Aspiration Biopsy of the Kidney*

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with comments by

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Aspiration biopsy of tumor tissue is a classical procedure for examination of the nature of neoplastic disease but this method has not been applied extensively to diseases of the parenchymatous organs, in which only liver and spleen biopsy has been employed to any great extent. The liver biopsy technic as described by Iversen and Roholm in 1939 has proved to be a useful aid in the differential diagnosis between obstructive jaundice and parenchymatous jaundice. Moreover, this technic has increased our knowledge of the histopathology of the liver both in acute and chronic hepatic disorders.

Apparently no attempt has thus far been made to perform investigations of renal tissue by aspiration biopsy. The literature on the subject contains reports only on the results of biopsies of kidneys obtained in the course of surgical treatment of hypertension but no investigations in intrinsic renal disorders have been published. Therefore we have attempted aspiration biopsy of renal tissue in the hope that additional information about the histopathology of the kidney could be obtained in this way. In the following pages an account will be given of the results obtained so far.

Even if microscopic examination does not afford complete information about the functional state of an organ, there can hardly be any doubt that comparison of the results of functional tests and the corresponding histologic picture constitutes one of the best means of becoming acquainted with the pathologic processes and their influence on the function of the organ. Consequently, we have made comprehensive renal function tests in connection with biopsy of the kidney.

The conditions in which the renal biopsy technics will presumably be of greatest value are those mild renal disorders which only rarely come to autopsy and also the initial stages of the severe, acute renal disorders. A group of diseases especially useful to examine in greater detail by means of biopsy is that of the acute anuria occurring after shock, intrarenal damage, poisoning with sulfonamides or corrosive sublimate, enteritis, and from many other causes. At present it is common usage to classify all these conditions under the term "lower nephron nephrosis"; but it is doubtful whether such generalization is permissible, and a closer investigation of the histological changes in milder, non-fatal cases of this nature is much needed.

The histologic picture obtained by postmortem technics generally used is frequently affected by autolysis, permitting

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an estimate of only the coarsest vascular, connective tissue and inflammatory changes. Like other cells with marked metabolic activity the tubular cells of the kidney are subject to great agonal and postmortem changes. These are not of the nature of actual putrefaction but are presumably metabolic processes which continue after death and follow a more or less abnormal course, thus changing the structure of the cells. In the case of biopsy of the kidney, fixed in a suitable manner, the histologic picture will, on the other hand, show the structure of the kidney as it was in vivo.

**TECHNIC**

**Biopsy of the Kidney.** The instruments used for this purpose were the same as were described by Iversen and Roholm for liver biopsy: (1) syringe, needle, and a 2 per cent procaine solution for local anesthesia; (2) a lancet; (3) a needle measuring 180 mm. in length, the external diameter being 1.9 mm., with a pointed stylet and a very sharp, slightly serrated edge; (4) a 20 ml. tight-fitting syringe the piston of which can be fixed in all positions by means of a special fixation device.

Before the biopsy is obtained, intravenous (if desired, direct) pyelography is performed with a lead mark on the skin approximately over the site of the right kidney. By means of exposures in two planes with the patient in the sitting position the site of the kidney and its distance from the lead mark are determined, after which the site of the puncture is marked off. With the patient in the same position the skin is disinfected and under local anesthesia a small incision is made in order to facilitate introduction of the needle. The needle is introduced nearly up to the surface of the kidney, according to the distance measured in the x-ray; the stylet is removed, syringe and needle are assembled and the piston is pulled back and secured by means of the fixation device. The needle is pushed in by screwing it another 3 or 4 cm. into the tissue, and then needle and syringe, in which the vacuum is retained, are pulled out. The barrel of the syringe will, as a rule, contain a cylinder of renal tissue measuring from 10 to 20 mm. in length. The specimen is fixed immediately on a small piece of cardboard in 95 per cent alcohol (per cent by weight) which, because of the thinness of the tissue, will complete the fixation in a very short time. It is important that the tissue not be allowed to dry up in the course of these manipulations.

**Renal Function.** Immediately after the biopsy of the kidney we have made renal function studies which, in addition to the urea and creatinine clearances comprise, among other things, the inulin clearance as a measure of the glomerular filtration rate, para-amino hippuric acid clearance as a measure of the effective renal blood-flow, and TmPAM expressing the tubular excretory mass for p-amino hippuric acid; also, Addis’s concentration test. The technic employed for the renal function tests will not be dealt with in detail here but reference may be made to previous publications on this subject.4-6

**Risks in Biopsy of the Kidney.** At the time of this writing eighty biopsy attempts have been made in sixty-six patients. Sufficient kidney tissue to permit histologic examination was obtained in only forty-two cases. Most of the failures were encountered in the beginning. With greater experience we now get a positive result in at least two-thirds of the cases. Complications other than transient hematuria have not occurred in any of the cases. In most cases the hematuria has been of only six to twelve hours’ duration, and some-
times it can be ascertained only by means of microscopic examination. In one case a small clot was passed.

