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Percutaneous renal biopsy in children

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PERCUTANEOUS RENAL BIOPSY IN CHILDREN

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INTRODUCTION

Physicians are often faced with patients complaining of symptoms of renal disease, which are not clearly diagnostic of any of the many recognized renal syndromes. Since hematuria, proteinuria, pyuria, edema, polyuria, oliguria, and hypertension, among others, may occur as prominent findings in many circumstances of disease and trauma, it is not surprising that diagnostic problems are encountered. As renal disease progresses, the resultant scarring produces a distorted, noncharacteristic kidney, which until recently was the pathologists source of information from which he had to study the natural history of various renal diseases. The correlation of this kidney with the sequence of events seen clinically was often an impossible task. One well-known clinician once stated, "It is not possible to diagnose accurately during life the anatomical changes that will be found in the kidney after death."[28] Such was the feeling of most physicians for many years and the histologic changes occurring throughout the natural history of most renal diseases remained quite vague. Even in 1958 Vernier[45] stated that " diseases of the kidney presently constitute one of the major unsolved problems in medicine."

The opportunity to correlate the clinical signs and symptomatology and the data obtained from laboratory

tests with the morphologic changes which develop in the kidney during various phases of a disease is afforded by percutaneous renal biopsy. Direct biopsy has no peer in diagnostic accuracy or in supplying information relative to diseases of many organ systems. "Whatever the theoretic dangers of biopsy, the alternative of radical treatment of a patient or abandoning him to a hopeless prognosis without proof of malignant tissue involvement is far more serious."[4]

HISTORY

The first kidney biopsy reported in the literature was done in Canada by Dr. Norman Gwyn in 1923. He took several renal biopsies during the course of abdominal operations upon patients with kidney stones. At the presentation of his paper in 1923, he emphasized the importance of biopsy in making diagnoses which might otherwise be impossible. He believed that " a kidney can always suffer the loss of a millimetre of substance."[15]

The first closed or percutaneous renal biopsy was reported by Ball [3] in 1934. He thought that practically all areas of the kidney are accessible to the needle without risk to the patient. He emphasized taking the biopsy through the margin of a lesion if possible, in order to obtain the greatest amount of information by comparing the abnormal histology side-by-side with the

normal histology.

In 1943 Castleman et al[9] reported a large series of open renal biopsies in which he was trying to determine the role and nature of renal vascular lesions in the production of hypertension. He concluded that hypertension not infrequently exists with no evidence of renal vascular disease to explain it, almost a reversal of his findings two years previously on a much smaller series in which he concluded that renal vascular disease was evident in all of their cases of hypertension long before any renal failure occurred.[8]

In 1944 Alwall performed aspiration biopsies of the kidney upon thirteen patients using the technique described by Iversen in 1939 for biopsy of the liver.[1] This method involved pushing the needle into the kidney, which had been previously located with an intravenous pyelogram, applying suction by locking the syringe, and then withdrawing the needle with a screwing motion. Although he got back adequate tissue in ten out of thirteen biopsies, one of his patients went into shock and died and he promptly discontinued this practice. However, in 1952, after several successful series of renal biopsies had been reported, Dr. Alwall wrote an article stating that with modern shock therapy and modern treatment of acute renal failure this patient probably

would not have died and after reviewing the articles written by Iversen and Brun, he believed a re-investigation for the justifiability of that technique was in order.

The first series of biopsies done to study intrinsic renal disorders was reported by Iversen and Brun in 1951.[21] They did the biopsy with the patient in a sitting position after first localizing the kidney in two planes with an intravenous pyelogram. At first they obtained satisfactory results in only 38.2% of Biopsies, but they improved to nearly 67% after they had acquired more experience with the technique. These investigators were the first to suggest that the term lower nephron nephrosis was probably not justified. They stated that the lesion did not look like nephrosis and that their lab studies and renal biopsies showed that the proximal tubules were as much if not more affected than the lower or distal tubules. They suggested the term tubular nephritis be used for cases with normal glomeruli, interstial inflammation, and heme casts in the distal tubules. Up to the present time reports of experience with over four thousand renal biopsies have appeared in the literature, but only about three hundred of these have been in children.

VALUE OF RENAL BIOPSIES

Renal biopsy is a very useful procedure today for

studying renal disorders from both the clinical and research viewpoints. Dodge et al[11] have recently stated that for the present, renal biopsy is primarily a research procedure, but many investigators[29,25,30,9,21] have already proclaimed its value in the diagnosis, prognosis, and selection of treatment in many renal diseases. Freedman and Andrews[16] have also emphasized the importance of renal biopsy in medico-legal cases, for example in a post-traumatic case who is subsequently found to have an abnormal urine analysis. If the kidney lesions were chronic it could easily be shown on a biopsy that the trauma was not the cause of the urine disorder and therefore wasn't compensible. Freedman also mentions that renal biopsy may eliminate the need for other more expensive investigations, especially surgical exploration.

