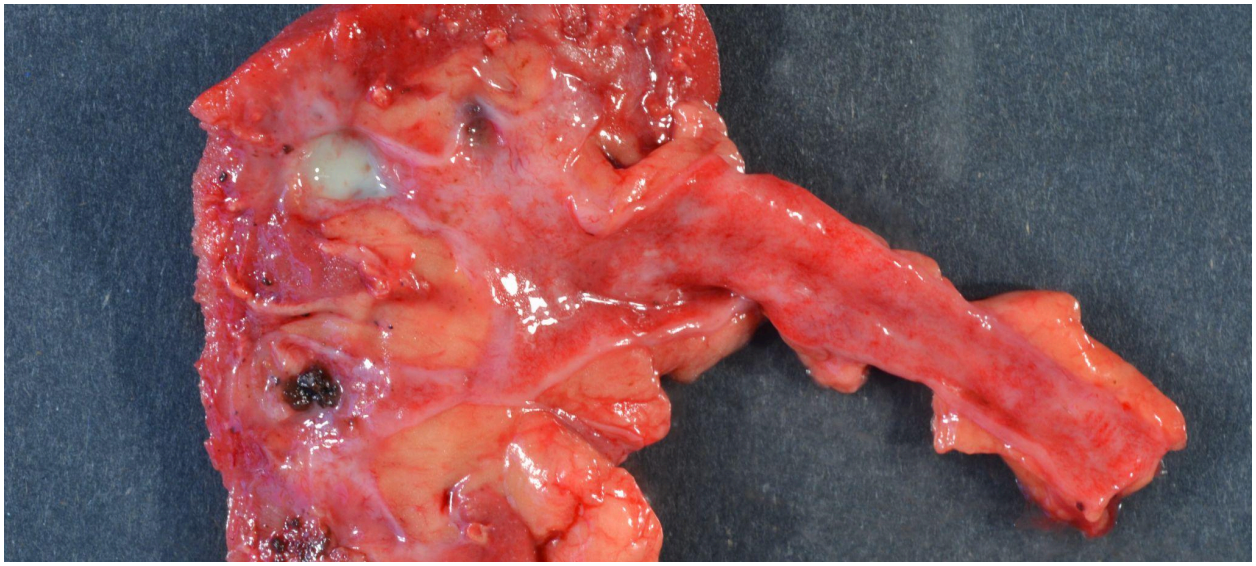

Pyelonephritis

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Background:

Pyelonephritis is inflammation of the kidney, classically from infection. Pyelonephritis can be acute, chronic, or acute-on-chronic. Approximately 95% of the time, acute pyelonephritis is caused by bacterial infection via retrograde urine flow from the ureters. Rarely, acute pyelonephritis may be caused by hematogenous bacterial spread from a source other than the kidney. Chronic pyelonephritis can develop due to recurrences or complications of acute pyelonephritis, especially in patients with structural abnormalities of the urinary tract. With timely antibiotics, prognosis is usually excellent.

Quick Tips at Time of Autopsy

Clinical History

Check the medical record for pre-mortem diagnostic information

- Urinalysis may demonstrate pyuria. Nitrite production suggests the causative organism is *E.coli*.
- Pre-mortem urine/blood cultures could also identify the causative agent.
- Abdominal/pelvic CT imaging with contrast may demonstrate perinephric inflammation with cortical filling defects in cases of acute pyelonephritis.
    - Imaging is not required for diagnosis, but it is indicated in certain patients (e.g. renal transplant patients, septic shock).
    - Imaging is also useful to detect obstruction and hydronephrosis.

- Identify underlying risk factors including urinary tract obstruction or reflux, diabetes mellitus, indwelling urinary catheters, extremes of age, and women who are sexually active or pregnant.
    - Those at risk for mortality from severe infection include male patients, older patients with impaired renal function, and those with associated disseminated intravascular coagulation (DIC).

External Exam

- Any external drains (nephrostomy tubes) should be documented and remain in place for subsequent internal confirmation of their site of termination.

