CLINICAL PROGRESS

Clinical Use of the Percutaneous Renal Biopsy

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Since the first practical method of renal biopsy by the percutaneous route was developed,1,2 at least 2,000 cases have been recorded. Perhaps several times that number of biopsies have actually been performed. Although the percutaneous renal biopsy is well established as a research procedure, it is not so well established as an ordinary diagnostic procedure. It is the purpose of this review to discuss the use of the percutaneous renal biopsy as a diagnostic tool and to discuss the changes in concept of renal disease that have resulted from its use in investigation.

Risks and Indications

As with all operative procedures, the percutaneous renal biopsy carries certain risks. Even though local conditions vary widely a limited evaluation of the risk is feasible. In at least 3 institutions a series of 500 or more biopsies without mortality has been accumulated. In many other institutions the percutaneous renal biopsy has been performed in 200 or more cases without mortality. On the other hand several deaths have occurred on the first attempt or in a small series. The natural reluctance to report this tragedy has kept some of this experience from the literature. It would appear that in experienced hands the risk of mortality should be less than 0.1 per cent.

In several of those deaths that have been reported or are known to us the actual mechanism of death is not known. Several reported deaths may have been unrelated to the biopsy procedure. Of the known causes of death, hemorrhage and shock are of first importance.

Morbidity, however, has been experienced in almost every series. Hemorrhage of some degree probably occurs after every biopsy. In terminal or near terminal patients an antemortem biopsy is accompanied by evidence of blood loss ranging from 10 to 50 ml. The local tissue forces in the region of the posterior aspect of the kidney seem quite capable of tamponade and control of this amount of bleeding.3 In most cases the only evidence of bleeding from the biopsy site is the appearance of blood in the urine. Hematuria is usually microscopic in amount and persists no longer than 36 hours. Bleeding produced by transection of small arteries in the kidney has occasionally been observed. These hemorrhages usually halt spontaneously.

More serious accidents also occur. Occasionally the needle has been known to penetrate the pelvis of the kidney. This is discovered by the reflux of urine through the biopsy needle or from recovery of mucosal tissue in the biopsy specimen. Although this would seem to be a serious event it is usually uncomplicated unless the urinary tract is obstructed. Occasionally the hilar vessels have been opened by the percutaneous needle. Bleeding from this source is potentially serious, especially if the renal vein is involved. Although bleeding from the hilar vessels is more serious than from others, hemorrhage from any source may be alarming. Hemorrhage has on occasion required operative intervention for control. The incidence of severe hemorrhage requiring some form of treatment (transfusion or surgery) has been surprisingly low. Significant bleeding occurs less frequently than once in 100 biopsy attempts. Many of these severe hemorrhages are self limited and require only simple trans-
fusion. It has been thought that the incidence of hemorrhage is much higher in cases of malignant hypertension, uremia, primary bleeding dyscrasias, obstructive uropathies, and polycystic disease.

Immediate or delayed pain occurs in a small number of patients. The pain may be either colicky or it may be constant and localized in the flank. It is rarely severe.

Edema does not by itself seem to increase the risk of the percutaneous biopsy; many patients with the nephrotic syndrome have been biopsied without difficulty. It is also surprising that infections in and around the kidney are apparently not complicated by biopsy. Fever after biopsy even in the presence of pyelonephritis is extremely rare.

The size or age of the patient also does not seem to limit the procedure. At least 1 patient of 450 pounds, has been biopsied successfully.3 The percutaneous renal biopsy has been carried out successfully at every age from 1 year into the seventh decade. It is probable that at both ends of this age range the risks are increased. It is usual though not always necessary in smaller children to carry out the procedure under heavy sedation or anesthesia.

In addition to certain reservations in the selection of patients with hypertension, bleeding dyscrasias, etc., a careful study of the x-ray films of the kidney will probably prevent a small number of accidents that would occur because the kidney is in an abnormal location. A single kidney would seem to be sufficient cause for avoiding a biopsy. It also appears to be a sound practice to carry out the procedure in the hospital and to keep the patient under observation and at bed rest for 48 hours subsequent to the biopsy.