Being able to see the histological lesion is especially important where renal diseases are concerned because of the non-specificity of most renal symptoms and signs. Another major difficulty is that primary renal disease is remarkably asymptomatic at times. There are also very few urinary findings which are very specific. A few that are very suggestive, but not necessarily specific are: red blood cell casts, which strongly suggests acute glomerulonephritis; albuminuria of greater than 5 grams per 24 hours is characteristic of the nephrotic

syndrome- etiology unknown; papillae, a good but rarely seen sign of acute necrotizing papillitis; hemosiderin, bacteria, glitter cells, and birefringent fat casts. Other laboratory findings which are quite suggestive include L.E. cells in disseminated lupus erythematosus, decreased serum albumin in nephrotic syndrome, increased serum globulin often seen in lupus or amyloidosis, and long-standing chronic infections suggesting amyloidosis. The more common findings of hematuria, proteinuria, edema, oliguria, polyuria, and hypertension are much more nonspecific.

Although certain tests of renal function, such as the determination of the glomerular filtration rate, are at times useful in the patient who presents a diagnostic problem, it has been the experience of Dodge[13] that the histologic change comes before any functional loss is detectable and that the renal biopsy is therefore a more sensitive index of the presence of renal disease. In 1943 Talbott and his group[42] found a quite constant correlation between microscopic evidence of renal vascular disease and renal function measured by quantitative procedures, but they stated later that only in grade four renal vascular disease was the renal blood flow seriously reduced, and their findings indicated also that constriction of the efferent glomerular arteriole wasn't present in early renal vascular disease.

Muehrcke et al[28] state that their main reason for doing a renal biopsy is to establish a more accurate diagnosis. This investigator has stated that he is willing to do a renal biopsy on any patient with diffuse renal disease who will co-operate and is able to undergo the procedure. These authors feel that a renal biopsy is a much more accurate method for culturing organisms in patients with suspected pyelonephritis than are urine cultures. They state that an occult kidney infection can only be diagnosed accurately by means of a renal biopsy and Kark and his group agree[23] in that they state that it is not unusual to find a positive culture from a biopsy in a patient with a sterile urine analysis.

Muehrcke described five patients with hematuria and proteinuria in whom pyelonephritis was not suspected and a positive bacteria culture was obtained. Kark[23] had a very interesting case along the same line. He described a 24 year old male who had complained of fatigue, gross hematuria, loss of weight, transient edema, polyuria, and nocturia of two years duration. He was anemic and ran a low fever most of the time. He had had ten sterile urine cultures and seventeen sterile blood cultures done in those two years. The clinical diagnosis was either subacute bacterial endocarditis or chronic glomerulonephritis. A renal biopsy revealed

a pure culture of hemolytic enterococci which were sensitive to tetracycline and with adequate treatment he was restored to complete health in two weeks.

Vernier[46] lists the group of diseases occurring in children in which he found the biopsy to be of greatest value and this included various forms of glomerulonephritis, the nephrotic syndrome, and the renal diseases associated with systemic lupus erythematosus, diabetes mellitus, and anaphylactoid purpura (Henoch-Schonlein syndrome). Parrish and Howe[32] found in a study in 1953 that a renal biopsy established the diagnosis in 52% of a series of patients when the clinical impression had been incorrect, and that the biopsy confirmed the clinical impression in 39% of the cases. Kark[23] has come up with unexpected diagnoses in such diseases as sarcoidosis, tuberculosis, glomerulosclerosis, amyloidosis, various collagen diseases, and pyelonephritis in many patients in whom he believes could not have been correctly diagnosed without a biopsy until much later stages in the disease. Pyelonephritis is a common and treatable cause of malignant hypertension, if caught early, some investigators reporting pyelonephritis in as high as 40% of all cases of hypertension.

A renal biopsy is also valuable in determining a prognosis in cases of nephrotic syndrome, hypertension, pyelonephritis, lupus erythematoses, toxemia, diabetes

mellitus, and acute anuria. Brun and Raaschou emphasize the use of a renal biopsy in the aid of selection of patients with acute anuria for hemodialysis.[5] They determine first from the biopsy if the patient has a reversible kidney disease as a "shock kidney," an irreversible acute kidney disease, or a terminal stage of a chronic kidney disease. They recommend hemodialysis only in cases of acute renal diseases with mild morphological changes, and they believe in these cases that hemodialysis can be of great importance. They state that with the therapy available today, if the glomeruli are destroyed or almost completely destroyed, there is no possibility of recovery and that then hemodialysis is seldom indicated, certainly not for long periods of time. They believe that tubular lesions are reversible to a much greater degree than are glomerular lesions, and that if tubular lesions exist with acute renal failure, treatment by hemodialysis should be repeated as frequently as required, possibly "to the bitter end."

Dodge[12] and Iversen[21] believe that steroids can be of definite value in the treatment of the nephrotic syndrome, but that they are successful only in cases with normal glomeruli or those with membranous glomerulonephritis or Ellis Type II glomerulonephritis. In those cases in which the changes similar to chronic glomerulo-

nephritis are seen, they have never found evidence that steroids have been helpful.