Gross Examination

- When hydronephrosis is suspected, the genitourinary block should be removed intact (i.e. the kidneys, ureters, and bladder should be removed intact).
- After removing the block, open the ureters lengthwise to look for stones and/or tumors.
- You can use the pattern of dilation in the genitourinary block to characterize the pathology and localize lesions
    - Dilation of the bladder, ureters, and bilateral kidneys suggests blockage in the urethra.
    - Bilateral kidney and ureter hydronephrosis without bladder distention suggests bladder obstruction.
    - Unilateral kidney hydronephrosis (with or without ureteral dilation) suggests ureter or ureteropelvic junction obstruction.

Gross findings of acute pyelonephritis

- Kidneys are enlarged and edematous.
- Purulence can be seen variably involving the medulla, scattered throughout the parenchyma as abscesses, and/or collecting in the calyces.
    - Straight yellow streaks in the medulla correspond to collecting ducts filled with pus; this is typically seen in ascending infections.
    - Small, subcapsular abscesses (typically only a few mm wide) are more commonly seen with hematogenous spread of infection.
- Severe infection can cause papillary necrosis, with gray-white to yellow discoloration.
- Perinephric abscesses can also be seen.
- Emphysematous pyelonephritis may cause empty (gas-filled), rounded spaces in the cortex and perinephric fat.

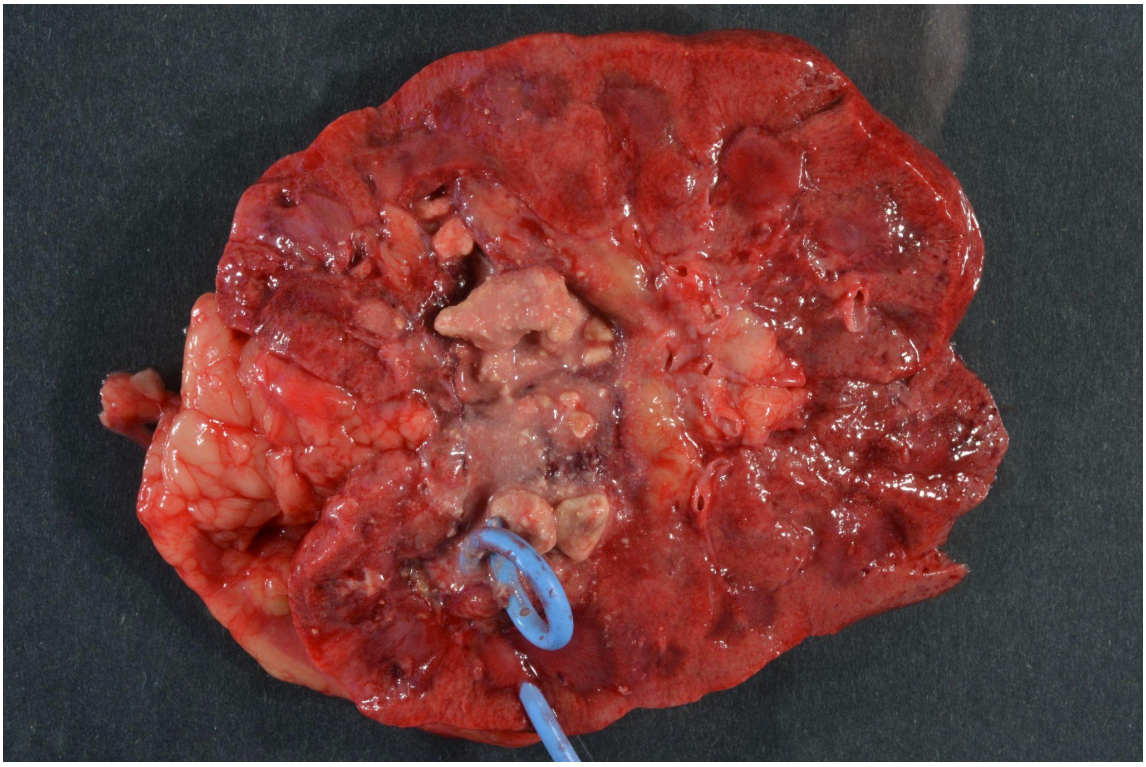

Image: A kidney with acute pyelonephritis associated with stones in the renal pelvis. The stones can be seen here coated with and adjacent to purulent material. Inferiorly in the photo a blue nephrostomy tube is present and in the correct place (with the tube ending the in the pelvis). (Image credit: Meagan Chambers/University of Washington).