Postmortem examination sooner or later after the biopsy could be made in ten cases. In three of these cases a small hematoma, corresponding to 5 to 10 ml. of blood, could be demonstrated in the perirenal fatty tissue but in most cases no trace of the biopsy could be demonstrated. Injury to the renal tissue was not found in any of the cases.

Because of the location of the large vessels and of the spleen the biopsy was made from the right kidney in all cases but one. Biopsy was not made in patients with hemorrhagic diathesis or with severe obstruction to the urinary flow from the kidney to be examined.

RESULTS

The following is a report of the preliminary results of biopsy examinations in six patients suffering from various renal disorders. As our knowledge of the histologic changes in preparations of this nature is still slight, only the most brief description of our findings will be given.

The histologic picture differs in several respects from that usually found in microscopic examination of kidneys obtained at autopsy, and, therefore, the results of two biopsies from patients with normal renal function will be given first. (Figs. 1 and 2.)

The biopsy material obtained by means of this technic differs from the usual postmortem material chiefly in the following respects: (1) The tubules, in particular the proximal and distal convoluted tubules, have a large lumen; they convey the impression of being "dilated" especially when the diuresis is low. (Fig. 1.) With increasing diuresis the lumina of the proximal tubules are narrowed. (2) The delimitation of the cells toward the lumen in the proximal convoluted tubules is very poor. In many cases there seem to be remnants of protoplasm in the tubule, and no actual limit can be drawn between cell and lumen. (Fig. 2). (3) The capillary coils of the glomeruli convey the impression of being gaping; most frequently they contain no blood. (4) Precipitates, resembling protein, may be found in the capsular spaces even in cases in which no proteinuria is found.

CASE 1. A thirty-nine year old woman, previously in good health, after a febrile abortion developed moderate jaundice and severe anuria. The period of oliguria lasted about two weeks during which the serum urea rose to 505 mg. per cent. On the eighth day of the disease biopsy of the right kidney was made. The output of urine was 70 ml. during these twenty-four hours.

The patient was treated with parenteral feeding with a 50 per cent glucose solution, correction of the electrolyte equilibrium, blood transfusion, antibiotics, etc., and was discharged in good health two months later.

Figure 3 shows the histologic picture. The glomeruli appear to contain no blood in the coils but are apparently normal otherwise. The proximal convoluted tubules show a low epithelium and a wide lumen but do not differ distinctly from the normal. In Henle's loops and in particular in the distal convoluted tubules numerous heme casts are seen, often containing lymphocytes, leukocytes and remnants of nuclei. The epithelium is well retained everywhere; however, in the tubules containing casts it is often flattened. There is no necrosis of the tubular cells anywhere.

In the interstitial tissue there is slight edema and in several areas a marked cell infiltration, chiefly lymphocytes and
histiocyes but very few plasma cells. The interstitial cell infiltration seems to be without any relation to the occurrence of casts. *Histologic diagnosis*: tubular nephritis.
Table I shows the results of renal function tests made on the thirteenth, nineteenth, thirty-second and sixty-second days, respectively, after the onset of anuria. To begin with, all the renal function tests showed much reduced values but the glomerular filtration rate (inulin clearance) was comparatively less impaired than the tubular secretion (TmPAHA) so that the ratio I/Tm (glomerular filtration rate:tubular excretory mass) is much increased at the beginning, and falls only slowly toward normal. Two months after the episode of anuria the filtration rate was about 50 per cent, the tubular secretion 33 per cent of normal.

Comment. Anamnesis and clinical course are in complete accordance with the clinical picture described as lower nephron nephrosis. The histologic findings are also in conformity with this, but the changes demonstrated are strikingly slight considering the almost completely suspended renal function. Characteristic are the high values of the ratio I/Tm at the beginning of the disease and the slow change of this ratio, indicative of the fact that the disease has impaired tubular function to a greater degree than glomerular function.

Case II. This was a twenty-three year old man who, without any preceding recognized disease, had for one year been suffering from frequency of micturition with frothy urine, periodic fatigue and functional dyspnea. Proteinuria was noted one week before admission to the hospital. The following findings were made in the department: Anemia (Hgb. 58 per cent), hypertension (blood pressure, 190/100), uremia (blood urea 237 mg. per cent), isosthenuria and considerably reduced clearances. Biopsy of the kidney showed completely and partially hyaline glomeruli with shriveling and agglutination of the capsular space and thickening of Bowman’s capsule, considerable atrophy of the tubules and increase of interstitial tissue and diffuse interstitial cell infiltration, chiefly with lymphocytes. (Fig. 4.) Histologic diagnosis: chronic glomerular nephritis.

