Ministry of Health of the Republic of Belarus
Educational Institution
“Gomel State Medical University”

Department of Pathological Anatomy

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METHODICAL GUIDELINES

for conducting a practical class
in the academic discipline “Pathological Anatomy”
for students
of the 3rd year, Faculty of International Students (instruction in English),
enrolled in the specialty
7-07-0911-01 “General Medicine”

Topic: “Renal pathology: glomerulonephritis, pyelonephritis. Nephrotic and nephritic syndromes”

Duration: 3 hours

Approved at the meeting of the Department of Pathological Anatomy
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EDUCATIONAL AND INSTRUCTIONAL GOALS, OBJECTIVES, AND MOTIVATION FOR MASTERING THE TOPIC

Educational Goal:

- To study the definition, classification, etiology, pathogenesis, morphology, clinical presentation (nephrotic and nephritic syndromes), complications, and outcomes of glomerulonephritis and pyelonephritis. To analyze glomerulonephritis: classification (primary vs. secondary, acute vs. chronic, by histologic pattern). To examine the following types: acute poststreptococcal glomerulonephritis (diffuse proliferative), rapidly progressive (crescentic) glomerulonephritis, membranous glomerulonephritis, minimal change disease, focal segmental glomerulosclerosis (FSGS), membranoproliferative glomerulonephritis, IgA nephropathy (Berger disease). To describe the morphological features by light microscopy, immunofluorescence (IgG, IgA, IgM, C3), and electron microscopy (electron-dense deposits, foot process effacement). To define nephrotic syndrome (proteinuria >3.5g/day, hypoalbuminemia, edema, hyperlipidemia, lipiduria) and nephritic syndrome (hematuria, hypertension, oliguria, azotemia, red blood cell casts). To analyze pyelonephritis: acute pyelonephritis (suppurative inflammation of renal parenchyma, caused by ascending infection – E. coli, Proteus, Klebsiella; morphology: abscesses, streaks of pus, papillary necrosis) and chronic pyelonephritis (tubulointerstitial inflammation, scarring, deformed calyces, chronic kidney disease). To discuss complications: renal failure, hypertension, end-stage renal disease.

Instructional Goal:

- Within the framework of the educational process for this academic discipline, the student must acquire not only theoretical knowledge, practical skills and abilities in the specialty but also develop their personal potential. They should cultivate qualities of responsibility and patriotism, be prepared to actively participate in the economic, socio-cultural, and public life of the country, recognize the social significance of their future professional activity, understand the norms of medical ethics and deontology, and learn to observe academic and labor discipline. In the course of studying the educational material, students should realize the importance of maintaining a healthy lifestyle and, as an example in the future, when performing professional duties, set an example for those around them and their patients.

Objectives: Upon completion of the practical session, the student must:

***Know*:**

- The classification of glomerulonephritis;
- The morphological features (light microscopy, immunofluorescence, electron microscopy) of each major type of glomerulonephritis;
- The definition and clinical features of nephrotic and nephritic syndromes;
- The etiology, pathogenesis, and morphological features of acute and chronic pyelonephritis;

- The complications and outcomes of glomerulonephritis and pyelonephritis.

Be able to:

- Distinguish between nephrotic and nephritic syndromes based on clinical and laboratory findings;
- Identify glomerular changes (hypercellularity, thickening of basement membrane, crescents, sclerosis) on renal biopsy;
- Recognize the macroscopic features of chronic pyelonephritis (scarring, deformed calyces);
- Diagnose pathological processes and diseases based on the description of macroscopic and microscopic changes in organs and tissues of the body.

Master:

- Basic techniques for working with a microscope;
- Skills in clinical-anatomical analysis;
- The fundamentals of synthetic generalization of morphological diagnostic signs of diseases and their correct interpretation in cause-and-effect relationships.

Motivation for Mastering the Topic:

Renal diseases, particularly glomerulonephritis and pyelonephritis, are important causes of acute and chronic kidney disease, hypertension, and end-stage renal disease requiring dialysis or transplantation. Glomerulonephritis is a leading cause of nephrotic and nephritic syndromes in both children and adults. Pyelonephritis is a common infectious disease that can lead to sepsis, papillary necrosis, and chronic kidney disease. Knowledge of the morphological features of renal pathology is essential for nephrologists, urologists, internists, pathologists, and primary care physicians for accurate diagnosis, treatment, and prognosis.

QUESTIONS

1. Classification of kidney diseases. Etiology. Pathogenesis. Proliferation of cells in the glomeruli. Nephrotic and nephritic syndromes. Acute tubular injury.
2. Postinfectious glomerulonephritis. Definition. Etiology. Pathogenesis. Morphology. Complications and outcomes.
3. IgA-nephropathy (Berger’s disease). Definition. Etiology. Pathogenesis. Morphology. Complications and outcomes.
4. Rapidly progressive glomerulonephritis (RPGN): anti-GBM disease (Goodpasture syndrome), immune-complex-mediated glomerulonephritis, ANCA-associated vasculitis. Definition. Etiology. Pathogenesis. Morphology. Complications and outcomes.
5. Minimal change disease (lipoid nephrosis). Definition. Etiology. Pathogenesis. Morphology. Complications and outcomes.
6. Membranous glomerulonephritis. Definition. Etiology. Pathogenesis. Morphology. Complications and outcomes.