Image: Acute pyelonephritis superimposed on chronic kidney disease. The kidney is atrophic overall with purulence best appreciated in the upper left calix. (Image credit: Meagan Chambers/University of Washington).

Gross findings of chronic pyelonephritis

- Irregular scars in a “jigsaw” pattern can be present in the cortex.
    - Cortical scars in an ascending infection frequently overlie the pelvic calyces.
- Dilated and blunted renal pelvis and/or calyces.
- Cortical thickness can be reduced to ~2-3 mm.

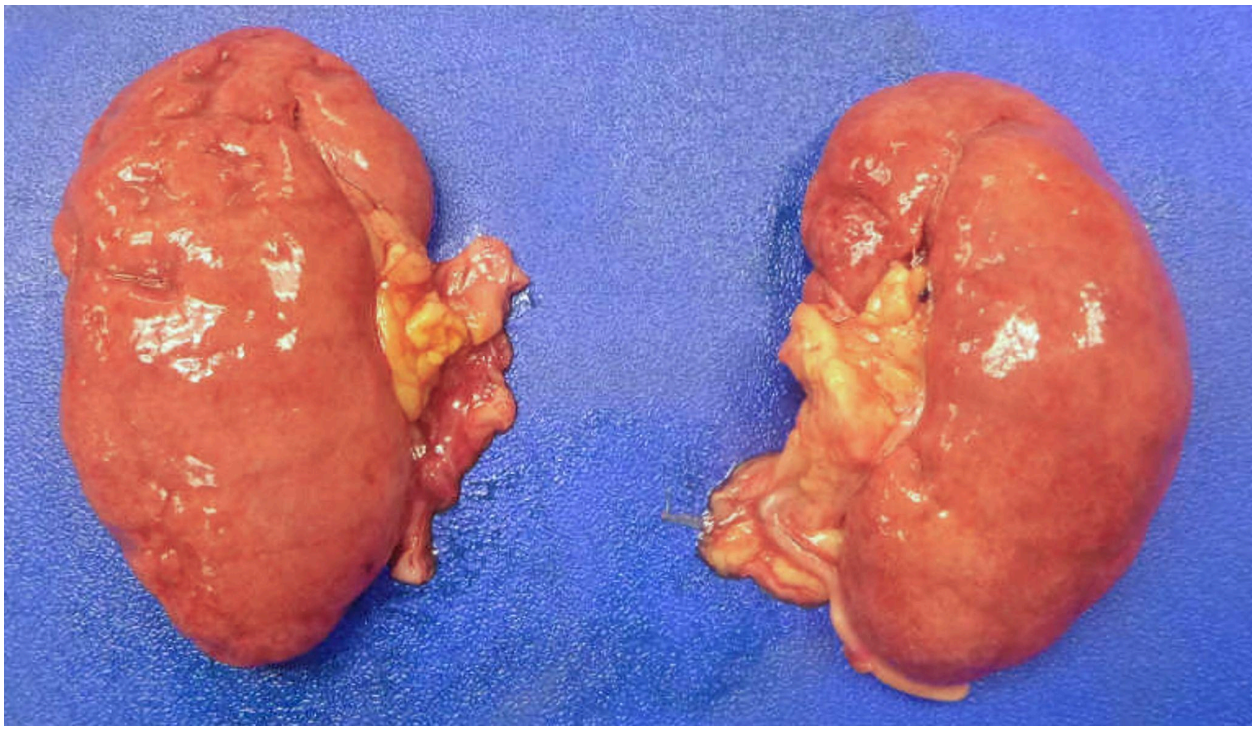

Image: Broad based scarring on upper and lower pole of right kidney (left side of image) representing chronic pyelonephritis (Image credit: Billie Fyfe/Robert Wood Johnson Medical Center).