CONTRAINDICATIONS TO DOING A RENAL BIOPSY

There have been many contraindications to doing renal biopsies suggested by about as many different authors, but almost all of these investigators agree that there are three absolute contraindications. Those are: 1) An uncooperative patient

2) A patient with a non-correctible bleeding tendency

3) A patient with only one functioning kidney.

Other conditions in which most investigators do not do a renal biopsy and with their presence extreme caution is certainly necessary if a biopsy is thought to be warranted are:

1) Severe calcific atherosclerosis[28]

2) Perinephric abscess[28]

3) Hydronephrosis or pyonephrosis[28]

4) Large renal cysts[28]

5) Renal neoplasm[28,35]

6) Aneurysm of the renal artery[28]

7) Known focal disease[44]

8) Pregnancy[17]

9) Children under two years of age- Vernier's experience has shown him that these children are

not able to co-operate to the extent which is necessary and that the margin for error is smaller due to the smaller renal mass.[46]

10) Uremia has been a fairly constant member on this list[28,46] but in the last few years more investigators are doing biopsies on patients in uremia with few complications.[6,22] Several authors set the limit on a patient with oliguria and a blood non-protein nitrogen which is over 100 mg.% and rising. Arnold states that there is a higher incidence of post-biopsy hemorrhage in patients with malignancies, uremia, bleeding disorders, obstructive uropathies, and polycystic kidneys.[2] However Kark[22] has reported doing a renal biopsy on a patient with a blood non-protein nitrogen of 259 mg.% and rising with no resultant hemorrhage. Ross believes that acute uremia with unknown etiology is an indication for doing a renal biopsy.[34] He reported that he had no increased frequency of hematuria or other complications with his patients with uremia.

11) Patients with severe hypertension have been reported to develope complications more frequently than those without.[22]

Yamauchi[47] had a fatality in 1957 after a renal biopsy in which he thought the major complication was

a pre-existing hypovolemia and he has since published an article in which he suggests that this should be considered a contraindication until it is corrected by transfusion. He states that hypovolemia is frequently seen in the nephrotic syndrome due to edema and that its correlation with blood hematocrit is poor. He suggests doing a blood volume study on all patients upon whom a renal biopsy is contemplated and especially those patients with the nephrotic syndrome. He believes that patients with hypovolemia are predisposed to shock should any hemorrhage occur. Most biopsies are done on the right kidney if possible because of the proximity of large vessels and the spleen on the left.

Pyelonephritis has been mentioned as a contraindication to doing a renal biopsy, especially in the older literature when it was generally believed that this procedure would cause a bacteremia and a dissemination of the infection. Brun and Raaschou[6] did a study of the temperature rise occurring in patients with pyelonephritis and a series of patients without pyelonephritis following renal biopsy. They found that in 3.2% of their patients with pyelonephritis the temperatures rose to 100.4°F. and the temperatures in the control group rose to 100.4°F. in 3.6% of the cases, suggesting that no bacteremia had occurred in those patients with pyelonephritis. They

also concluded from this study that the pyelonephritis was not activated by a renal biopsy.

Arnold[2] reported no increase in risk in doing a biopsy on a patient with edema or infection and that size and age of a patient did not affect results. There is apparently no contraindication to doing repeat biopsies upon the same patient. Brun[6] has done as many as eleven biopsies on one patient and Vernier[45] reports doing four biopsies in a series on a child with no deleterious effects. Brun also reported that the creatinine clearance was not affected in a series of patients following a renal biopsy. Vernier[46] noted that no change in glomerular filtration rate or renal blood flow occurred following his renal biopsies.

Brun and Raaschou[6] also reported an autopsy series of 96 patients who had died within six months of having had a renal biopsy and they could find only 23 of the sites, all of which were only small scars. There were no lacerations and 24 minor hematomas found.

TECHNIQUE OF DOING A RENAL BIOPSY

Because many patients disliked the sitting position developed by Iversen and many either felt faint or complained of pain, Muehrcke, Kark, and Pirani developed a new technique for doing renal biopsies in 1955 which

is still used by most American clinicians with some minor variations today.[29] One of their major objections to Iversen's sitting position was that the kidneys are quite mobile in this position, making it difficult and more risky to obtain tissue. This they corrected by placing the patient in a prone position with sandbags under his abdomen to fix the kidneys firmly in place against the solid paravertebral tissues.

Preliminary Studies

1) The patient should be thoroughly questioned about any bleeding tendencies he might have.

2) A complete urine analysis with a culture of the urine for bacteria should be done.

3) An intravenous pyelogram to localize the kidneys and to assure the clinician that both are functioning is mandatory.

4) Studies of the coagulation and hemostatic mechanisms, usually the bleeding, clotting, and prothrombin times and a platelet count are adequate.

5) A PSP or some other good test of renal function is necessary.

6) A biochemical blood analysis, especially for non-protein nitrogen, blood urea nitrogen, and serum creatinine should be done.

7) Type and cross-match 500 cc. of blood to be on-hand if necessary.