Several methods of doing the biopsy have been described. At the present time the Franklin modification of the Vim Silverman needle is probably most widely used. The patient is usually placed prone with his abdomen on a sand bag. This position seems to immobilize the kidney partially. With an exploratory spinal needle the kidney may be located by the respiratory excursions of the needle, once the needle reaches the kidney. In most patients the capsule of the kidney is perceived by the type of resistance it offers the needle. Specific technics are discussed elsewhere.4

With all known precautions and with experience a small mortality (of the order of 1 in 1,000 cases) appears to be the minimum risk. This being so, when is the percutaneous renal biopsy indicated as a diagnostic procedure?

The Problem of Making a Clinical Diagnosis

Unless a patient is in uremia or in the nephrotic syndrome, the primary renal diseases are remarkably asymptomatic. Obviously a patient with lupus nephritis may have other stigmata of systemic lupus erythematosus; a patient with the Kimmelstiel-Wilson lesion will probably have overt diabetes; but a large number, perhaps the majority of patients with primary renal disease who are accustomed to receive close medical attention are discovered by routine urinalysis. This appears to be less true of children than of adults.

In a patient without signs or symptoms there are relatively few abnormalities of the urine which help in formulating a specific diagnosis. The list of such findings is unfortunately quite short.

Red cell casts and hemoglobin casts have long been interpreted as indicating an acute glomerulitis. Albuminuria greater than 5 Gm. per 24 hours usually indicates one of the diseases capable of producing the nephrotic syndrome. This is also true of birefringent fat in cells and casts. Glitter cells are often associated with pyelonephritis. Papillae in the urine are a good though very rare sign of acute necrotizing papilitis. Bacteria in a fresh clean urine suggest chronic pyelonephritis. Hemosiderin in cells suggests a form of renal siderosis.

Other laboratory findings in an asymptomatic patient are also of assistance. A high blood globulin points strongly to amyloid or systemic lupus; a low albumin suggests an early nephrotic syndrome and usually though
not invariably limits the diagnosis to those diseases which produce this syndrome. The finding of I. E. cells suggests lupus. Long-standing chronic infection suggests amyloid. Most laboratory findings only suggest a renal disease; usually they do not establish a specific diagnosis.

Even patients with marked renal insufficiency and uremia and patients with the nephrotic syndrome may have little to suggest a specific diagnosis. Any one of a large number of disease entities may produce the nephrotic syndrome. A list of diseases producing the nephrotic syndrome should include lipid nephrosis, chronic glomerulonephritis, systemic lupus, diabetes mellitus, polyarteritis nodosa, renal vein thrombosis, amyloid disease, and certain drugs and toxins. The nephrotic syndrome has been reported to occur with other entities but this occurs rarely and the possibility always exists that a primary renal disease of another sort was overlooked. The pure lipid nephrosis, for instance, may be diagnosable only by the electron microscope.

Although every biopsy attempt involves risk, it does not always produce a diagnostic piece of tissue. From 60 to 90 per cent of all biopsy attempts produce from 5 to 30 or more glomeruli. This varies from operator to operator. Although this may be sufficient tissue to give a very useful and spectacular diagnosis, it may also contribute nothing of clinical value.

The small size of the biopsy specimen often forces a great deal of attention on 1 or 2 elements of the total pathologic process. This results in a change in emphasis over that of the study of pathologic anatomy on large sections of kidney. In some respects the renal biopsy gives a worm’s-eye view of renal pathology. The discussion that follows emphasizes single-element pathology and is organized as follows: (1) membranous glomerular lesion, (2) proliferative glomerular lesions, (3) vascular changes, (4) intracytoplasmic changes, (5) tubular changes, and (6) interstitial changes. Pathologic lesions in these areas give the most help in making a diagnosis.

It is obvious of course that a change of any one type is related to changes in all areas of the nephron. Membranous glomerular changes lead to proteinuria; the increased urinary protein is frequently accompanied by hyaline droplet changes in the tubules. Tubular regressive changes may lead to atrophy with condensation of the stroma in which case vascular involvement could be produced. In a similar fashion glomerular proliferative or vascular changes could start the cycle.