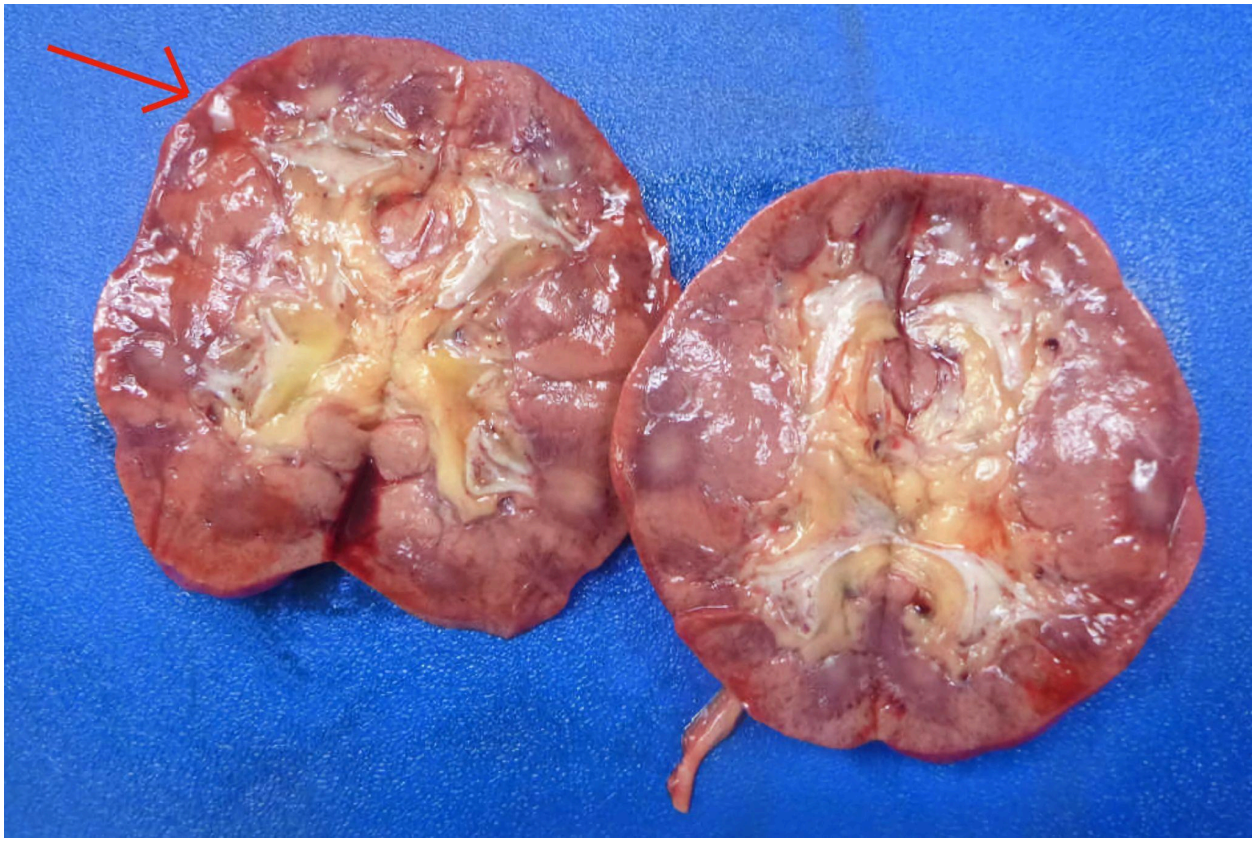

Image: Right and left kidneys with cortical abscess and pus in the collecting ducts, representing acute on chronic pyelonephritis (Image credit: Billie Fyfe/Robert Wood Johnson Medical Cente).

