The kidneys are a pair of organs located in the back of the abdomen. Each kidney is about 4 or 5 inches long – about the size of a fist. The kidneys’ function is to filter the blood. All the blood in our bodies passes through the kidneys several times a day.
Glossary

• Acute Interstitial Nephritis – An abrupt inflammation of the connective tissue inside the kidney, often causing acute kidney injury/acute renal failure. Allergic reactions and drug side effects are the usual causes.

• Acute Kidney Injury (AKI)/Acute Renal Failure – A sudden worsening in kidney function. Dehydration, a blockage in the urinary tract, or kidney damage can cause AKI, which may be reversible.

• Chronic Kidney Disease (CKD) Stages 1-4/Chronic Renal Failure – A permanent partial loss of kidney function. Diabetes and high blood pressure are the most common causes.

• CKD Stage 5/End Stage Renal Disease (ESRD) – Complete loss of kidney function, usually due to progressive CKD. People with CKD Stage 5/ESRD require regular dialysis for survival.

• Diabetic Nephropathy – High blood sugar from diabetes progressively damages the kidneys, eventually causing CKD. Protein in the urine (nephrotic syndrome) may also result.

• Glomerular Filtration Rate (GFR) – The rate at which the kidneys filter wastes and extra fluid from the blood, measured in milliliters per minute.
<table>
<thead>
<tr>
<th>Stage</th>
<th>Qualitative Description</th>
<th>Renal Function (mL/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage-normal GFR</td>
<td>≥90</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage-mild ↓ GFR</td>
<td>60-89</td>
</tr>
<tr>
<td>3</td>
<td>Moderate ↓ GFR</td>
<td>30-59</td>
</tr>
<tr>
<td>4</td>
<td>Severe ↓ GFR</td>
<td>15-29</td>
</tr>
<tr>
<td>5</td>
<td>End-stage renal disease</td>
<td>&lt;15 (or dialysis)</td>
</tr>
</tbody>
</table>
Glossary

• Glomerulonephritis – Overactive immune system attacks the kidney, causing inflammation and some damage. Blood and protein in the urine are common problems that occur with glomerulonephritis. It can also result in kidney failure.

• Hypertensive Nephrology – Kidney damage caused by high blood pressure. CKD may eventually result.

• Kidney Cancer – Renal cell carcinoma is the most common cancer affecting the kidney. Smoking is the most common cause of kidney cancer.

• Kidney Stones (nephrolithiasis) – Minerals in urine form crystals (stones), which may grow large enough to block urine flow. It’s considered one of the most painful conditions. Most kidney stones pass on their own but some are too large and need to be treated.

• Minimal Change Disease – A form of nephrotic syndrome in which kidney cells look almost normal under the microscope. The disease can cause significant leg swelling (edema). Steroids are used to treat minimal change disease.

• Nephrogenic Diabetes Insipidus – The kidneys lose the ability to concentrate the urine, usually due to a drug reaction. Although it’s rarely dangerous, diabetes insipidus causes constant thirst and frequent urination.
<table>
<thead>
<tr>
<th>Glossary</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nephrotic Syndrome</strong> – Damage to the kidneys causes them to spill large amounts of protein in the urine. Leg swelling (edema) may be a symptom.</td>
</tr>
<tr>
<td><strong>Papillary Necrosis</strong> – Severe damage to the kidneys can cause chunks of kidney tissue to break off internally and clog the kidneys. If untreated, the resulting damage can lead to total kidney failure.</td>
</tr>
<tr>
<td><strong>Polycystic Kidney Disease</strong> – A generic condition resulting in large cysts in both kidneys that impair their function.</td>
</tr>
<tr>
<td><strong>Pyelonephritis (infection of kidney pelvis)</strong> – Bacteria may infect the kidney, usually causing back pain and fever. A spread of bacteria from an untreated bladder infection is the most common cause of pyelonephritis.</td>
</tr>
<tr>
<td><strong>Renal Cyst</strong> – A benign hollowed-out space in the kidney.</td>
</tr>
</tbody>
</table>
Kidney Tests

- **Urinalysis** – A routine test of the urine by a machine and often by a person looking through a microscope. Urinalysis can help detect infections, inflammation, microscopic bleeding, and kidney damage.

- **Kidney Ultrasound** – A probe placed on the skin reflects sound waves off the kidneys, creating images on a screen. Ultrasound can reveal blockages in urine flow, stones, cysts, or suspicious masses in the kidneys.

- **Computed Tomography (CT scan)** – A CT scanner takes a series of X-rays and a computer creates detailed images of the kidneys.

- **Urine and Blood Cultures** – If an infection is suspected, cultures of the blood and urine may identify the bacteria responsible. This can help target antibiotic therapy.

- **Ureteroscopy** – An endoscope (flexible tube with a camera on its end) is passed through the urethra into the bladder and ureters. Ureteroscopy generally cannot reach the kidneys themselves, but can help treat conditions that also affect the ureters.

- **Kidney Biopsy** – Using a needle inserted into the back, a small piece of kidney tissue is removed.
Kidney Treatments

- **Antibiotics** – Medicines that treat kidney infections caused by bacteria. Often, cultures of the blood or urine can help guide the choice of antibiotic therapy.

- **Nephrostomy** – A tube (catheter) is placed through the skin into the kidney. Urine then drains directly from the kidney, bypassing any blockages in urine flow.