**The Problem of Pathologic Interpretation**

Several factors contribute to the problem of interpreting the pathologic changes found on renal biopsy and diminish the usefulness of the biopsy procedure. In part this is due to the lack of a depth of general experience in interpreting renal biopsy material and the current lack of agreement between the classical pathologic and clinical entities. Almost every group with extensive experience with the renal biopsy has had early difficulty in specifically characterizing changes that are obviously pathologic and relating them to current pathologic concepts. Some of this difficulty resolves as local experience accumulates, but some is apparently due to the lack of recognized standards for many stages of disease which heretofore were seen at the autopsy table only, and then usually in the terminal period of the disease. These difficulties are being resolved by serial renal biopsies in long-term studies with good clinicopathologic correlation.

Some of the problems of interpretation are currently insurmountable and no clear way of overcoming them is now apparent. The biopsy sample is usually taken at random. If the lesions are focal and scattered they will be discovered only by chance. The lesions of Kimmelstiel-Wilson disease and sclerodema, for example, are often so focal that a very large specimen would be needed to insure inclusion of a diagnostic lesion. Others, such as glomerulonephritis, with more uniform diffuse involvement will be discovered if a reasonably good sample is obtained. Although the electron microscope is not generally con-
considered a clinical tool, its role in the resolution of some of the problems of the renal pathology has become very important, for it provides information that is not currently available in any other way. The problem of random sampling is magnified several fold in studies with the electron microscope. Because if its increasing importance the findings with electron microscopy will be discussed along with those of light microscopy.

**Membranous Lesions of the Glomerulus**

One of the most intriguing problems in renal physiology and consequently in renal pathology has to do with the role of the basement membrane in the separation of the colloidal elements of the blood from the crystalloids and water. This filtration presumably occurs across the basement membrane. A disturbance in filtration leads to the most important clinical signs of renal disease, namely, azotemia and proteinuria. The light microscope even with the best of stains does not reveal enough of the structure of the basement membrane to indicate the physiologic function that is disturbed in any given disease entity. In fact, in at least one important disease with heavy proteinuria (lipid nephrosis) the basement membrane may on occasion appear to be normal by light microscope.

In a number of other diseases the basement membrane appears to be thickened. Some types of basement membrane thickening have a characteristic appearance. Of these systemic lupus erythematosus and the early changes in the diabetic kidney are probably the most important. In contrast to these conditions a number of patients have alterations of the basement membrane which must be classified simply as membranous glomerulonephritis. The clinician sometimes has a difficult time relating this pathologic diagnosis to the established clinical entities. At the present time it is clear that for a number of patients with membranous glomerulonephritis a clear pathologic-clinical correlation has not been made. It is possible that some of these represent a new and as yet undescribed entity. It would of course be unsound to fasten on the changes of the basement membrane as the pathognomonic feature of most renal diseases, but in the absence of other changes such as cellular proliferation, etc., the basement membrane may be the only feature upon which to build a diagnosis. Frequently membranous glomerulonephritis becomes a miscellaneous category of renal diseases known to be associated with the nephrotic syndrome.

**Lipid Nephrosis**

For nearly 30 years the diagnosis of lipid nephrosis has been the subject of controversy. Until specific changes were revealed by the electron microscope there were no pathologic or clinical features with enough specificity to convince all observers of the existence of this entity. Frequently, in the early stages of the disease, no pathologic abnormalities could be determined in the glomerulus with use of the light microscope. Some observers have even thought this to be a variant of chronic glomerulonephritis.

The electron microscope has changed all this. To understand the changes that are now attributed to lipid nephrosis, one has also to understand the anatomy of the basement membrane and the associated endothelial and epithelial cells which compose the filtering apparatus of the glomerulus (fig. 1). Normally the basement membrane is approximately 0.1 μ in thickness. It increases in thickness with age and it is apparently derived from the glomerular endothelial cells. The epithelial cells which line the outer surface of the capillary tuft are quite unique at the magnification of the electron microscope. These cells possess many branches which divide into secondary branches or foot processes called podocytes. The podocytes look as if they provide mechanical support for the basement membrane.