Ancillary Testing

Cultures may be indicated for confirmation of the presumed infectious diagnosis. If the causative pathogen is already known from pre-mortem cultures, post-mortem cultures may not be indicated. However, they can be useful in evaluating the response to antibiotics. For additional information on the use of postmortem cultures at autopsy, see the Postmortem Cultures article.

- Common pathogens include gram-negative bacteria: *E. coli* (most common), *Proteus*, *Klebsiella,* and other *Enterobacter* species.
- *Pseudomonas* is also a common culprit, often hospital-acquired and in association with instrumentation of the urinary tract (e.g. urinary catheters).
- The rare cases that are seeded by hematogenous infections are most commonly caused by *Staphylococcus aureus* or fungi (*Candida* and *Aspergillus*).

Quick Tips at Time of Histology Evaluation

The pattern of inflammation may provide clues to the route of infection

- Bloodborne infections often show abscess formation throughout the tissue, sparing the renal pelvis.
- Ascending urinary tract infections show prominent inflammation of the renal pelvis, medulla, and collecting system while sparing the glomeruli and blood vessels.

Histologic findings of acute pyelonephritis

- Neutrophilic inflammation in a patchy distribution involving the tubules (including neutrophilic casts) and the interstitium
- Chronic, mixed inflammation after a few days of infection
- Variable amount of abscess formation and necrosis
- Acute tubular injury
    - Distinguishing acute tubular injury and autolysis can be challenging but kidney injury molecule-1 (KIM-1) staining is positive in acute tubular injury and negative in autolysis.
    - Additionally, in shock/acute tubular injury the epithelial cells are adherent to basement membrane with associated tubular dilation and cytoplasmic blebs in contrast to autolysis where the tubular epithelium is detached from the basement membrane. (In advanced tubular injury the epithelial cells do slough off, although they tend to do so in a whorling pattern which is distinct from autolysis). Additionally, autolysis should be a uniform process, while acute tubular injury is typically patchy.

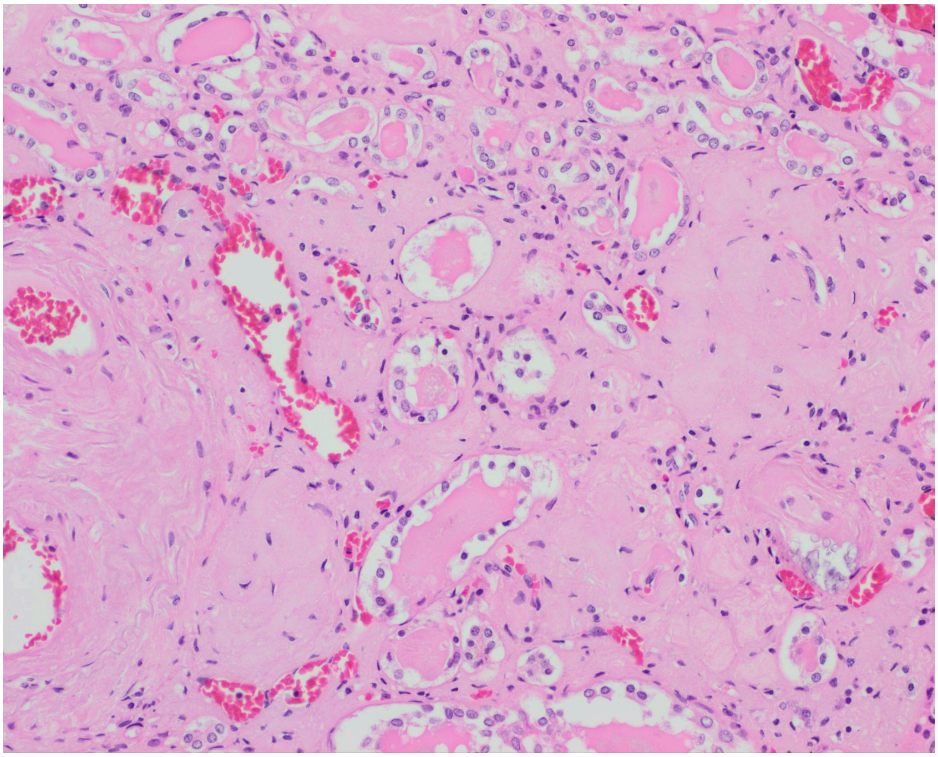

Image: Dilated tubular lumens with epithelium adherent to the basement membrane and cytoplasmic blebs is consistent with acute tubular injury (in this case from acute

pyelonephritis superimposed on chronic kidney failure). (Image credit: Meagan Chambers/University of Washington).

