The Renal Biopsy

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• *Context.*—**The first renal biopsy was carried out more than a century ago, but its widespread introduction into clinical use, beginning in the 1950s, helped develop nephrology into the powerful subspecialty of internal medicine that it is today. In the past 25 years, the use of the spring-loaded biopsy gun, in combination with newer visualization techniques, including ultrasound and computed axial tomography scanning, has led to greater tissue yield and to a much lower risk of complication. During this same time, our understanding of renal pathology has increased many fold. Correct fixation and processing of renal biopsy tissue is critical, and the laboratory must be skilled with renal biopsy light microscopy, immunohistochemistry, and transmission electron microscopy preparation.**

***Objectives.*—To provide an overview of the renal biopsy, including the techniques and its complications, and to summarize proper laboratory methods for processing renal biopsy tissue.**

***Data Sources.*—This article is based on a review of the literature and on the experience of the author.**

***Conclusions.*—The experienced nephropathologist, knowledgeable in both renal medicine and pathology and thus able to correlate subtle tissue-derived information with appropriate clinical data, remains the most important key to the development of an accurate clinicopathologic diagnosis.**

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The first renal biopsy was likely performed in 1901 in New York City, NY, as part of a renal decapsulation procedure for the treatment of Bright disease.[1] Similar material was obtained soon after in Toronto,[2] Liverpool,[3] and Glasgow.[4] Although the tissues were examined and, in some instances, the histologic information was used to modify treatment, these open renal biopsy materials were secondary to the main purpose of the procedure. Castleman and Smithwick[5] (and later Heptinstall[6]) examined a large series of open renal biopsies taken at the time of dorsolumbar sympathectomy, a procedure used to treat hypertension. The reports provided insight not only on the renal vascular pathology associated with hypertension but also on the reliability of the biopsy material by comparing samples taken from both kidneys.

RENAL BIOPSIES

The Aspiration Technique

The percutaneous aspiration needle biopsy had been successfully used to acquire liver material as early as 1895 (reviewed in Iversen and Brun[7]), but it was not until 1939 that Paul Iversen and Kaj Roholm published the first large, systematic series of liver biopsies.[8] Other organs, not as large and as easily accessible as the more superficial liver, were thought to be poor candidates for this procedure. However, in 1944, Nils Alwall began using the aspiration technique to biopsy the kidney after first localizing it using an x-ray. He collected tissue successfully in 10 (77%) of 13 patients but did not publish his results until 1952.[9] It was the publication in 1951 of the results of 133 aspiration biopsies of the kidney by Poul Iverson and Claus Brun, one of the first nephrologists, that led to the keen interest in diagnostic renal biopsies that quickly followed[10] (commentary in Iversen and Brun[7]). Interestingly, only 50% (67/133) of the biopsies in this first series had sufficient renal tissue for evaluation.

The Needle Biopsy

The use of the Vim-Silverman cutting needle, with the patient prone, was described by several investigators (reviewed in Cameron and Hicks[11]), but the information did not become widespread until Kark and Muehrcke published their series in the *Lancet* in 1954.[12] They demonstrated a marked improvement in tissue yield (48 [96%] of 50 samples had diagnostic tissue) and that the procedure was safe. This report[12] led numerous nephrologists to learn this technique and eventually resulted in the influential CIBA Symposium on Renal Biopsy, Clinical and Pathological Significance, held in London, England, in March of 1961.[13] The renal biopsy rapidly became a key part of renal evaluation, so much so that only 2 years after the CIBA symposium, Roland and Dimond[14(p140)] remarked on the critical contributions of the renal biopsy to the "diagnosis, treatment, and management of patients ill with renal disorders. It has illuminated the anatomy, pathology, and biochemistry of the kidney in health and disease." Today, the renal biopsy is recognized to have played a critical role in the development of nephrology as a subspecialty.[11]

Current Practices

A spring-loaded, automated, cutting-needle biopsy "gun" was developed in the early 1980s.[15] It was quickly adopted for renal biopsies because of its ease of use, decreased risk of renal laceration, and lessened pain report-