Functional tests (Table II) showed much reduced values for all functions examined; the ratio I/Tm was somewhat lower than the normal, presumably indicating that the glomeruli were comparatively more injured than the tubules.

The patient was treated with a high-calorie diet poor in nitrogen with good effect for six months, after which the uremia suddenly became aggravated and the patient died in a week. Postmortem examination showed chronic glomerular nephritis.

Comment. According to the anamnesis, which revealed no acute precursory stage or preceding tonsillitis, the case

<table>
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<tr>
<th>Case</th>
<th>Day of Illness</th>
<th>C\textsubscript{\text{in}} ml/min.</th>
<th>C\textsubscript{\text{urea}} ml/min.</th>
<th>C\textsubscript{\text{PAHA}} ml/min.</th>
<th>Tm\textsubscript{\text{PAHA}} mg/min.</th>
<th>C\textsubscript{\text{PAHA}} (24 hr.) ml/min.</th>
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<td>13</td>
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<td>19</td>
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<td>9.4</td>
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<td>600</td>
<td>75</td>
<td>100</td>
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Inulin clearance (C\textsubscript{\text{in}}), urea clearance (C\textsubscript{\text{urea}}), p-amino hippuric acid clearance (C\textsubscript{\text{PAHA}}), maximal tubular excretion of p-amino hippuric acid (Tm\textsubscript{\text{PAHA}}), 24-hour endogenous creatinine clearance (C\textsubscript{\text{crea}} 24 hr.) and the ratio inulin clearance (I/Tm), which represents the glomerular activity in relation to the tubular activity. All values corrected to 1.73 m\textsuperscript{2} body surface.
must be classified as one of chronic glomerular nephritis (of type 2 according to Ellis's classification). The histologic findings after biopsy corresponded to the postmortem findings. The functional tests seemed to show a slight preponderance of the glomerular injury over injury to the tubules.

Case III. This was a sixty-two year old woman who had been suffering from diabetes for fourteen years and was treated with insulin for seven years. For one year proteinuria and decreasing vision had been noted. On admission a mild diabetes was found, with little or no glucosuria although the dose of insulin was less than half the dose given a year before. Moderate hypertension and anemia were present.

Ophthamoscopy showed numerous globular microaneurysms and scattered, yellowish-white, fresh cotton-wool exudations; further, there was universal narrowing of the arteries.

Biopsy of the kidney (Fig. 5) showed several hyaline glomeruli with surrounding interstitial connective tissue and atrophic tubules. In several of the glomeruli hyaline precipitations of the Kimmelstiel-Wilson type were seen, embedded in the basal membranes, most of them of the diffuse type, a few, however, being nodular. Histologic diagnosis: intercapillary glomerulosclerosis (Kimmelstiel and Wilson). Functional tests (Table II) showed a fairly equal decrease of the functions examined to between a half and two-thirds of normal.

Case IV. This was a twenty-eight year old woman who because of hyperthyroidism had had a thyroideotomy in 1936 and because of relapse had been operated on again in 1940. After the last operation she developed postoperative tetany with serum calcium at a level of 6.4 mg. per cent. She was treated effectively with calcium and A.T. 10. Since 1947 she had been given an ultraconcentrated vitamin D2 preparation. At the beginning there was control of the serum calcium but later there was no control. For a year before admission the patient had been tired and anemic and was suffering from nausea, vomiting and anorexia. On admission the blood urea was 54 mg. per cent, serum calcium 18.4 mg. per cent, hgb. 67 per cent. Intravenous urography showed no concrements, no calcification of the renal parenchyma and normal excretion of the contrast medium in normal pyelograms. X-rays of the femur and the humerus showed normal structure of the bones. Biopsy of the kidney was made twice at an interval of three weeks. On the first occasion the specimen consisted almost exclusively of medullary tissue (Fig. 6) in which precipitation of calcium was seen in several collecting tubules. A slight diffuse lymphocyte cell infiltration could also be observed. A second specimen consisted of cor-

<table>
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<th>Case No.</th>
<th>Diagnosis</th>
<th>( C_{in} ) ml/min.</th>
<th>( C_{crea} ) ml/min.</th>
<th>( C_{PASHA} ) ml/min.</th>
<th>( T_{PASHA} ) mg/24 hr.</th>
<th>( C_{ure} ) (24 hr.) ml/min.</th>
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<tr>
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tical tissue which showed nothing unquestionably abnormal apart from a slight increase of connective tissue and some cell infiltration at the transition to the medulla. **Histologic diagnosis:** renal calcinosis.