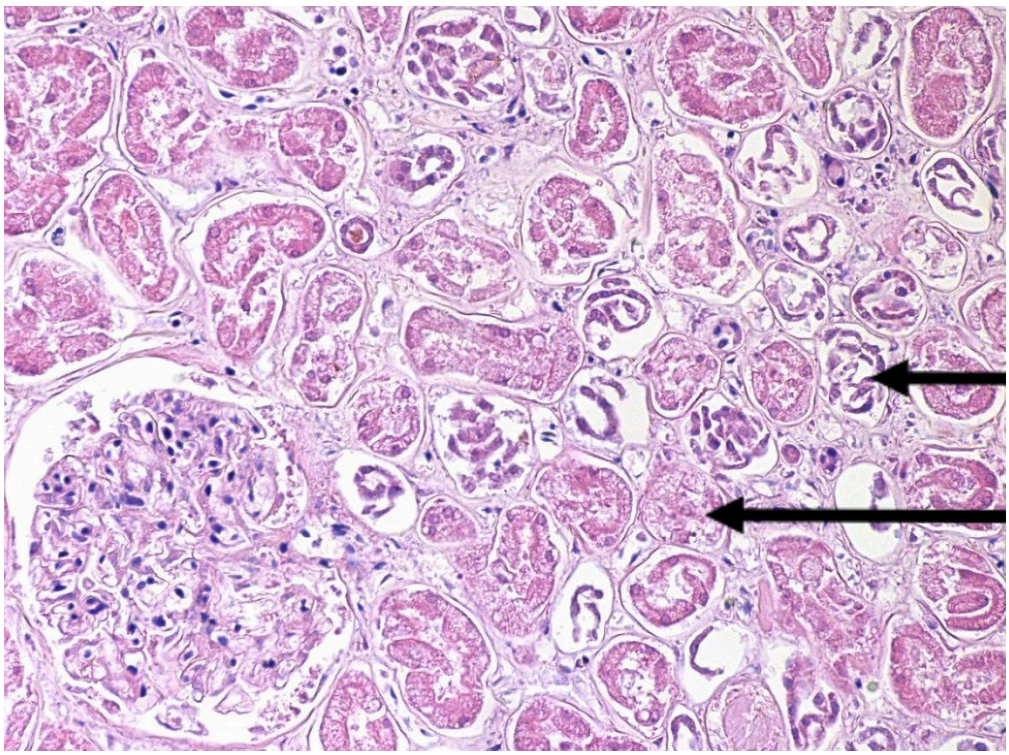

Image: some tubules contain necrotic (top arrow) vs. autolytic (bottom arrow) tubular epithelium. Here, the necrotic epithelium has sloughed off the basement membrane but in characteristic whorls which distinguish it from the admixed tubules with autolysis.(Image Credit: Alex Williamson).