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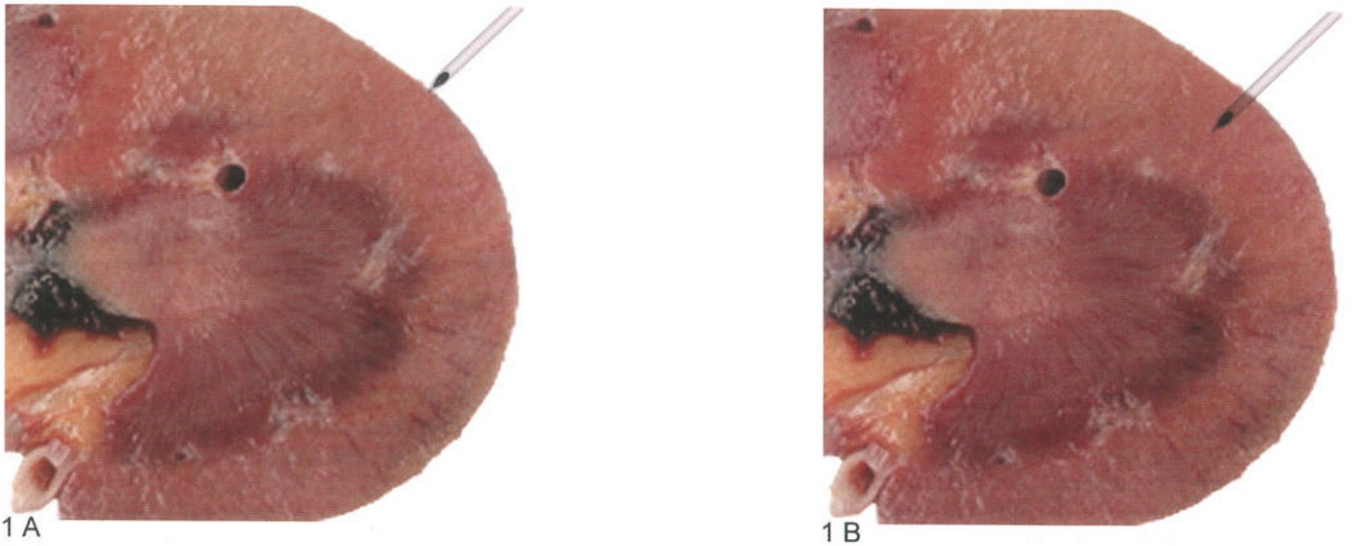

Figure 1. *A, Gross appearance of a kidney showing the lower pole with the biopsy needle correctly positioned. B, Pushing the needle through the capsule can result in the needle starting in midcortex as shown. Note the large vessel in the center of sample that could easily be reached by the needle if it were displaced only slightly. Photographs courtesy of Stephen M. Bonsib, MD.*

ed by patients (reviewed in Burstein et al[16]). The use of the biopsy gun, in combination with advanced imaging techniques, primarily ultrasound (reviewed in Geddes and Baxter[17]) has led to an increase in safety and yield.[16,18–23] The impression among renal pathologists is that there has also been an increase in the number of renal biopsies (oral communications), but there is no published data to verify this conclusion.

Native kidney biopsies are performed with the patient prone and transplant kidney biopsies with the patient supine. In general, a prebiopsy ultrasound scan is used to localize the optimal biopsy site.[22] The lower pole of the native left kidney and the most visible or easily accessed pole of the transplant kidney are the usual targets. Following local anesthesia, the skin is lanced and the biopsy needle inserted. Using real-time ultrasound guidance, the needle is advanced to the kidney, and the biopsy gun is activated.

The number of biopsy attempts varies widely. The questions of how much kidney is enough or how many attempts to obtain good tissue are sufficient have a very unsatisfying answer—"It depends!" Sometimes one pass is all that is required for adequate material. Usually 2 or 3 attempts produce the desired result, with some operators limiting themselves to no more than 5 tries.[19,20,22–24] It does seem that fewer passes are required today with the combination of the biopsy gun and the newer ultrasound equipment.[23]

Sample Size and Needle Gauge

A renal biopsy that yields inadequate tissue is obviously a very unpleasant result, and all care should be exercised to avoid this situation. Not only is there no tissue for diagnosis but also the complication rate is the same or possibly greater if the biopsy is too deep because of the presence of larger vessels in the medullary region.