8) A retrograde pyelogram should be done if uremia is present (BUN over 40 mg.%).[46]

9) About 45 minutes pre-operatively the patient is given about 90 mg. of Seconal and 50 mg. of Demerol.

10) The patient is asked to void just prior to taking the biopsy.

11) The full cooperation of the patient is essential and all of the details of the procedure should be explained to him, as well as practicing breathing maneuvers.

A blood pressure cuff is then placed on his arm and a running record of the blood pressure and pulse is kept for the next 24 hours. The patient is placed in a prone position with a sandbag under his abdomen but not pressing on his rib cage. This usually fixes the kidney against the structures on the back so that it can be palpated.

Localizing the Kidney

From the intravenous pyelogram a site is chosen at the lower outer pole of the right kidney and this spot is marked on the X-ray film with a small cross. A line is then drawn over the spinous processes of the vertebra and this is labeled Line B. Another vertical line is drawn parallel to line B through the lateral border of the right kidney and labeled Line A. A third vertical line, Line S, parallel to the other two, is then drawn through the proposed site and the distances between lines A & B (distance X), lines S & B (distance Z),

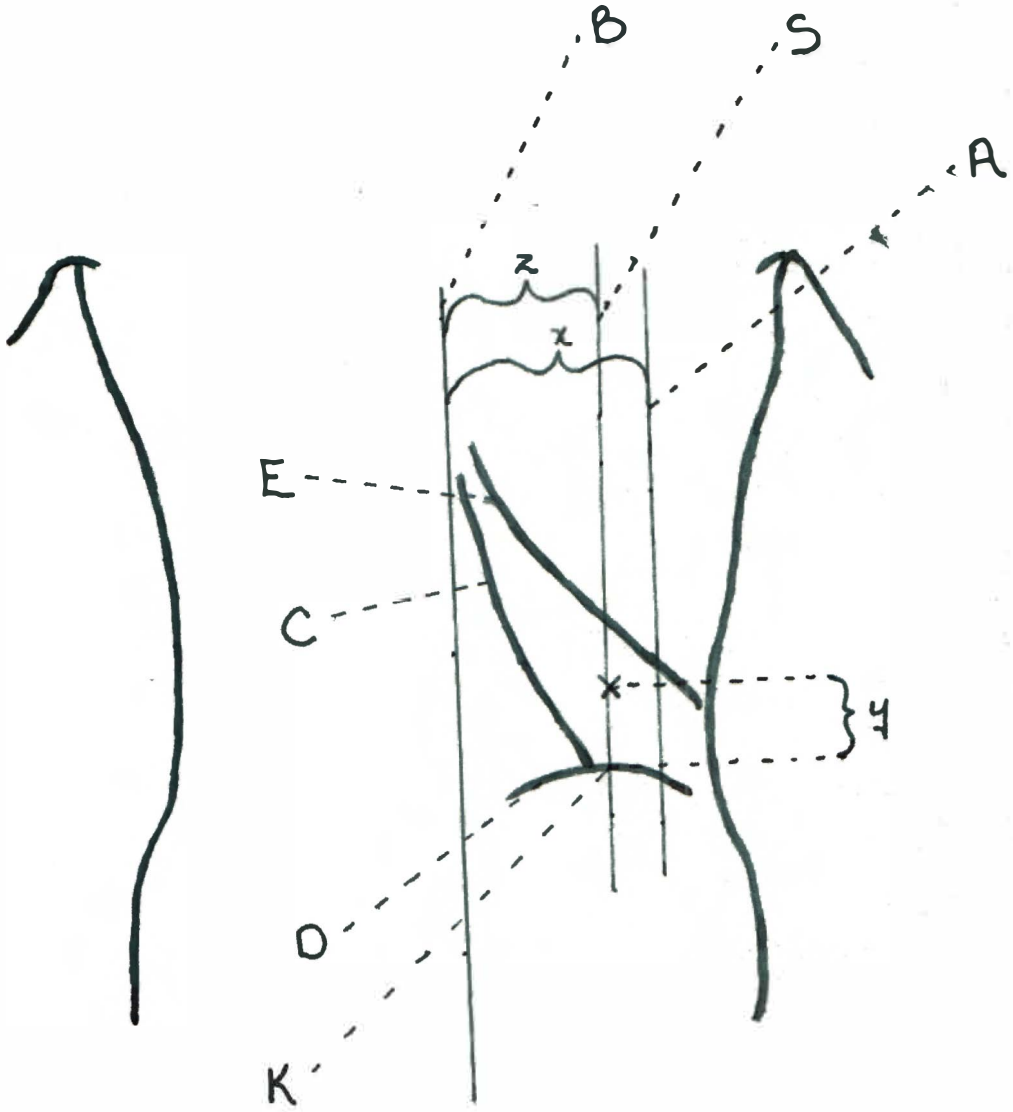

Figure I. - A diagram of the landmarks on the back which are used to localize the kidney. (A) Lateral border of the right kidney (B) Line through the spinous processes (C) Lateral border of the quadratus lumborum (D) Iliac crest (E) Last rib (K) Point K (S) Line through proposed site

and the distance between the site and the crest of the ileum along line S, (distance Y), are measured on the film and recorded.

