MEMORANDUM

TO: Physicians submitting renal biopsies to the UNC Division of Nephropathology in Chapel Hill, NC

FROM: Volker Nickeleit, M.D. (Director), Sharan Singh, M.D. (Associate Director), J. Charles Jennette, M.D. (Executive Director)

The UNC Division of Nephropathology evaluates approximately two thousand specimens per year. Most are referred from nephrologists in community practice via their community hospital and local pathologist. Preliminary diagnoses are faxed to the referring nephrologists within one business day of the receipt of specimens. In addition, pertinent diagnoses are communicated immediately by telephone. A detailed final report is faxed and mailed to nephrologists and pathologists after completion of all studies together with histologic preparations and relevant images. The UNC Division of Nephropathology is CAP and CLIA approved. The UNC Division of Nephropathology has flexible billing options and provides both direct patient billing and institutional billing (see Section 6 on page 5 for detailed billing information). All reports can also be accessed via a secure online HIPAA-compliant server anytime, anywhere.
For obtaining the most adequate biopsy material, we strongly recommend using 15- or 16-gauge needles rather than 18-gauge needles. Small 18-gauge needles do not reduce the risk of complications but rather substantially limit the diagnostic yield of a kidney biopsy, i.e., they often generate small, inadequate specimens. In addition, 18-gauge needles can cause so-called “squeezing artifacts” due to sheer stress when obtaining the biopsy cores which can substantially impair subsequent morphologic studies.

In general, 3 biopsy cores each measuring approximately 12 mm to 15 mm should be obtained for histologic evaluation. Adequate sampling, including a good insight into the arterial tree (i.e., large interlobular arteries, branches of arcuate vessels), is of particular importance when evaluating renal transplant biopsies.

Tissue adequacy at time of biopsy can be assessed with a 10X to 15X hand lens, dissecting microscope, or smartphone camera. Adipose tissue presents as clusters of fat droplets and skeletal muscle as dark colored tissue that is easily disrupted in fascicles when prodded. “Simple” magnification often also allows for the identification of renal cortex (glomeruli present as punctuated blushes or raised hemispheres; see arrows in figure) and medulla (collecting ducts present grossly as “striations”).

ELECTRON MICROSCOPY
10% fresh (non-recycled), neutral buffered formalin is supplied for electron microscopy. Place biopsy tissue in vial and cap tightly. Invert the vial several times to assure that tissue is floating freely in the fixative.

LIGHT MICROSCOPY
10% fresh (non-recycled), neutral buffered formalin is supplied for light microscopy. Place the biopsy tissue in the vial. Replace the cap tightly and invert the vial several times to guarantee that the tissue floats freely in the liquid and is not stuck to the lid.

IMMUNOFLUORESCENCE MICROSCOPY
A transport medium (Michel’s solution, IF transport medium) is supplied ready for use. Place tissue in vial, cap tightly, and invert the vial several times to assure that the tissue is floating freely. Tissue can be kept in this medium for at least 5 days (at ambient temperature or refrigerated).

Michel’s transport medium is designed for preserving biopsies for immunofluorescence studies only. Biopsies that have been placed (even briefly) in Michel’s will not fix properly in formalin or glutaraldehyde and will show severe fixation artifacts.
Needle or wedge biopsies should be processed immediately after tissue collection. Never allow the tissue sample to dry out. If there is any delay, keep tissue moist on a cool saline-moistened gauze. Do not submerge the biopsy tissue in water or saline, as this will introduce artifacts. Do not use Michel's transport medium or any other fixative as a holding solution prior to partitioning the sample.

Appropriation of tissue for light (LM), immunofluorescence (IF), and electron microscopy (EM) is an important step to optimize the diagnostic yield of a renal biopsy. Note: In general, only a small segment of cortex (approximately 3 mm) is required for EM analysis. Tissue sampled for EM studies is processed separately, and it is not thoroughly analyzed by standard light microscopy.

Tissue for the three methods of examination can best be obtained as follows: (see diagram)

In general, three long (approximately 12 mm to 15 mm) biopsy cores are divided. One or two cores are fixed entirely in formalin for light microscopy. Small segments (approximately 2 mm) from both ends of the remaining core are fixed in formalin for electron microscopy (this approach makes EM sampling of glomeruli likely since one end of the biopsy core should contain cortex), and the rest of the core is preserved in Michel's medium for immunofluorescence microscopy. In case only 2 cores are obtained, the "best" one (i.e., most glomeruli, cortex rather than medulla, minimal fat) should be fixed in formalin for LM studies.