Real-time imaging allows an accurate approach to the kidney. The tendency is to reach the outer cortex (Figure 1, A), and then, to go just a little deeper "to be sure." The normal adult renal cortex is only 10 mm. Thus, that last push ends with the needle well into the cortex (Figure 1, B). Because the needle extends slightly before beginning to cut, the resulting sample may have little or no cortex. An assistant (eg, pathologist, technician, nurse) trained in the use of a dissecting microscope can usually quickly determine whether a sample is adequate (see below).

The biopsy gun is supplied with various needle gauges, but practically, only the 14- through 18-gauge needles should be considered. The internal diameter of the 18-gauge needle is 300 to 400 μm, the 16-gauge needle is 600 to 700 μm, and the 14-gauge needle is 900 to 1000 μm.[25] The average diameter of a normal glomerulus from a newborn is about 100 μm. Glomeruli reach the normal adult size of 200 to 250 μm by about 8 years of age. So, the internal diameter of the 18-gauge needle is only slightly larger than the average glomerulus in an adult. More problematic is the volume of tissue available with the smaller needles. Not only is there less tissue per section (Figure 2, A and B), there are fewer sections. Finally, 18-gauge needles produce a significantly greater percentage of fragmented or lost glomeruli (Figure 2, C).[25] It is thus apparent that 14- or 16-gauge needles are ideal in adults, whereas 16- or 18-gauge needles are more appropriate in children younger than 8 years.

Biopsy Complications

Renal biopsy using the spring-loaded biopsy gun with ultrasound guidance appears to be a safe procedure.[20,23,26] Following a biopsy, hematuria is present in about 35% of patients, but gross hematuria is seen in less than 0.5% of patients. A perirenal hematoma is found in as many as 65% of patients, depending upon the diligence of the search, because most are silent. Transfusion is required in less than 1% of biopsies, renal loss in less than 0.1% of cases, and loss of life is extremely rare.[21,26–30]

Other Renal Biopsy Techniques

Most renal biopsies can be done percutaneously. Still, this approach may be contraindicated, such as, for example, in patients with bleeding diatheses.[31–35] A transjugular retrograde approach to the kidney can be attempted with a small biopsy instrument introduced by catheter.[34,35] With

