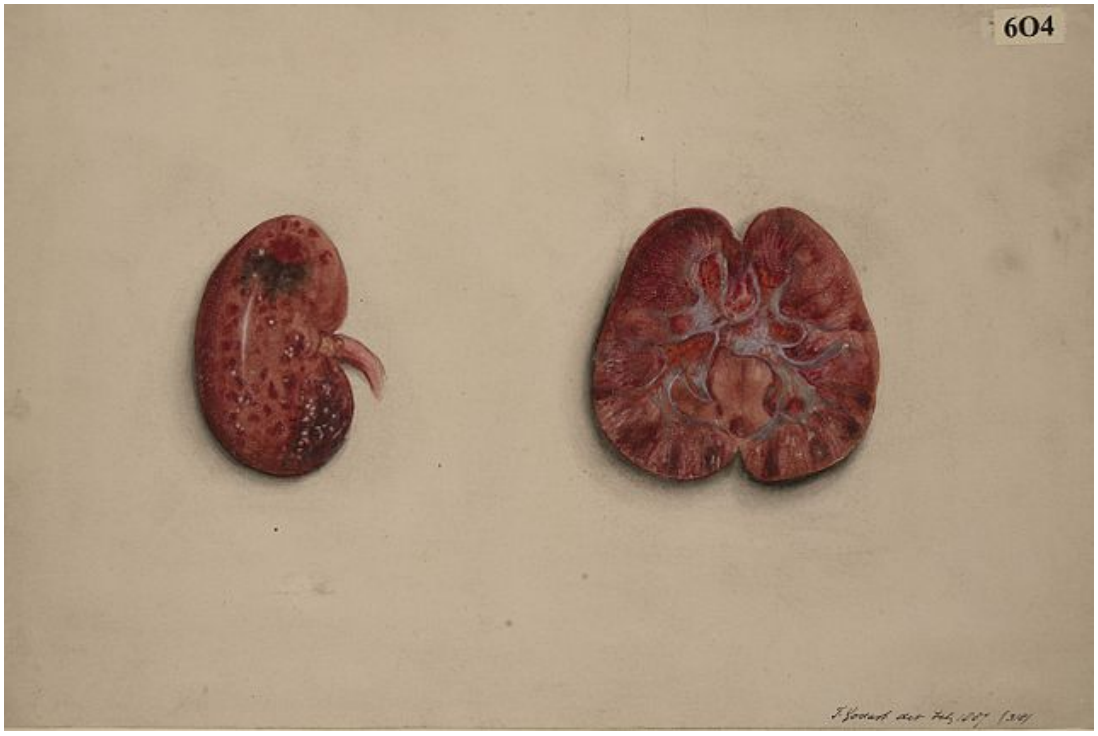
Interstitial Nephritis (Tubolainterstitial Nephritis) — Pathophysiology and Laboratory Investigations

See online here

Tubulointerstitial nephritis is an inflammatory condition affecting the tubules and interstitium while sparing the glomerulus. Acute and chronic pyelonephritis, along with drug-induced interstitial nephritis, is the predominant cause of tubulointerstitial nephritis. Urine examination shows characteristic eosinophiluria and WBC casts. The treatment involves the discontinuation of the offending drug, along with steroids, while treatment is mainly supportive in the chronic type. Progression to end-stage renal disease is seen in the majority of tubulointerstitial disorders.