7. Membranoproliferative glomerulonephritis (MPGN). Definition. Etiology. Pathogenesis. Morphology. Complications and outcomes.

8. Focal segmental glomerulosclerosis (FSGS). Definition. Etiology. Pathogenesis. Morphology. Complications and outcomes.

9. Interstitial nephritis. Definition. Etiology. Pathogenesis. Morphology. Complications and outcomes.

10. Pyelonephritis. Definition. Etiology. Pathogenesis. Morphology. Complications and outcomes.

11. Hydronephrosis. Definition. Etiology. Pathogenesis. Morphology. Complications and outcomes.

COURSE OF THE SESSION

Before delving into the specifics of individual glomerulopathies, it is essential to familiarize oneself with the **terminology** regarding damage to the glomerular apparatus of the kidneys. Damage can manifest in various forms:

1. **Focal**: Referring to a condition where a portion of the glomeruli is affected, while others remain unaffected.
2. **Diffuse**: Signifying widespread damage affecting all glomeruli.
3. **Segmental**: Characterized by localized damage affecting only a segment of the glomerulus.
4. **Global**: Indicating extensive damage affecting the entire glomerulus.

These **terms are often combined** to describe the nature and extent of lesions. For instance, the term "focal segmental lesion" implies that changes are not uniformly distributed across all glomeruli and are limited to specific segments.

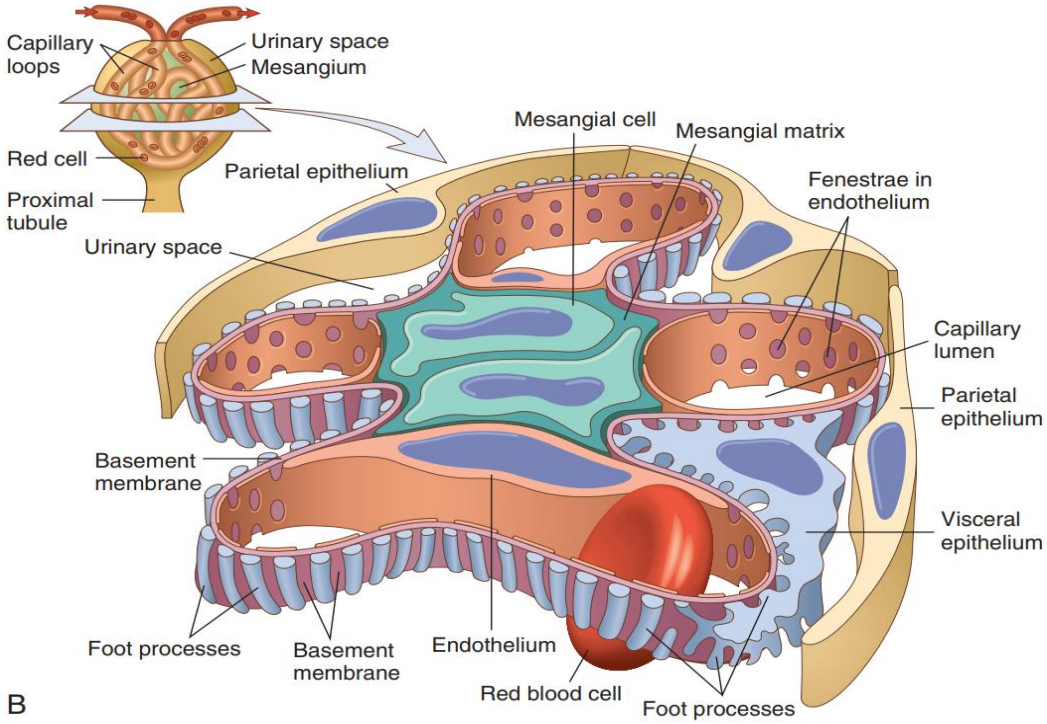
In the context of differential diagnosis for glomerular diseases, **accurate identification of morphological changes during biopsy** assumes paramount importance. There exist various types of morphological changes that may coexist in different diseases.

1. **Mesangial Cell Proliferation**: Characterized by an increase in the number of nuclei (exceeding four) within the central region of the glomerular lobule. Mesangial cells actively participate in phagocytic processes within the glomerulus. This proliferation often accompanies inflammatory responses and can contribute to the deposition of extracellular matrix, leading to glomerulosclerosis.

2. **Endothelial Cell Proliferation**: Results in the narrowing or occlusion of the vascular lumen. This process, known as endothelial proliferation, is commonly observed in conditions like thrombotic microangiopathy and can lead to compromised blood flow within the glomerulus, further exacerbating renal dysfunction.