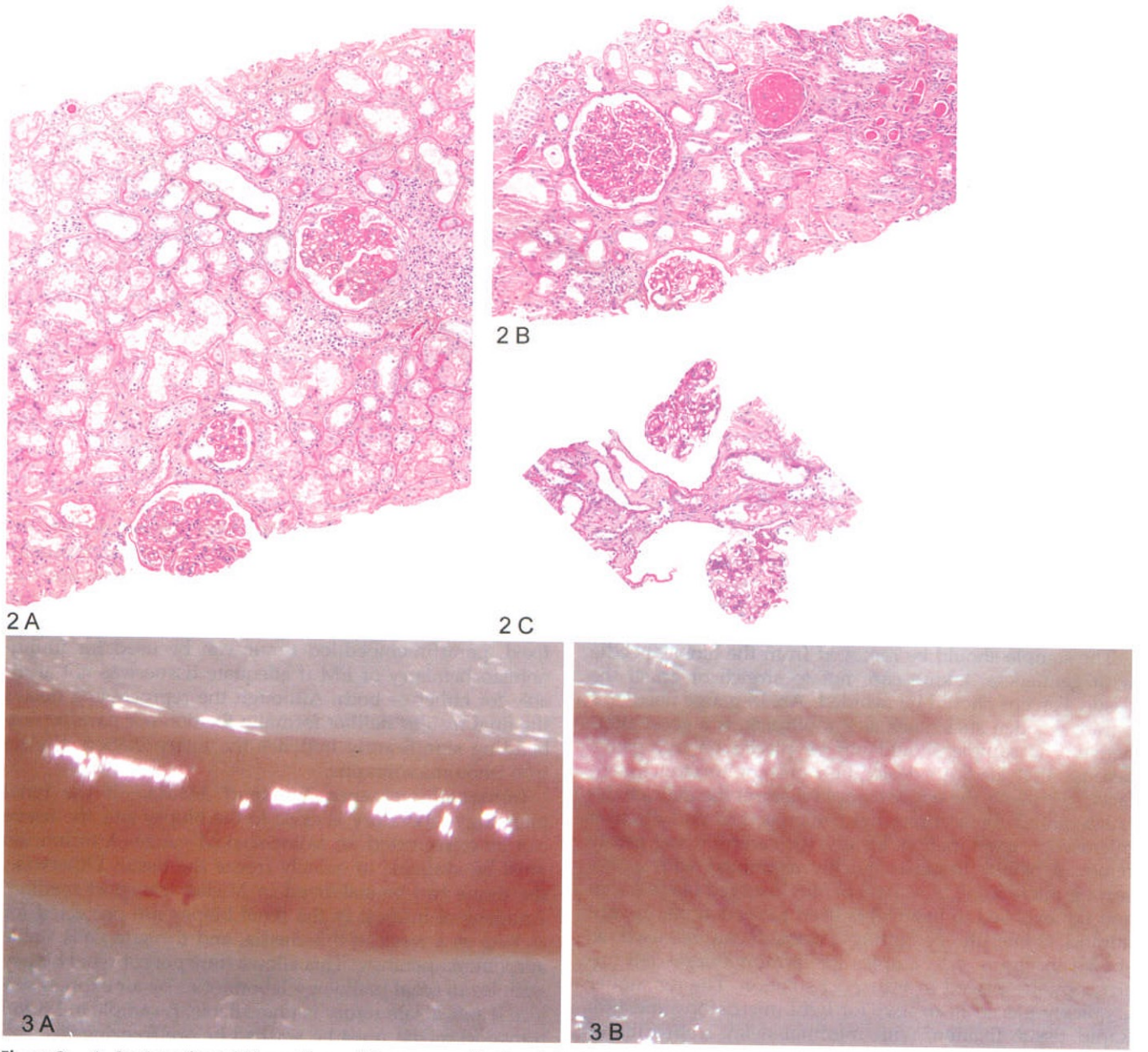

Figure 2. *A, Section of renal biopsy from a 16-gauge needle. B and C, Sections of a renal biopsy from an 18-gauge needle. There is much less overall volume in the 18-gauge samples. Fragmentation and potential glomerular loss are also shown (periodic acid–Schiff, original magnifications ×100).*

Figure 3. *A, Gross appearance of renal cortex showing reddish, circular structures, typical of glomeruli. B, Gross appearance of renal medulla, showing reddish streaks and lacking typical glomerular structures (original magnifications ×10 [A] and ×20 [B]). Photographs courtesy of Alexis Harris, MD, and Myra Zucker.*

this technique, any bleeding that may occur does so into the circulation and is, therefore, of no consequence, per se. Alternatively, a laparoscopic technique can be used.[36–38] Here, a posterior approach, with introduction of a laparoscope, is used. The biopsy is then performed under direct visualization, followed by hemostasis, before closing the wound.

RENAL BIOPSY SAMPLE PREPARATION

Intraoperative Sample Preparation

To provide an accurate diagnosis, the renal pathologist needs to evaluate a renal biopsy with immunohistochemical techniques, light microscopy, and transmission electron microscopy (EM). Separation of biopsy material for each of these techniques occurs optimally at the time of the biopsy, which is best accomplished using a dissecting microscope. A trained observer can recognize glomeruli, allowing sufficient material to be placed quickly in the appropriate media for all 3 modalities (Figure 3, A and B).

Lacking a dissecting microscope or training in its use, the operator may elect to section each biopsy sample into halves for immunohistochemical and light microscopy after removing small sections of each for EM (Figure 4). Some centers still mistakenly attempt longitudinal sectioning. This was appropriate when the needle aspiration tech-