The following landmarks are then marked on the skin:

a) Line B

b) The lateral border of the quadratus lumborum muscle, which becomes Line C.

c) Iliac crest (D)

d) Last rib (E)

e) Line A - which is the distance X from Line B and parallel to it.

f) Line S - which is the distance Z from Line B and parallel to it and passes through the biopsy site. This line passes over the iliac crest at point K.

g) The distance Y is then measured from point K along Line S to determine the biopsy site on the skin, which is again marked with a small cross. This cross should fall into the triangle defined by the lateral border of the quadratus lumborum muscle,and the last rib.

The Biopsy

The skin is now disinfected around the proposed site and a completely aseptic technique is used until the completion of the biopsy. The biopsy set, which should be sterile, should include:

1) Vim-Silverman biopsy needle with the Franklin modification.

2) One 6 inch 20 gauge infiltrating needle

3) One ½ inch 26 gauge needle

4) One ½ inch 20 gauge needle

5) Both a 5cc. and a 10cc. syringe

6) Several 4x4 inch gauzes and a few applicator sticks

7) Biopsy towels

8) A scalpel, which has been sterilized separately.

The first step is to raise a wheal with 1% procaine using the 26 gauge needle. The 6 inch 20 gauge needle is then used for an exploring needle. The patient is asked to take several deep breaths and then to hold his breath in deep inspiration while the exploring needle is slowly advanced toward the kidney. When the tough layer of the lumbodorsal fascia is penetrated, the patient is asked to take a couple more deep breaths and again to hold his breath in inspiration. The needle is then advanced slowly to the hard renal capsule. Three good criteria for determining when the needle has penetrated the kidney according to Vernier[46] are recognizing contact with the hard renal mass, noting the vibration of the needle with the pulsation of the kidney, and most important, seeing the paradoxical movement of the hub of the needle with the patient's respiration, i.e. moving

caudally with expiration and cephalad with inspiration. Note the depth of the exploring needle and mark this same depth with a broken applicator stick for reference. Infiltrate this pathway with procaine on the way out being careful not to inject procaine into the kidney. Re-insert the exploring needle once for a check on accuracy and the effectiveness of the anesthetic.

Next make a small incision through the skin with a scalpel parallel to the last ri . The biopsy needle is then inserted to the kidney and advanced about two centimeters while the patient holds his breath in deep inspiration. The patient breathes once to verify its position and again he holds his breath in inspiration. The stylet is removed and the cutting prongs are inserted to full depth. Without advancing the cutting prongs furthur, the outer needle sheath is pushed down over the prongs, biting the biopsy tissue free from the organ. The cutting prongs are then pulled out slightly, allowing a small amount of blood from the renal parenchyma to enter the outer sheath. The needle is quickly withdrawn and pressure with gauze is applied over the biopsy site. All manipulations are done quickly but deliberately.

The operator must not push the needle sidewise or handle it while it is moving with respiration, lest the

renal tissue be torn. No twisting motion should be applied while removing the tissue and no more than three attempts at obtaining renal tissue should be tried at any one sitting.

A cylinder of tissue 1.5-2.0 cm. by 1.0-1.5 mm. is usually obtained. This is examined under a hand lens to be sure both medulla and cortex are present; the glomeruli appear as minute raised structures. The blood in the sheath is washed out into the culture medium with a sterile syringe. The tissue is immediately fixed in a 10% neutral formalin in saline solution and can be stained with any of the routine stains such as hematoxylin and eosin, Mallory-azan for connective tissue, periodic acid-Schift for basal membranes, casts, and the tubular brush border, Oilred-O for lipids, Congo red and crystal violet for amyloid, or Van-Gieson-Weigert for elastic and collagen fibers.

Post-operative Care

The patient remains on the sandbag for thirty minutes post-operatively for hemostasis. A frequent running record of his clinical status, blood pressure, and pulse is kept for 24 hours while the patient is kept in the supine position at bedrest in the hospital for this time. He is questioned frequently for the presence of pain in his shoulder, abdomen, back, or genitalia. A sample

of a catheterized urine specimen which is passed in the first 24 hours post-operatively should be sent to the laboratory.

If the patient should develope signs of renal colic or pass any blood clots in his urine, the authors recommend forcing fluids for a day or two and irrigating the bladder. If gross hematuria is present for longer than 24 hours, prophylactic antibiotics should be started and the patient kept in bed for three days after bleeding has ceased. Although the authors have had no cases with massive bleeding, they recommend immediate vigorous treatment should this occur. They usually give their patients codeine with aspirin for backache and meperidine for renal colic.

Ginsburg[17] has recently published an article advocating doing renal biopsies under direct radiological control. This idea was actually expressed by Lusted[26] in 1956 in the American Journal of Roentgenology. These authors feel that measurements taken from an intravenous pyelogram film are not accurate enough when dealing with an organ as small as the kidney, and that anyone is bound to hit the hilum or the kidney pelvis occasionally.