Definition of Interstitial Nephritis

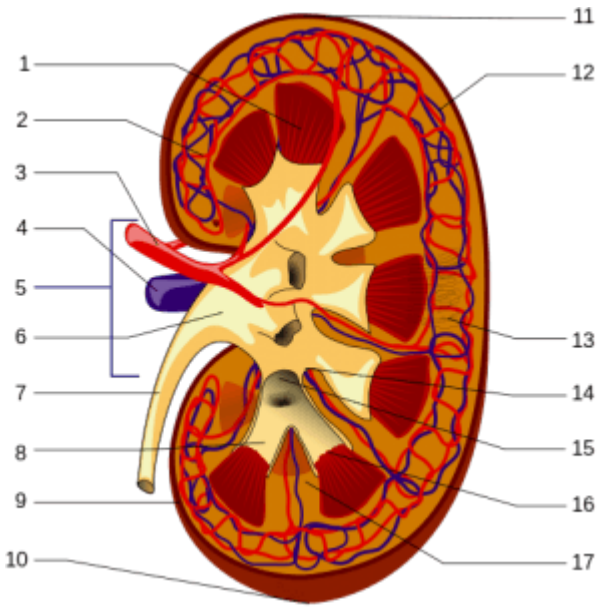


Image: “Structures of the kidney: 1.Renal pyramid 2.Interlobular artery 3.Renal artery 4.Renal vein 5.Renal hilum 6.Renal pelvis 7.Ureter 8.Minor calyx 9.Renal capsule 10.Inferior renal capsule 11.Superior renal capsule 12.Interlobar vein 13.Nephron 14.Minor calyx 15.Major calyx 16.Renal papilla and 17.Renal column” by Piotr Michał Jaworski. License: CC BY-SA 3.0

Interstitial Nephritis as Inflammation

Inflammation of the **tubules and interstitium,** while sparing the **glomerulus,** is called as tubulointerstitial nephritis.

Epidemiology of Interstitial Nephritis

Spread of Interstitial Nephritis

Tubulointerstitial nephritis contributes to 10 to 15% of all the **kidney** diseases in the United States. Women are at greater risk for drug-induced **interstitial nephritis** when compared to men.

Etiology of Interstitial Nephritis

Acute Interstitial Nephritis

Drugs

- Antibiotics: Sulfonamides, vancomycin, rifampin, beta-lactam antibiotics
- NSAIDs
- Diuretics (thiazide and loop diuretics)
- Anticonvulsants (phenytoin, valproic acid, and carbamazepine)

Infections

- Bacterial (streptococcal, staphylococcal)
- Viral (EBV, CMV)

Autoimmune Disorders

- Systemic lupus erythematosus
- Sjogren's Syndrome

Acute Obstructive Disorders

- Light chain nephropathy
- Acute urate nephropathy

Chronic Interstitial Nephritis

- Reflux nephropathy
- Sickle cell disease
- Drugs and toxins
    - Phenacetin and NSAIDs
    - Cyclosporine and tacrolimus
    - Exposure to heavy metals (lead, lithium)

Pathophysiology of Interstitial Nephritis

Type I and type IV hypersensitivity reactions are associated in the pathogenesis of drug-induced interstitial nephritis. These drugs act as **haptens** and, during secretion, they covalently bind to the extracellular components of the tubule. When these haptens are immunogenic, they result in tubulointerstitial injury.

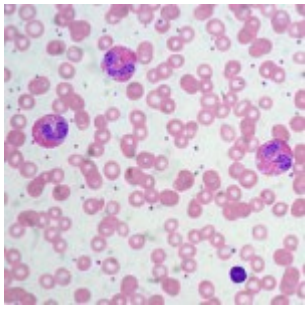


Image: "Eosinophils in peripheral blood in a patient with eosinophilia of unknown etiology." by Ed Uthman, MD, Houston, Texas, USA. License: CC BY 3.0

Presence of **eosinophilia,** rash and increased Ig E levels indicate the presence of type I hypersensitivity reaction, while the presence of **granulomatous infiltrate** in some tissues indicates the presence of type IV hypersensitivity reaction. Dosage of the drugs administered is independent on the incidence of the disease. Discontinuation of the drug results in the reversal of some changes.

Clinical Presentation and Symptoms of Interstitial Nephritis

Acute tubulointerstitial nephritis presents as an acute renal failure following the exposure to the offending drug. **Nephrotic range proteinuria** is seen in

patients with NSAIDs induced tubulointerstitial nephritis.

Presence of rash, **eosinophilia,** and **eosinophiluria** should be investigated for the presence of the offending antibiotic, especially in hospital admitted patients for other medical conditions.