For renal transplant biopsies, 2 long tissue cores are needed for light microscopy and 1 additional core for IF studies. Transplant biopsy tissue in formalin for EM studies is only required if a glomerular disease process is suspected or if biopsies taken > 1 year post transplantation to search for allograft glomerulopathy or the presence of multi-layering of peritubular capillary basement membranes.

If very limited tissue is available, more than one diagnostic procedure can be performed on tissue preserved with one of the aforementioned methods. For example:

- Tissue submitted in Michel's transport medium for immunofluorescence microscopy can be processed for light microscopy (although this will result in some artifacts), or
- Tissue fixed in formalin can be processed for either electron microscopy or light microscopy. (Optimally, please send sufficient tissue in both vials.)

In all cases with a suspected glomerular disease process and suboptimal tissue sampling, it is usually best to submit the entire small biopsy core in Michel's transport medium. Limited, small transplant biopsies should be entirely fixed in formalin.

Follow directions for using the kits supplied by the UNC Division of Nephropathology (see Section 1). If you do not use our kits, please be sure to label the containers with the name of the preservative as well as the patient's name and their date of birth.

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**PARTITIONING OF RENAL BIOPSY NEEDLE CORES**

General rule: try to obtain three biopsy cores (each 12 mm to 15 mm long) with a 15- or 16-gauge needle.

Take the most tissue for LM, less for IF, and the least for EM.

(Note: EM is least helpful in transplant biopsies without clinical suspicion of a glomerular disease process).

First core (and second core if a total of three cores are taken) for formalin fixation (for LM):

Second core (or third core if a total of three cores are taken) to be divided for preservation in Michel's transport medium (for IF) and formalin fixation (for EM):
Referral forms to be submitted with each biopsy specimen are included in the UNC renal biopsy kit (see section 1), can be faxed from our office, or can be downloaded from the Nephropathology website (http://www.uncnephropathology.org). Please use the current appropriate form, depending on whether the biopsy is taken from a native kidney or a transplant kidney. Please be sure that the information is legible and complete in order to facilitate the diagnostic interpretation.

Specimens should be labeled with the patient’s name and a second identifier (e.g., date of birth), as required by CAP. Adequate clinical information is crucial for optimal and fast diagnostic workup.

Please also provide current contact information for rapid communication of biopsy results, including names, telephone numbers, and fax numbers of referring nephrologists and pathologists.

**REQUIRED INFORMATION:**

1. Patient’s full and correct name, date of birth, and sex (if possible, also include race for identification purposes)
2. The date of biopsy and type of kidney (native or transplant kidney)
3. List of underlying clinical problems and current laboratory data
4. Name, address, phone number, and fax number of the referring institution that will receive the reports, glass slides, and the invoice (unless patient is directly billed)
5. Name, address, phone number, and fax number of the referring nephrologist who requested/performed the biopsy and who will receive the reports and will be informed immediately by telephone of any pertinent diagnoses

We accept specimens during our regular working hours: Monday through Friday from 8:00 am to 5:00 pm. Please notify the UNC Division of Nephropathology at 919-966-2421 prior to sending a biopsy specimen in order to guarantee optimal specimen tracking. The UNC Division of Nephropathology is closed Saturdays, Sundays, and on major holidays. In case of medical emergencies or weekend/holiday deliveries, tissue processing and interpretations can be pre-arranged upon request (call 919-966-2421).

**UNC Division of Nephropathology**

**409 Brinkhous-Bullitt Building**

**CB# 7525**

**Chapel Hill, NC 27599-7525**

Priority Overnight service by FedEx (approximate delivery time at UNC of 10:30 am) has been the most effective means of transporting specimens. Please always retain a copy of the pre-paid FedEx airbill for proper specimen tracking.

If you are using a local courier, specifically instruct them to obtain a signature from a UNC Division of Nephropathology staff member upon delivery of the specimen.
REPORTING OF RESULTS

All preliminary and final reports are available via our secure online web access. Referring physicians can set up automatic email alerts for all newly available reports for their patient management.

A preliminary diagnosis is faxed to the referring nephrologist and the pathology department of the referring institution indicated on the referral form within one business day of specimen receipt. In addition, pertinent findings crucial for patient management are also immediately communicated by phone.