In lipid nephrosis the foot processes are smudged and confluent, with little other change in the glomerular capillary. Unfortunately this can be determined only at a magnification produced by the electron microscope. This means that in the ordinary survey of patients in the nephrotic syndrome or
of patients who have a clinical spectrum that can be associated with lipid nephrosis a specific pathologic diagnosis may not be made by the light microscope except by exclusion.

The specific lesion demonstrated by the electron microscope now must be correlated with the actual clinical course of these patients. It would be premature at this time to translate previous clinical experience with the disease entity of lipid nephrosis to the present group of patients with lipid nephrosis diagnosed by the electron microscope.

One group of authors has reported the disappearance of albuminuria by therapy with steroids to be associated with a return to normal of the podocytes in the glomerulus.6 We have observed, however, 2 patients in distinct remission of the disease in whom the confluent, smudged podocytes were still marked. The disturbance of podocytes would not seem to be sufficient to account for the massive albuminuria frequently seen in this disease.

Systemic Lupus Erythematosus

Although this disease has many striking and bizarre clinical features and sometimes is an easy clinical diagnosis, there is an increasing number of patients now recognized in whom the onset of the disease is either so insidious or the symptom complex so unusual that a diagnosis cannot be made immediately. The natural history of systemic lupus is undoubtedly much longer than it was once thought to be,7 and it is quite possible that the disease may present as a nephritis of ob-
FIG. 2. Changes in the glomerular capillary of a 45-year-old woman with a 1-year history of systemic lupus erythematosus. There are proliferative endothelial cell changes (END), osmophilic inclusions (INCL) in cytoplasm of endothelial cells at the basement membrane (BM), occlusion of the capillary lumen, and mild thickening of the basement membrane. This glomerulus was severely damaged and other areas had fibroepithelial crescents. × 9,500.

severe etiology, or in fact it may present with obscure symptoms with few findings in the urine. In either case, with or without an abnormal urine, a diagnostic anatomic change may exist in the kidney. Lupus nephritis, unlike many of the other nephropathies, does not produce a urinary sediment that is easily correlated with the degree of activity in the kidney tissue itself. When wire-loops are clearly identified, there is generally little difficulty in making a diagnosis. Unfortunately, glomerular changes such as proliferation of the endothelial and epithelial cells, generalized thickening of the basement membrane, hyaline thrombi, focal necrosis, fibroepithelial crescents, fibrinoid changes, and so on, all of which are not clearly pathognomonic of systemic lupus, may be all that is discovered on renal biopsy; the diagnosis may remain in doubt despite a fairly large biopsy. If, as occasionally happens (10 per cent), a hematotoxicophyl body is found, the diagnosis is secure.8 Figure 2 shows changes in the glomerular capillary of a patient with lupus as seen under the electron microscope.

Chronic Glomerulonephritis

Chronic glomerulonephritis has been a popular clinical diagnosis for many years in patients who present few systemic complaints but in whom there is evidence of nephritis not due to primary infection or hypertension. It may be, as suggested by Earle and Seegal,9 that chronic glomerulonephritis is due to a number of different causes; if so, we must then consider the diagnosis of chronic glomerulonephritis as a pathologic diagnosis with the kidney reacting in a single manner to different stimuli. It is our impression that chronic glomerulonephritis is much less common than one would predict on the basis of autopsy studies. This is probably due to the fact that much earlier lesions are being seen by percutaneous biopsy than are seen at
the autopsy table. The stigmata of other disease may now be more easily and frequently identified. This has cut heavily into the group previously diagnosed as chronic glomerulonephritis. On the basis of the membranous changes a specific diagnosis of chronic glomerulonephritis cannot be made (fig. 3). It is necessary to show, in addition to the membrane changes, endothelial or epithelial cellular proliferations. It is helpful to have synchiae and hyalination of the glomeruli. It is unfortunate that no pathognomonic feature, either clinical or histologic, exists for chronic glomerulonephritis so that some landmark may be used to establish the proper boundaries of this entity. At the present time it is not even possible to depend on the history of the patient, for it is rare to find one who gives a definite history of an acute episode of glomerulonephritis. In fact it is not even certain how often an episode of acute glomerulonephritis actually initiates the chronic disease.