They propose doing all of the preliminary studies that Muehrcke suggests except that the pyelogram is not

necessary. The patient is placed in the prone position with sandbags as before. After the patient is checked for sensitivity, 25cc. of Renografin 60 are injected intravenously. Good visualization is obtained in ten minutes under the image amplifier and the presence of both kidneys is assured. The point of a hemostat is placed over the lower pole of the kidney as checked by the radiologist. The exploring needle is inserted again as before and again checked by the radiologist. If it is 1-2 cm. below the lower pole calyx, it is considered satisfactory. The remainder of the biopsy is carried out as described by Muehrcke. This method can be done with a retrograde pyelogram as well if an intravenous pyelogram fails to give visualization.

The advantages of this method are its greater accuracy, the fact that one should always be able to obtain renal tissue, and you should be able to get a repeat biopsy from the same place. The chief disadvantage is the need of an expensive image amplifier which more and more hospitals are now acquiring.

Some authors[15] have recently been advocating the use of a modified Menghini needle for doing renal biopsies. With this needle the biopsy is cut and then withdrawn by suction. They suggest that it should help to reduce morbidity, although they have no large series to support this belief as yet.

COMPLICATIONS OF RENAL BIOPSY

In their article on the "Technique of Renal Biopsy" Muehrcke et al state that renal biopsy used to be a dangerous procedure due to poor localization of the kidney and the repeated stabs necessary to obtain renal tissue. With their new technique, the prone position and fixed kidney, the use of the exploring needle, and the better cutting needle the morbidity of the procedure has been reduced substantially and for the majority of patients it is a painless procedure with no post-operative complications. It is definitely not a procedure for general or casual use and statistics show that there have been several deaths in the smaller series of biopsies and that in the large series done by those with more experience there have been virtually no mortality and a very low morbidity rate. Arnold[2] has remarked that the mortality rate should be less than one in a thousand and that significant bleeding should occur in less than one in one hundred biopsies. It has been shown that when the small arteries of the kidney are transected, they usually quit bleeding quickly and spontaneously. In Slotkin's review of 5000 renal biopsies,[41] there were four deaths reported which is less than 0.1%. This compares favorable with Terry's reported mortality rate of 0.12% in over 7000 cases

of liver biopsy.[43]

Following is a list of most of the literature reports of renal biopsies done on adults and children for a comparison of the number of biopsies done with the percentage of complications and adequacy of biopsy. Note the much better results that Brun achieved after he changed to doing biopsies in the prone position.

AUTHOR	NUMBER BIOPSIES DONE	ADEQUACY OF BIOPSY	DEATHS	GROSS HEMA-TURIA	HEMA-TOMA	COMPLI-CATIONS
Dodge [11]	205	92%	1	5.2%	0.4%	
Muehrcke [28]	179	80%				9.8%
Iversen [21]	215	38%*				
Vernier [46]	250	-		10%	0.8%	2%
Parrish [32]	100	58%*				
Chugh [10]	60	60%		10%	4%	
Schwiebinger [39]	44	55%				
Smythe [40]	72	71%				
Ross [36]	124	76%				
Greene [18]	58	86%**				13.8%
Moser [27]	60	71%				8.3%
Pearl [33]	401	75%				4.0%
Kark [22]	500	80%		5.2%	0.6%	9.8%
Brun [6]	500	67%-40%*	4****	7.9%	0.2%	
Schreiner [38]	150	91%		15%		
Slotkin [41]	5000***	-		2-50%	0.5%	

*— Sitting position
**— Reported a much lower percentage early in experience
***— From 70 departments of Urology
****— Due to hemorrhage in already ill patients

TABLE 1 - A Representative List of Results of the Complications of 7918 Renal Biopsies Done in Adults and Children.

Kark[22] reported 83.6% of his biopsy patients out of 500 biopsies had no symptoms or complications, 6.6% had slight symptoms, and 9.8% had definite symptoms or complications. He agrees with almost all investigators that practically all patients have a microscopic hematuria which clears up spontaneously in six to twelve hours. He listed the following complications in his series of 500 biopsies:

Deaths	0
Operations necessary	0
Anuria	0
Bacteremia	0.2%
Gross hematuria	5.2%
Prolonged hematuria	0.6%
Renal colic	2.8%
Perirenal hematoma	0.6%
Back pain	4.4%
Mild ileus	0.4%
Pain during biopsy	4.4%
Transfusion	0.4%

Bacteremia can occur after a biopsy of an infected kidney, but is very uncommon. Jackson had only two cases of transient bacteremia following 220 biopsies of pyelonephritic kidneys. All of his cases of gross hematuria cleared up spontaneously in 6-12 hours. In his cases with prolonged microscopic hematuria he emphasizes that the wound must be given a chance to heal. The patient is kept flat on his back in bed for ten days while he is given broad-spectrum antibiotics and plenty of fluids. Renal colic is usually due to

small blood clots in the ureters and responds quickly to an increased fluid intake and diuresis.