- **Nephrectomy** – Surgery to remove a kidney. Nephrectomy is performed for kidney cancer or severe kidney damage.

- **Lithotripsy** – Some kidney stones may be shattered into small pieces that can pass in the urine. Most often, lithotripsy is done by a machine that projects ultrasound shock waves through the body.
Kidney Treatments

- **Dialysis** – Artificial filtering of the blood to replace the lost function of damaged kidneys. Hemodialysis is the most common method of dialysis in the U.S.

- **Hemodialysis** – A person with complete kidney failure is connected to a dialysis machine, which filters the blood and returns it to the body. Hemodialysis is typically done three days per week in people with ESRD.

- **Peritoneal Dialysis** – Placing large amounts of a special fluid in the abdomen through a catheter, allows the body to filter the blood using the natural membrane lining the abdomen. After a while the fluid with the waste is drained and discarded.

- **Kidney Transplant** – Transplanting a kidney into a person with ESRD can restore kidney function. A kidney may be transplanted from a living donor, or a recently deceased organ donor.
Normal Kidney Biopsy
AKI

Dusky red medulla

Pale cortex
Science that Supports Causation

• In 1992, Ruffenach and others were the first to publish a report of omeprazole (Prilosec)-induced AIN. See Stephen J. Ruffenach et al., *Acute Interstitial Nephritis Due to Omeprazole*, 93 Am. J. Med. 472, 472 (1992) (“We describe here what we believe is the first case of acute interstitial nephritis due to omeprazole.”); see also id. at 473 (“Physicians who prescribe omeprazole should be aware of the association between acute interstitial nephritis and omeprazole.”)

• “Since that time, numerous biopsy-confirmed case reports and retrospective descriptive reports have been published suggesting a connection between PPI use and AIN.” Donald G. Klepser et al, *Proton Pump Inhibitors and Acute Kidney Injury: a nested case-control study*, 14 BMC Nephrology 1, 2 (2013) (citing reports).
Science that Supports Causation

• Between 1992 and 2004 there were over 20 reported cases of biopsy-proven AIN secondary to omeprazole (Prilosec) use. See Nimeshan Geevasinga et al., *Acute interstitial nephritis secondary to esomeprazole*, 182 Med. J. Austl. 235, 235 (2005); see also id. at 236 (“Early recognition of [PPI-induced AIN] may prevent the development of irreversible renal injury.”).

• See Nimeshan Geevasinga et al., *Proton Pump Inhibitors and Acute Interstitial Nephritis*, 4 Clinical Gastroenterology Hepatology 597, 599 (2006) (“This is the first report to highlight that all 5 of the commercially available PPIs have been implicated in causing AIN … In our series, 18 of 28 cases of biopsy-proven AIN were associated with PPI use); see also id. at 602 (“As the use of PPIs increases, medical practitioners and pharmacists need to appreciate the potential for PPIs to cause AIN.”)
Science that Supports Causation

• See Ian J. Simpson, et al.; 2006, Proton Pump Inhibitors and Acute Interstitial Nephritis: Report and Analysis of 15 cases, 11 Nephrology 381, 381 (2006) (“[T]he present review over 2002-2005, in the greater Auckland area [of New Zealand], indicates that PPI are now the most commonly identified cause of AIN and that this is a consequence of extensive use in the community … the failure to detect deterioration early may reduce the chance of complete renal recovery from PPI-induced AIN.”)

• See Linda Härmak et al., Proton Pump Inhibitor Induced Acute Interstitial Nephritis, 64 British J. Clinical Pharmacology 819, 823 (2007) (“AIN is a complication associated with all PPIs. It is important for health professionals to be aware of this adverse drug reaction, because accurate and timely diagnosis and withdrawal of the offending drug can prevent potentially life-threatening renal failure.”) (emphasis added).
Science that Supports Causation

• A 2013-published study demonstrated an association between PPI use and AKI. See Donald G. Klepser et al, Proton Pump Inhibitors and Acute Kidney Injury: a nested case-control study, 14 BMC Nephrology 1, 5-6 (2013) (concluding from a study of 854 renal disease cases, most of which were renal disease diagnoses of acute renal insufficiency and acute renal failure, that “patients with an incident of renal disease diagnosis were nearly twice as likely to have been exposed to PPIs compared to those without renal disease.”).

• A 2015 study reported increased incidence of long-term PPI use associated with AIN and AKI; it found a higher ratio of AIN and AKI among patients given PPIs than among controls. Tony Antoniou et al., Proton Pump Inhibitors and the Risk of Acute Kidney Injury in Older Patients: A Population-Based Cohort Study, 3 CMAJ Open E166, E170 (2015).
Science that Supports Causation

• A 2016 study linked PPIs to AKI and CKD. See Benjamin Lazarus et al., *Proton Pump Inhibitor Use and the Risk of Chronic Kidney Disease*, 176 JAMA Internal Medicine 238, 245 (2016) (“[W]e found that PPI use is an independent risk factor for CKD and AKI.”)

• Another 2016 study, published in the Journal of the American Society of Nephrology, found that people who did not have kidney problems and recently started taking PPIs were two times more likely to develop kidney failure and thirty percent more likely over five years to develop CKD. See Yan Xie et al., *Proton Pump Inhibitors and Risk of Incident CKD and Progression to ERSD*, 27 J. Am. Soc’y Nephrology 1, 4-6 (2016).
Conclusion

Examining Science and Causation will be key to Proton Pump Inhibitor Litigation