**Diabetes Mellitus**

The concept of diabetic renal disease is also undergoing a considerable evolution. For a long time the initial and prominent feature of diabetes was the disturbance of the carbohydrate metabolism of the patient. It is becoming increasingly more apparent that specific pathologic changes occur in diabetes which are not associated with overt hyperglycemia or even at times with an abnormal glucose tolerance test. This has been clearly recognized for several decades in the case of necrobiosis lipoidica diabetica. This skin lesion may antedate the discovery of an abnormality in carbohydrate metabolism by a number of years. It is also well known that embroyopathy antedates the discovery of the typical findings of diabetes.

In the past it has been common to attribute the renal disease of diabetes to the long-standing disturbance in carbohydrate metabolism. It has been suggested that nephropathy is made worse by poor control. However, with the advent of the renal biopsy and access to kidney tissue in patients who may be observed over a long period of time, it is now apparent that renal lesions characteristic of diabetes mellitus may occur prior to the onset of the disturbance in carbohydrate metabolism.11

Unfortunately the changes in the diabetic kidney are very complicated. It is probable that the several types of pathologic change seen in diabetes are not even very closely related. It appears that the vascular changes, the glomerular changes, tubular changes, and interstitial changes may occur in several different sequences. The severity of any one change does not correlate well with the severity of another. One change in the glomerular basement membrane as seen on biopsy is well correlated with the overt state of diabetes mellitus, and offers the best starting place from which to unravel the complexities of the diabetic kidney.

The change known as the Kimmelstiel-Wilson lesion,12 which is a nodular cellular lesion, is one of the very few pathognomonic lesions of the kidney. Actually the description of the Kimmelstiel-Wilson lesion in the past has been dependent upon the light microscope and a fairly advanced lesion has been necessary for clear identification. As it has been more recently studied by the electron microscope the Kimmelstiel-Wilson lesion appears to begin as an intracytoplasmic change in the endothelial cell.13 These changes would appear to be diagnostic. The important thing, of course, is that the cytoplasmic changes may be seen to involve the basement membrane and eventually to produce the intralobular nodule of the classical Kimmelstiel-Wilson type. The recognition of less extensive lesions by electron microscopy has made it possible to reinterpret the light microscope findings and to identify much earlier lesions with the light microscope.

The interpretation of the frequently prominent vascular changes in diabetes is very difficult. Hyalinization of the efferent arteriole is a characteristic14 that is often useful in larger sections but is much less useful with the biopsy specimen. There is otherwise nothing in the nature of the vascular changes that distinguishes them from the changes also due to aging or hypertension. The vascular
FIG. 3. **Top.** A glomerulus showing extensive nonspecific membranous glomerulonephritis from a 28-year-old man with a 2-year history of fatigue and nephrotic syndrome. These lesions are difficult to distinguish from lupus nephritis by light microscopy. The electron micrograph however is quite different from systemic lupus erythematosus, as is shown in figure 3B. (Hematoxylin and eosin) × 430. **Bottom.** Two glomerular capillaries showing the extensive accumulation (INCL) of material along the basement membrane (BM) extending into the cytoplasm of the epithelial cells (EP). The electron micrograph distinguishes this lesion from the lesion shown in figure 2, which we believe to be typical of systemic lupus erythematosus. It has not yet been possible to correlate this anatomic change with an accepted clinical entity. × 10,000.
lesions, therefore, are not specific in type and their presence does not usually make a specific diagnosis.

Since some of the relationships between pathologic changes in the kidney are yet uncertain, they must be interpreted with this uncertainty in mind. The diffuse membranous lesion of Bell, which he believes to antedate the nodular Kimmelstiel-Wilson lesion, the hyalin acellular fibrinoid lesion of Koss, sometimes called the glomerular fibrinoid cap, or the exudative lesion of the glomeruli in diabetes and some of the tubular lesions, particularly those described by Kimmelstiel recently, have yet to be accorded a high degree of specificity. Micro-aneurysms in the glomeruli are frequently associated with the specific nodular Kimmelstiel-Wilson lesions and retinal aneurysms.