Perirenal hematoma is probably the most severe and troublesome complication which follows renal biopsy. The bleeding is usually into the perirenal fat pad and may give pain and shock out of proportion to the amount of blood which has extravisated. The pain is severe and not well-controlled with narcotics. The first symptoms are usually nausea and vomiting with spasm and guarding of the muscles in the back. There is often a mass palpable. The symptoms usually last 2-3 days and then subside. A urologist should be called in early, so that he can have the benefit of following the patient in case more vigorous treatment is thought to be indicated. If the estimated blood loss is quickly replaced, the patient usually makes an uneventful recovery.

Another serious complication of renal biopsy is that of delayed hemorrhage, which was reported by Dodge to be very rare, but two cases of which have been reported by Slotkin[41] in the literature recently. One of these cases involved a severe retroperitoneal hemorrhage of 1000 cc. of blood which occurred on the tenth day postoperatively. At operation a freely bleeding laceration was found. The other case was done by Felton[14] in 1959.

His patient did well until the ninth day post-operatively when he suddenly went into profound shock secondary to delayed rupture of the kidney, necessitating an emergency nephrectomy.

Eight deaths have been reported in the literature which were associated with renal biopsy. The first death was reported by Alwall[2], who later said it probably was due to a retrograde pyelogram. Zelman[48] described a death in a patient upon whom both a liver and a kidney biopsy had been done. At autopsy both sites were found to have bled, but the massive bleeding was around the site of the liver biopsy. Reubi reported a death in 1954 but gave no details regarding the case. Felton's[14] patient with the delayed hemorrhage and Yamauchi's[47] patient with a hemorrhage complicated by hypovolemia have been mentioned previously. Schreiner[38] described a death in an anuric patient with widespread necrotizing arteritis. The death reported by Dodge[11] was in a patient who had been anuric for ten days prior to biopsy, and continued to be anuric for twelve more days until he died. The eighth patient, reported by Ogilvie[31], had severe arteriolar nephrosclerosis and died eight days post-operatively.

PATHOLOGY

Because of the different areas of the kidney biopsied and the difference in the angle which the biopsy needle passes through the kidney cortex, the contents of different biopsies varies greatly from one to the other. The glomerulus is usually considered the most essential structure which must be present to make an accurate diagnosis and the number of glomeruli necessary in order for the biopsy specimen to be considered adequate has been a subject of much debate. Schwiebinger[39] believes that a biopsy should be four centimeters long and include capsule, the entire cortex and medulla, and some pelvic epithelium. He reports his success at achieving this is 55%. Parrish and Howe[32] believe a biopsy should contain more than twelve glomeruli with their convoluted tubules, loop of Henle, interstial tissue, arterioles, and small arteries. He reported an adequate biopsy in 58%. Vernier[45] believes an adequate biopsy should contain ten or more glomeruli and Muehrcke[28] and Kark[22] believe that five or more glomeruli are adequate. Dodge[11] in his study of diseases of children with renal biopsies, considered five to ten glomeruli as adequate and reported adequate biopsies in 92%.

Kellow et al[24] in a study of 308 biopsies on 103

autopsy cases comparing the diagnosis with the number of glomeruli present in the biopsy specimen seemed to indicate that the number was not an important factor and they concluded that four glomeruli was all that was necessary to pick up the histological abnormality. They found that 76% of their biopsies accurately reflected the histological abnormality compared to an autopsy specimen and that the correct diagnosis was made in 69% of the cases. They found that 84% reflected the histological abnormality and 77% showed the correct diagnosis in diffuse renal disease. In pyelonephritis the histological abnormality was picked up in 44% of biopsies and in neoplastic disease the abnormality was found in 86% of the cases. Sala[37] has demonstrated better than 85% correlation of such a biopsy with the whole kidney as determined at autopsy in diffuse renal disease. Muehrcke[28] took needle biopsies at autopsy from ten different areas of one kidney which were then compared with each other and with larger sections and these compared excellently both for degree and type of histological findings. They believe, however, that a biopsy is not adequate in focal diseases such as acute pyelonephritis, tumor, tuberculosis, and abscess. They warned not to overevaluate the severity of the case if your biopsy happens to include a cortical scar from an old biopsy.

When looking at a biopsy specimen for abnormality, Pearl[33] suggests looking for the following features. In the glomerulus look for increased cellularity, basement membrane thickening, glomerular capillary size, and increased cellularity of Bowman's capsule. The tubules should be observed for degeneration or atrophy, dilatation, necrosis, and casts. The arterioles should be checked carefully for intimal and medial hyalinization and hypertrophy, and the interstial tissue observed for signs of edema, fibrosis, and inflammation.