Functional tests between the two biopsies (Table II) showed an equal lowering of the functions examined to a little less than half the normal. After discontinuance of administration of vitamin \(D_2\) renal function improved considerably.

**Comment.** After thyroidectomy a woman who was otherwise in good health developed hypoparathyroid tetany which was treated with an ultraconcentrated vitamin \(D_2\) preparation without control of serum calcium and dose. This resulted in injury to the kidneys, anemia and hypercalcemia. Precipitation of calcium in the kidneys could not be demonstrated by roentgenography but biopsy of the kidney revealed considerable calcium deposits in the collecting tubules.

**Case V.** This was a sixty-two year old man who contracted syphilis at the age of twenty-eight years and was treated with inunctions and salvarsan. At the age of fifty-one years the patient was admitted to a neurologic department for tabes dorsalis and Charcot's joints. A year before the present admission severe proteinuria and edema were noted. The condition then progressed until his admission when he had enormous edema and up to 1.7 per cent of protein in
the urine, serum albumin 0.9 gm. per cent, serum globulin 3.4 gm. per cent, blood urea 37 mg. per cent and sedimentation rate 131 mm. The patient lost 10 kg. in three weeks on a diet poor in salt. Biopsy of the kidney (Fig. 7) showed that almost all glomeruli contained subendothelial precipitations which stained red with gentian violet; the proximal convoluted tubules were normal, the distal somewhat dilated containing hyaline casts. *Histologic diagnosis:* kidney amyloidosis.

The functional tests showed a lowering to about half the normal values with almost equal distribution to the glomerular and tubular functions (Table II).

*Comment.* According to the anamnesis and clinical findings the diagnosis of amyloidosis of the kidneys was considered probable, and the biopsy of the kidney confirmed the diagnosis. The functional tests showed no characteristic functional pattern.

**OBSERVATIONS**

The examples given in the preceding pages are sufficient to show what the technic of biopsy of the kidney can afford. It is, of course, of minor importance to decide whether a chronic nephropathy is of one or another form. At present this is of no great importance to therapy. In acute anuria, on the other hand, information about the nature and
degree of the renal injury is of great importance and may perhaps decide the choice of method of treatment.

As already mentioned, our knowledge of the pathologic processes underlying the milder cases of anuria or oliguria is very scanty, and in our opinion it will hardly be possible to collect all such cases under the diagnosis "lower nephron nephrosis." This term is in itself objectionable insofar as the histologic findings, including those of autopsy materials, show severe interstitial inflammatory changes which do not conform very well to the term nephrosis. To this must be added that the injury is not confined to "the lower nephron" alone but also affects the proximal tubules. This appears, among other things, from the fact that the excretion of para-amino hippuric acid, which there is good reason to believe takes place in the proximal tubules, is much impaired, and that alkaline phosphatase, normally present in large quantities in the proximal tubules and in Henle's loops, is lacking or only present in small quantities in "lower nephron nephrosis." 

On the other hand, a function such as hydrogen ion secretion, which is supposed to take place in the distal portion of the tubules, is apparently unimpaired. At any rate, the urine is, as a rule, highly acid in these patients.

It would undoubtedly not be justifiable to attribute to the localization of the casts any significance in regard to the site of the disease, as the casts must be present in the areas where the urine first attains a sufficient concentration of the substances forming the constituents of the casts.

Therefore, we have for the time being decided on the term tubular nephritis to designate the cases of acute renal injury in which relatively normal glomeruli, interstitial inflammation and heme casts in the distal convoluted tubules are demonstrated.

In our opinion it is probable that continued examinations of biopsies of the kidneys of such patients can solve some of the problems in connection with the mechanism of origin and pathophysiology of these disorders. With greater experience in estimating the changes of the cells and with a more highly developed histologic technic, it will no doubt be possible to obtain valuable information.

It is, of course, quite obvious that by means of this technic we can become enlightened on the condition in only a small portion of the renal tissue, and that this restricts the value of the method. For practical purposes, however, it has appeared that the specimen of tissue removed is sufficiently large to be fairly representative in diffuse renal disorders.

SUMMARY

The authors describe a technic for aspiration biopsy of renal tissue in man. Biopsies from two normal individuals and from five patients with various renal disorders are reported in preliminary form. At the same time determinations of discrete kidney functions were made in these patients.

The authors consider that continued studies of material removed by aspiration biopsy of the kidney may contribute materially to solution of the pathophysiologic problems of the heterogeneous group of renal diseases generally termed "lower nephron nephrosis."

REFERENCES