To complicate the problem further, patients have now been observed with diabetes in whom renal damage is apparent without an abnormal urinary sediment. This dissociation of the histology and clinical findings can be discovered only by renal biopsy.

**Amyloid**

Occasionally the discovery of amyloid will come as a surprise; more often, however, it can be suspected because of the presence of a chronic infection or debilitating disease. Occasionally this histologic diagnosis will require special stains of the kidney tissue. Also, early lesions of amyloid may be confusing. In our material an extension from either side of the basement membrane of the glomerular capillary has been demonstrated by electron micrographs of an early lesion before the light microscope reveals amyloid deposits. The electron micrograph once more plays a real though limited role in making a diagnosis. The kidney biopsy now ranks in importance with the liver biopsy as a means of making a diagnosis of visceral amyloid.

**Toxemias of Pregnancy**

These entities have presented long-standing difficulties in diagnosis in the past. It is obvious that pre-existing renal disease may contribute to the clinical picture seen in pregnancy, and it is also obvious that some of the renal changes are produced by the pregnancy itself. A large series of renal biopsies examined by the light microscope have consistently failed to separate other renal diseases from eclampsia. It will remain to be seen what the electron microscope can do to separate these conditions from eclampsia, but it is clear that occasionally the signs of chronic glomerulonephritis or pyelonephritis will be discovered and the diagnosis therefore made.

**Proliferative Glomerular Lesions**

**Acute Glomerulonephritis**

One concept of acute glomerulonephritis is that of an inflammation of glomerular capillaries accompanied by a striking acute proliferative change of the cells and a varied amount of exudation. Endothelial change is frequently most marked but epithelial proliferation is common.

It is thought that the clinical diagnosis of acute glomerulonephritis is a fairly clear diagnosis. A history of upper respiratory infection, hematuria, recovery of the β-hemolytic streptococcus, an elevation of the antistreptolysin-titer, and the characteristic facial edema, hypertension, and reduced kidney functions give a high order of confidence about the diagnosis. Unfortunately, this constellation of clinical and laboratory findings is not always complete or unequivocal. It is probable that an exacerbation of chronic glomerulonephritis, obstructive uropathies, focal nephritis, and acute renal failure have all been confused with acute glomerulonephritis. The appearance of birefringent fat in cells and casts suggests another diagnosis.

Although the acute proliferative and exudative reaction of the glomerulus is most characteristic, tubular and interstitial involvement is frequent. The proliferative change in the endothelium of the glomerular capillaries is a prominent feature producing narrowing of the lumen and ischemia with almost certainly a marked effect on renal blood flow.

From the point of view of the diagnosis of acute glomerulonephritis, the percutaneous renal biopsy is of very great assistance. Since
the disease is uniform and diffuse, a small number of glomeruli may be sufficient to establish the diagnosis. Nonstreptococcal infections have been reported to give a classical pathologic picture of acute glomerulonephritis. Enough uncertainty surrounds many of the cases of presumed acute glomerulonephritis to warrant a percutaneous biopsy. The possibility of a recurrence of chronic renal disease masquerading as an acute episode of glomerulonephritis is often very real.

In addition to making the diagnosis, the biopsies done to date have revealed that glomerular disease persists much longer than was anticipated from the study of the urinary sediment. A case has been observed with resolving glomerular disease as long as 14 months after the urine became free of albumin and formed elements. As a corollary to this, it is quite likely that a number of cases of acute glomerulonephritis with systemic complaints exist in which the urine is normal. We as well as others have seen acute glomerulonephritis presenting both with unexplained episodes of acute hypertension without albuminuria and as an episode of acute anuria. In the latter instance, of course, no useful urinary sediment was obtained.

**Chronic Glomerulonephritis**

It would be difficult to point to the involvement of any one segment of the renal architecture as being most characteristic of chronic glomerulonephritis. It is true that glomerular proliferation is a prominent component, but widespread scarring is frequently present before the development of clinically recognized symptoms or signs. This disease is diffuse and widespread in the kidneys and renal biopsy is successful in revealing it unless the degree of change is such that specific characteristics are obliterated or become indistinguishable from those of other end-stage kidneys.