Several differences between autopsy and biopsy specimens were immediately noticed. Autopsy material is usually affected by autolysis. Tubular epithelial cells undergo marked changes post-mortem which are metabolic changes rather than putrefaction. A renal biopsy in which the tissue is fixed immediately will show the renal tissue as it is in vivo.[21] Some differences seen in biopsy specimens are:

1) The proximal and distal convoluted tubules have a large lumen, especially when the diuresis is low; with increased diuresis, the lumen becomes narrower.[21]

2) Delineation of the cell from the lumen is poor, i.e. no definite line can be drawn.[21]

3) The glomeruli usually contain no blood.[21]

4) Precipitates like protein can be seen in the

capsular spaces, even when proteinuria is not present.[21]

5) The height of the tubular epithelial cells varies considerably, therefore tubular nephrosis can not be based entirely on the swelling of these epithelial cells. Other changes such as clumping of the cytoplasm, vacuolization of the cytoplasm, and disruption of cellular membranes have been suggested as better criteria.[28]

Kark[23] has seen free red blood cells in Bowman's space only once in his large series of biopsies, but he has observed red blood cells in the tubules many times and in several instances the ruptured peritubular capillary was present in the biopsy specimen. Teaching on hematuria to date, based on autopsy material, is that it is due to glomerular bleeding. Kark's evidence tends to show that in some cases at least, bleeding is directly into the tubular lumen.

Kark has also done some studies on proteinuria. There are at present two schools of thought on the mechanism of proteinuria. One school believes that it is due to increased permeability of the glomerular filtrating membrane, while the other school thinks that it is a disturbance in the nearly complete reabsorption in the tubules of the normally filtered protein. Kark's biopsies on patients with consistently negative urinary proteins have shown proteinaceous material in the tubules

and in Bowman's space, therefore confirming the belief that protein is filtered normally by the glomeruli and reabsorbed by the tubules.[23]

CRITICISM OF RENAL BIOPSY

As with any new procedure which has some proven risk, renal biopsy has been criticized by many different clinicians for different reasons. Almost all investigators agree that it is not for casual use and must be done in a hospital. One of the major objections is that the doctor is putting the patient through a procedure which carries a possibility of severe hemorrhage and when he is through he may have no information that will help him treat the patient. These clinicians point out that many lesions of the kidney are quite non-specific and that many different diseases with different etiologies end up with a similar appearing kidney. They also argue that in early renal disease the lesions may not be definite enough to make a diagnosis. Rose[36] concluded in 1957 that renal biopsy was valuable in the study of renal diseases, but that it had limited value in the diagnosis, prognosis, and treatment of renal disease and that although it was found to be quite safe by this author, its practice should be limited to a few selected cases. An editorial in an

English journal which appeared in 1955 stated that they thought that renal biopsies offered interesting possibilities, but probably wouldn't achieve the importance that liver biopsy now holds since accurate diagnosis of renal disease is rarely of immediate and crucial importance.[30]

Arnold[2] believes that the main difficulty at the present time with renal biopsies is the lack of experience among pathologists in interpreting the lesions which are seen in the fresh biopsy specimen and therefore the difficulty correlating the obviously pathological lesions with present ideas about the clinical disease. Another difficulty in interpretation is the lack of standards at the present time in evaluating the severity of the various lesions. Another valid criticism of renal biopsy is the possibility that the physician may miss a focal disease entirely. Other objections which have been somewhat reduced by the work of several investigators recently are the fear of dissemination of infection, and the scepticism that a representative sample will be obtained.

SUMMARY AND CONCLUSIONS

1) Although renal biopsies were first used as long ago as 1923, they were not utilized as an adjuvant in the study of patients with renal disease until 1951. Since that time the results of over 7000

renal biopsies have appeared in the literature and only around 400 of these were done on children.

2) A technique of doing a renal biopsy was described which was originally reported by Muehrcke in 1955. This technique is now generally accepted as the safest and most efficient method used today.

3) Three contraindications were named which were held as absolute by most investigators. They are an uncooperative patient, a patient with any bleeding tendency, and the presence in a patient of only one functioning kidney.

4) The most common complication seen following a renal biopsy is microscopic hematuria. This has been reported to be present in most patients following a renal biopsy and usually clears up spontaneously in 6-12 hours. More serious complications are gross hematuria with an incidence of about 5%, and perirenal hematoma with an incidence of approximately 0.4%. Eight deaths have been reported in the literature which were associated with renal biopsy, but in several of these the renal biopsy was probably not the cause of death. Most physicians with experience with renal biopsy have found the procedure to be safe, painless, and atraumatic in the great majority of patients.

5) Despite the risks involved, renal biopsy is often the only method available for making a definite diagnosis. Vernier and Good, who have done over 250 biopsies in children, stress the value and safety of the procedure in the diagnosis and as a guide to the management of renal disease. It's greatest practical clinical importance today is in selecting patients with the nephrotic syndrome in whom treatment with glucocorticoids is likely to be most beneficial, in the patient with acute anuria to determine if his lesions are reversible with time, and as a guide to the effective treatment of pyelonephritis and lupus erythematosus.

6) The application of renal biopsy to the study of renal disease will give valuable information to the physician in the future which will not be obtainable by any other method of investigation.

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