All three modes of examination (LM, IF, and EM) will be completed within 1 week of specimen receipt unless special processing (e.g., additional stains and/or levels) is required.

Final reports include detailed descriptions of light, immunofluorescence, and electron microscopy as well as a diagnostic interpretation often explicated by a detailed comment.

All final reports are faxed to the referring nephrologist and the pathology department of the referring institution indicated on the referral form. Final reports are then mailed along with electron microscopy and immunofluorescence microscopy images to the referring nephrologist and the referring institution’s pathology department (who additionally receive glass slides). Digital images of interesting cases will be supplied upon request.

BILLING: CHARGES AND CPT CODES

FLEXIBLE BILLING OPTIONS ARE AVAILABLE WITH EITHER DIRECT PATIENT BILLING OR INSTITUTIONAL BILLING.

Direct Patient Billing: Please call (919-966-2421) or fax (919-966-4542) the UNC Division of Nephropathology to request direct patient billing. When a biopsy is sent, a copy of the patient’s insurance information and contact information (address and telephone) should be included with the specimen referral form.

For Medicare patients, our consultation charges are billed to Medicare, but Medicare regulations require billing of technical charges to the referring institution; these charges are $1,050 ($380 for LM, $395 for IF, and $275 for EM).

Institutional Billing: The total consultation charge is $1,400 ($470 for LM, $590 for IF, and $340 for EM). For each portion, if the specimen submitted is inadequate (non-renal tissue or lacking glomeruli) and results in no diagnosis, then there is no charge.

We do not bill separately for additional procedures, such as step sections through the paraffin block, tissue reprocessing, or special diagnostic studies including C4d staining. We believe our charges are fair and competitive based on the complexity of the procedures and are low enough for recovery of costs through primary site patient billing. Further, the exceptional value offered by the skill and knowledge of our world-class team enables us to stand out from other services.

Checks should be made payable to “UNC Faculty Physicians” and indicate that the payment is made for renal biopsy interpretation. Please mail them to: UNC Division of Nephropathology, 409 Brinkhous-Bullitt Building, CB# 7525, Chapel Hill, NC 27599-7525.

CPT Codes: We suggest the following:

- Light microscopy: 88305 (once for H&E stains) plus 88313 (once per stain used: usually 3 for PAS and 3 for trichrome)
- Immunofluorescence microscopy: 88346 (per antisera used)
  - Native kidney: typically once each for IgG, IgA, IgM, C3, C1q, fibrin, kappa light chains, and lambda light chains (8 total)
  - Transplant kidney: as per native kidney plus typically once each for C4d and HLA-DR (10 total)
  - Electron microscopy: 88348 (once)

CAP Accreditation Number: 13992-01
CLIA ID Number: 34D0655124
Federal Tax ID: 56-1732213

Important Billing Note:
The name of the entity for reporting tax information is “The University of North Carolina d/b/a UNC Faculty Physicians” not “UNC Division of Nephropathology”.

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The GDCN was established in 1985 to enhance communication and research efforts between nephrologists and the UNC School of Medicine (Division of Nephrology and Division of Nephropathology). The GDCN is organized by the UNC Kidney Center and co-directed by Dr. Ronald J. Falk, Professor and Chief, Division of Nephrology and Hypertension, and Dr. J. Charles Jennette, Professor and Chair of Pathology and Laboratory Medicine. The GDCN participants are approximately 300 nephrologists, most in private practice, from North Carolina, Virginia, South Carolina, Georgia, and Florida. The foundation of the GDCN is the ongoing enrollment of patients at the onset of their renal disease and subsequent long term follow-up.

All nephrologists who submit renal biopsies to the UNC Division of Nephropathology are invited to participate in the GDCN and to enroll eligible patients into ongoing collaborative clinical trials. Annual GDCN CME events allow nephrologists who submit specimens to the UNC Division of Nephropathology to meet UNC faculty and to discuss patient care issues and upcoming clinical trials. This group has many great resources from which to derive useful information. Drs. R. Falk and P. Nachman from the UNC Kidney Center are available for clinical consultation and discussion of specific patient management issues if uncommon and challenging interpretations are rendered by the UNC Division of Nephropathology.

Please feel free to contact the UNC Division of Nephropathology. We look forward to working with you.

HOURS: Monday through Friday
(except major holidays)
from 8:00 am to 5:00 pm ET

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For further detailed information, including downloadable referral forms, please visit our website at http://www.uncnephropathology.org