Clinical onset is more insidious in the chronic tubulointerstitial nephritis. Clinical history includes administration of offending agents for several years. They present with predominant symptoms of tubular dysfunction (polyuria). Proximal tubule defects can present as **Fanconi syndrome**.

Interstitial Nephritis with Uveitis

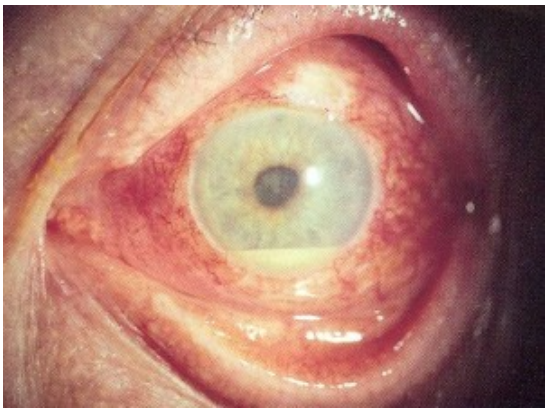


Image: "Hypopyon – leukocytic exudate in the anterior chamber of the eye." by EyeMD (Rakesh Ahuja, M.D.). License: CC BY-SA 2.5

It is an autoimmune disease seen in around 5% of those affected with tubulointerstitial nephritis. Clinical features include bilateral painful **uveitis** with **photophobia** and blurred vision. Uveitis can either precede or accompany the renal symptoms. Histopathology shows a characteristic **lymphocytic infiltrate.** Clinical symptoms are usually relapsing in adults and show good response to **glucocorticoids.**

Diagnosis & Laboratory Investigations of Interstitial Nephritis

Blood and Urine Examination

Eosinophiluria is the characteristic finding in acute tubulointerstitial nephritis. Urinalysis may show **proteinuria** and microscopic **hematuria**. The complete blood picture shows the characteristic increase in the number of **eosinophils,** and further blood examination shows increased **blood urea nitrogen** and **serum creatinine** in the presence of renal insufficiency.

Gross and Histopathology Findings

Renal biopsy is the definitive test for the diagnosis of acute interstitial nephritis. Findings include:

- Cellular infiltration with **eosinophils** and **monocytes**
- Sparing of the **glomeruli**
- Interstitial fibrosis

Chronic tubulointerstitial nephritis shows **interstitial fibrosis; tubular atrophy and arteriosclerosis** to varying degrees are seen.

Radiological Investigations

Papillary calcification with **garland pattern appearance** on a non-contrast CT scan is characteristically seen in **analgesic nephropathy**. Ultrasound and CT scan helps in identifying the presence of chronic kidney disease but does not help in the diagnosis of tubulointerstitial disorder.

Treatment of Interstitial Nephritis

Acute Interstitial Nephritis

Withdrawal of the offending agent is the primary treatment for acute interstitial nephritis. Treatment with **glucocorticoids** is recommended in the absence of improvement after the withdrawal of the offending agent.

Chronic Interstitial Nephritis

Treatment is usually supportive and is tailored based on the etiology. Offending drugs like analgesics are to be discontinued, immunosuppressive agents like **tacrolimus and cyclosporine** need to be replaced. Heavy metal poisonings, like lead, needs to be promptly identified and treated.

Prognosis of Interstitial Nephritis

Improvement is seen as long as the offending agent is removed from the circulation. The majority of the tubule interstitial disorders will progress to **end-stage renal disease (ESRD)**. The rate of progression to ESRD is slower when compared to other glomerular disorders.

References

Longo, D., Fauci, A., Kasper, D., & Hauser, S. (2015). Harrison’s Principles of Internal Medicine 19th edition. McGraw-Hill Professional.

Kumar, V., Abbas, A. K., & Aster, J. C. (2012). Robbins basic pathology. Elsevier Health Sciences.

Tubulointerstitial Nephritis via emedicine.medscape.com

Treatment of acute interstitial nephritis via uptodate.com

Notes