**Vascular Changes**

Differentiation between primary renal disease and renal vascular changes secondary to hypertension is often difficult to establish. A satisfactory separation may be possible by renal biopsy only in cases where proliferative glomerulonephritis clearly antedates the arteriolar nephrosclerosis. The focal nature of the vascular involvement makes biopsy evaluation difficult except in severe hypertensive states. In addition to the difficulty inherent in the interpretation of the pathologic changes, the patient with hypertension is a somewhat greater risk for biopsy than a patient with normal blood pressure. However, the percutaneous renal biopsy may provide life-saving information by revealing an unexpected pyelonephritis in a patient with severe hypertension.

**Progressive Systemic Sclerosis**

Progressive systemic sclerosis, classically considered to be a dermatologic lesion, has been shown to involve the gastrointestinal tract and to involve the kidney. The renal involvement is most pronounced in the intralobular arteries where there is marked acellular intimal thickening with secondary changes in the media. Fibrinoid necrosis may occur and extend to the glomeruli. If the involvement is extensive an infarction may occur. Since the lesions are focal, an evaluation by needle biopsy may be difficult. The differentiation from systemic lupus erythematosus may be made by biopsy as arteriolar involvement is infrequent in lupus as compared to progressive systemic sclerosis. There are occasional changes that are indistinguishable from those of malignant hypertension. Since the major renal involvement is late in the course of the disease, it is unlikely that progressive systemic sclerosis will be diagnosed by renal biopsy before clear stigmata of the disease are apparent in other organ systems. Several cases have appeared, however, with a fulminating course and with predominant involvement of the kidney.

**Venous Lesions**

In cases with renal vein thrombosis, biopsy may be helpful in support of the diagnosis in spite of the rather nonspecific changes, including interstitial edema, tubular atrophy,
and a diffuse thickening of the glomerular basement membrane. A specific diagnosis of visceral thromboangiitis obliterans may be made occasionally where there is ideal sampling.

Tubular Disease

Except for the Fanconi syndrome and a few other rare metabolic familial disorders, the most important tubular diseases are acute and generally not progressive. If the patient survives the acute episode, an equilibrium compatible with an extended life span is usually achieved. As a consequence, tubular disease (except for these rare hereditary disorders and the complications secondary to chronic pyelonephritis) are of clinical interest chiefly in the management of acute renal failure. Many centers now take biopsies from patients in acute renal failure as soon after the anuria develops as possible.

The anticoagulant therapy during external dialysis increases the risk of hemorrhage from a biopsy made within the previous 24 hours. It appears to be reasonably safe to carry out dialysis 48 hours or so after a biopsy. The usefulness of the information produced by the renal biopsy will of course vary.

After due consideration of the sampling error some prediction about the recovery of the renal lesion is sometimes possible from the biopsy. A number of cases of anuria have been observed in which the degree of morphologic change was much less than that expected from the clinical state of the patient. A great deal remains to be done in the study of the morphology of acute renal failure. This is an especially fertile area for electron microscopy.

Interstitial Changes

Clinically significant processes involving the stroma usually also produce changes in both the parenchyma and the pelvis. Many of the changes that result in renal impairment are progressive for long periods and have few signs and symptoms. Significant pyelonephritis is found in up to 10 per cent of autopsy cases. In Smithwick’s series of 1,251 biopsies between 1946 and 1955, 13 per cent were interpreted as showing pyelonephritis and this number was thought to be a conservative estimate. In a study by Kipnis et al. a small number of cases showed a good correlation between pathologic changes and renal function. Kark and co-workers have shown that cases not suspected of having pyelonephritis can be diagnosed by renal biopsy and the organism may be isolated by culture from the biopsy needle.

In the cases of familial nephritis that have come to autopsy the end-stage kidneys have been interpreted as characteristic of pyelonephritis.