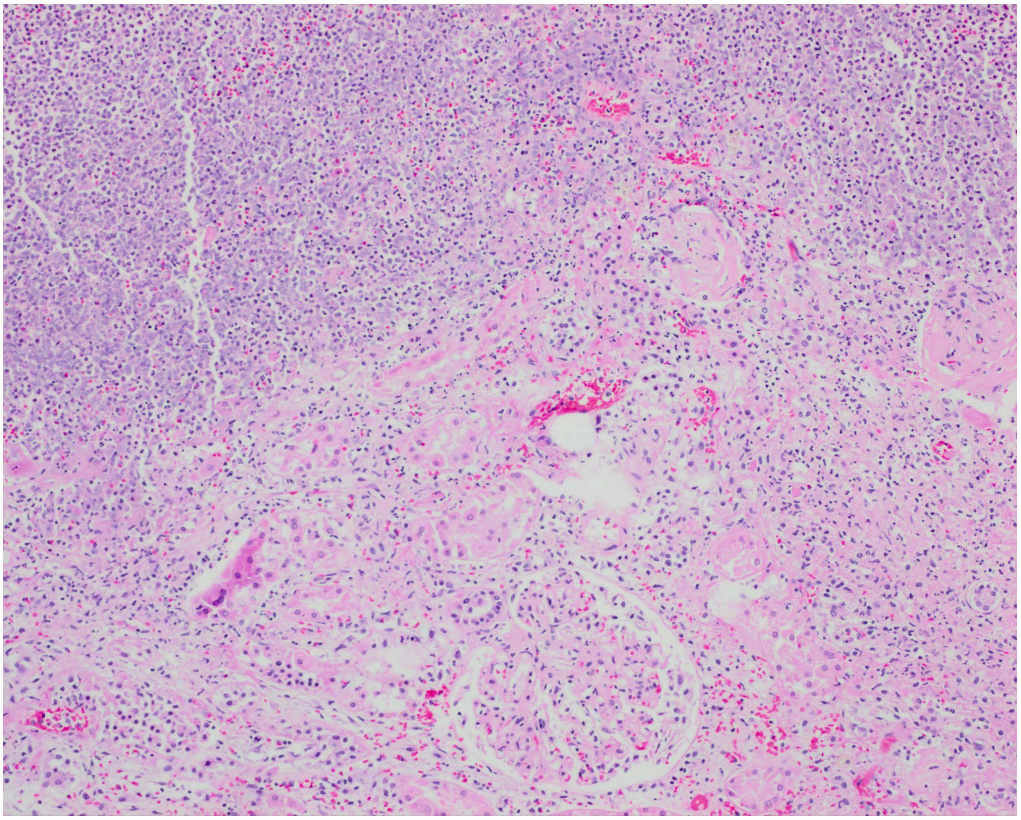

Image: Neutrophilic abscess with adjacent kidney parenchyma. (Image credit: Meagan Chambers/University of Washington).

Histologic findings of chronic pyelonephritis

- Mixed inflammatory infiltrate (lymphocytes, monocytes, and plasma cells)
- Clear demarcation between involved tissue and uninvolved tissue
- There may be “thyroidization” of the tubules: atrophic tubules contain hyaline casts made up of Tamm-Horsfall glycoprotein (resembles colloid in thyroid follicles).
- Variable periglomerular fibrosis with viable glomeruli

