg. of albumin per 100 ml. of urine and a classification of grade 4 albuminuria required more than 100 mg. of albumin per 100 ml. of urine. Therefore, the degree of albuminuria discussed in this paper is relatively severe.

SUMMARY

1. Albuminuria may be an integral part of the picture of congestive heart failure. Of 161 patients in whom the histologic renal findings were considered to be either normal or to be of such a nature as not to be responsible in themselves for albuminuria and in whom clinically obvious causes for albuminuria had been eliminated (group 1 of this study), 141 or 88 per cent had albuminuria.

2. The incidence of albuminuria was about equal among the various types of heart disease when heart failure existed.

3. A trend existed for the grade of albuminuria to parallel the grade of heart failure.

4. Based on a study of 21 patients, there seemed to be a correlation between the grade of albuminuria and the group of hypertension, according to fundoscopic examination.

5. No correlation was found between the grade of albuminuria on one hand and the systolic or diastolic values for blood pressure, the known duration of elevated blood pressure, the grades of hematuria or the values for blood urea on the other hand.

6. Among the 161 patients with heart failure in our group 1, there was no predominant renal lesion associated with any one cardiac lesion.
Albuminuria pote esser un parte integral del syndrome de congestive disfallimento cardíaco. Essev investigate 161 patientes in qui le constatazones historenal poteva considerar se como normal o essev de character a render impossibile considerar los como responsable per se pro albuminuria. In omnes, obvie causas de albuminuria habeva esseite eliminate. Sed 141 de illes (88 pro cento) habeva albuminuria. Le frequentia del albuminuria esseva distribuite plus o minus equalmente inter le varie typos de morbo cardíaco, in tanto que disfallimento cardíaco esseva involvite. Essev noteate le tendentia del grado del albuminuria a condecer se parallelmente al grado del disfallimento cardíaco. Un studio de 21 patientes parece indicar un correlation inter le grado del albuminuria e le grupo de hypertension secondo le examine fundoscopic. Nulle correlation esseva constatate inter—de un latere—le grado del albuminuria e—del altere latere—le valores systolic o diastolic del pression sanguinee, le cognoscite duration del elevate pression sanguinee, le grado de hematuria, o le valores de urea sanguinee. Inter le 161 patientes hie reportate, nulle specific lesion renal esseva predominantemente associate con ulle specific lesion cardíaco.

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