Because of the focal nature of the pathologic change in chronic pyelonephritis, a negative biopsy does not furnish conclusive evidence against the existence of chronic pyelonephritis nor does a positive finding on renal biopsy eliminate another underlying process.

Summary

The renal biopsy is undoubtedly a justifiable diagnostic tool though it has not yet reached full maturity in clinical practice.

Risks. For most patients the risks do not appear to be excessive. An added caution must be exercised in malignant hypertension but even here after careful appraisal of this added risk the biopsy may still be justified. The experience of the operator would appear to modify some of the risk.

Returns. The biopsy has often added to the confusion surrounding a given case because it may be uninterpretable or because it provides an unfamiliar complex of findings. This result is becoming less common with increasing experience.

Even when the histology of the kidney is not diagnostic, it may suggest something of clinical value about the nature of the disease process, such as the presence of vascular disease, focal nephritis, or tubular disease of unidentified nature. The use of the electron microscope has extended the range of the percutaneous biopsy considerably. It is unfortunate that the cost and complexity of this instrument have confined it to certain centers.

It should be remembered also that a number
of technical failures will occur, and the sampling error may be large.

Despite these real problems, the percutaneous renal biopsy is often the only way of establishing a diagnosis and makes its greatest contribution in the appraisal of the asymptomatic patient with proteinuria and an abnormal urinary sediment.

**Summario in Interlingua**

Biopsia renal es sin dubita un justificabile metodo diagnostic, ben que illo ha non ancora attingite su complete maturitae in le practica clinic.

**Riscos.** In le majoritae del patientes le riscos non pare esser excessive. Attention special es indicate in casos de maligne hypertension, sed mesmo hie un meticulous evaluation del risco additional arriva possibilemente al conclusion que le biopsia es justificate. Il pare que le riscos se attenda con le crescente experimenta del operante.

**Resultatos.** Il ha occurrirte frequentemente que le biopsia augmentava le confusion in un caso particular proque illo esseva ininterpretable o proque illo presentava un complexo infamiliar de constatationes. Iste situation deveni minus commun con le crescente experimenta del investigatores.

Mesmo se le constatationes reno-histologic non es diagnostic, illos pote suggester aspectos de interesse clinic con respecto al natura del processo morbide: per exemplo le presentia de’ morbo vascular, de nephritis focal, o de morbo tubular de natura occulte. Le uso del microscopio electronica ha grandemente estendite le applicationes de biopsia percutaneae. Il es infelice que le costo e le complexitate de iste instrumento ha resultate in le restriction de su a certe centros.

On debe expectar le occurrentia de mal-sucessos technice, e etiam le marginie de error causate per le obtention del specimen pote esser grande.

In despecto de iste problemas (que es real), le percutaneae biopsia renal es frequentemente le sol metodo possibile pro establir le diagnose. Illo facce su plus grande contribution in le evaluation del patiente asymptomatic con proteinuria e un anormal sedimento urinari.

**REFERENCES**

3. **Personal observations.**


The electrocardiograms of 50 normal children and of patients with pulmonic stenosis, atrial septal defect, and mitral stenosis were studied to determine the frequency of the rSr' pattern in normal children and to determine factors that might yield the rSr' complex with QRS duration 0.08 to 0.10 second found in certain cardiac defects. Forty-nine of 50 normal children revealed rSr' in at least 1 right chest lead. Direct leads from the epicardial surface of the right ventricle in 5 patients with atrial septal defects showed rSr' or rSr's' localized beneath the pulmonary valve. Intraepicardial electrocardiograms studied during withdrawal of the catheter showed a splintered complex of the delay R-wave variety in the region of the right ventricular outflow tract. In 5 of 8 patients, following surgical correction of valvular pulmonic stenosis, the lead V3R changed to rsR' pattern. The electrocardiographic changes seen following closure of atrial septal defects were variable. Of 10 patients with mitral stenosis who showed electrocardiographic evidence of right ventricular hypertrophy before surgery, 4 exhibited changes following surgery from a RS pattern to an rSr' pattern. The evidence is interpreted as supporting the concept that the rSr' pattern with QRS time of 0.08 to 0.10 second is due to hypertrophy of the right ventricular outflow tract.
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