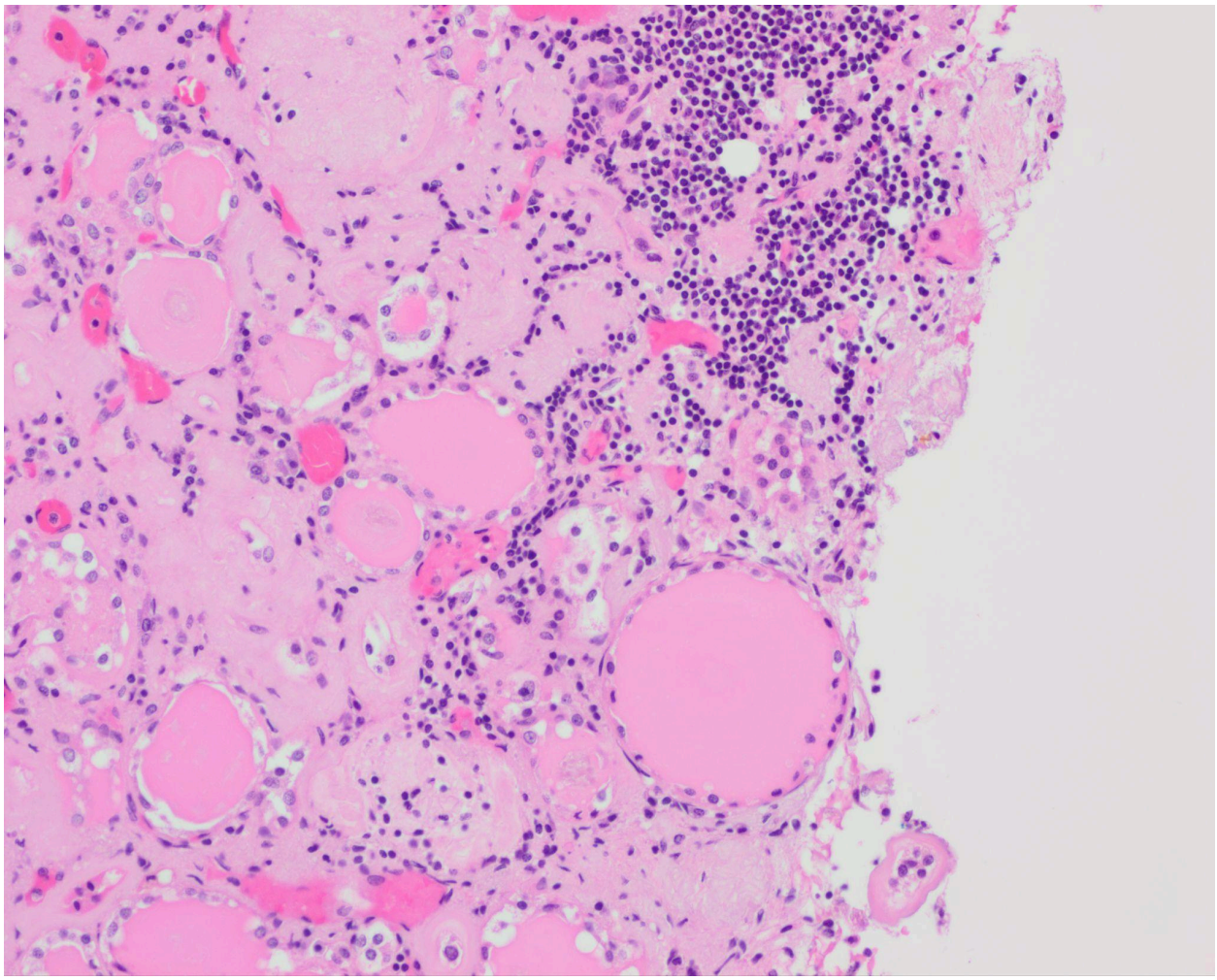

Image: Chronic pyelonephritis with thyroidization of some tubules, patchy chronic inflammation, and increased interstitial fibrosis. (Image credit: Meagan Chambers/University of Washington).

Histologic findings of superimposed (acute-on-chronic pyelonephritis)

- Grossly, there should be a mix of findings of acute infection (e.g. abscess formation) and chronic infection (e.g. irregular cortical scarring).
- Microscopically, there are neutrophils and atrophic tubules with hyaline casts.

Other histologic findings

- Xanthogranulomatous pyelonephritis is a rare form of chronic pyelonephritis, often occurring in the setting of stone obstruction from staghorn calculi caused by *Proteus mirabilis*. This form causes massive destruction of the renal parenchyma, with profuse lipid-laden macrophages.

- Evidence of underlying conditions may also be present in a kidney with pyelonephritis (acute or chronic) such as hypertension and/or diabetes.

Quick Tips at Time of Reporting

- A diagnosis of chronic pyelonephritis should be made with appropriate clinical correlation or gross findings, rather than histology alone.
- Recording whether antibiotics were used, which ones, and for how long prior to death can correlate with the disease burden in the kidneys and subsequently communicating therapy effectiveness to clinicians via the report.
- Example cause of death statement: “Complications of acute on chronic pyelonephritis, status post nephrostomy tube placement, due to urethral obstruction, due to prostatic carcinoma.”

Recommended References

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