3. **Epithelial Cell Proliferation**: When severe, it leads to the formation of cellular masses resembling crescents, which subsequently result in the occlusion of Bowman's capsule lumen. These crescentic formations, often seen in rapidly progressive glomerulonephritis, represent a hallmark of severe glomerular injury and are associated with a poor prognosis if left untreated.

Schematic representation of a glomerulus



Syndrome vs Symptom

A **syndrome** is a term used in medicine to describe a set of medical signs and symptoms that tend to occur together and are associated with a particular disease or condition. Essentially, it's a cluster of symptoms that frequently coexist and are indicative of a specific underlying cause.

On the other hand, a **symptom** is any subjective evidence of disease or abnormality. Symptoms can be physical or mental manifestations experienced by an individual that suggest the presence of an underlying condition. Symptoms are what the patient perceives and reports to healthcare providers during medical evaluation.

In essence, the key difference lies in the scope:

- a **syndrome encompasses a combination of symptoms** that tend to occur together,
- while a **symptom is a singular manifestation** experienced by an individual.

Syndromes in urology

1. **Nephrotic Syndrome**: Characterized by heavy proteinuria, hypoalbuminemia, edema, and hyperlipidemia. It often indicates glomerular damage and is associated with conditions like membranous nephropathy or minimal change disease.

2. **Nephritic Syndrome**: Manifests as hematuria, proteinuria, hypertension, and reduced glomerular filtration rate. It typically arises from inflammatory processes affecting the glomeruli, such as acute glomerulonephritis.

3. **Acute Kidney Injury (AKI)**: Marked by a sudden decline in kidney function, leading to electrolyte imbalances, fluid overload, and accumulation of waste products in the blood. AKI can result from various factors including ischemia, toxins, or infections.

4. **Chronic Kidney Disease (CKD)**: Characterized by a gradual loss of kidney function over time, often leading to irreversible damage. CKD is diagnosed based on decreased glomerular filtration rate and persistent proteinuria, and it is associated with numerous systemic complications.

5. **Chronic Renal Failure** or **Uremia**: Represents advanced stages of CKD where kidney function is significantly impaired, leading to uremia - a syndrome of systemic symptoms resulting from the retention of waste products and electrolyte imbalances in the blood.

Symptoms in urology

1. **Hematuria**: Presence of blood in the urine, which can indicate various underlying conditions including kidney stones, infections, or glomerular diseases.

- **Recurrent Gross Hematuria**: Episodes of visible blood in the urine occurring repeatedly over time, often suggestive of conditions like bladder cancer, kidney stones, or glomerular diseases.
- **Hematuria with Back Pain**: Hematuria accompanied by pain in the lower back, which may signify renal pathology such as kidney stones, infections, or renal tumors.

2. **Proteinuria**: The presence of abnormally elevated levels of proteins, primarily albumin, in the urine, typically defined as ≥30 mg/24 hours or a urine protein-to-creatinine ratio >0.2 mg/mg. This syndrome may manifest as persistent foamy urine, edema (periorbital or pedal), and hypoalbuminemia in nephrotic-range proteinuria (≥3.5 g/24 hours). Etiologies include glomerular diseases (e.g., minimal change disease, focal segmental glomerulosclerosis, membranous nephropathy), diabetic nephropathy, hypertensive nephrosclerosis, and tubulointerstitial disorders. Proteinuria may occur as an isolated finding or in conjunction with hematuria, suggesting glomerulonephritis or other intrinsic renal pathology.

3. **Symptomatic Renal Arterial Hypertension**: Elevated blood pressure associated with symptoms such as headaches, visual disturbances, or fatigue, indicating renal artery stenosis or other renal vascular diseases.

4. **Dysuria**: Pain or discomfort during urination, commonly associated with urinary tract infections, bladder inflammation, or urethral strictures.

5. **Polyuria**: Excessive urination, often indicative of conditions like diabetes mellitus or diabetes insipidus, where the body either produces excess urine (polyuria) or has difficulty concentrating urine.

Syndromes in urology

The **nephrotic syndrome** is defined as a clinical and laboratory symptom complex, characterized by:

- Proteinuria with urinary protein loss of 3 grams or more per day in adults, or equal to or more than 50 mg/kg/24 hours or 40 mg/m²/h (morning portion) in children.
- Hypoproteinemia with hypoalbuminemia (equal to or less than 25 g/l).
- Hyperlipidemia, encompassing hypercholesterolemia and triglyceridemia.

- Edema (though not obligatory, as incomplete or non-edematous nephrotic syndrome is possible).

Nephritic syndrome represents a complex of clinical and laboratory signs arising against the backdrop of inflammatory kidney diseases.

- Proteinuria (up to 2-3 grams/liter).
- Hematuria across a wide spectrum (microscopic or macroscopic).
- Arterial hypertension.
- Impaired kidney function (acute kidney injury or chronic kidney disease).

Morphology & Clinical Manifestations

Minimal change disease

Etiology/pathogenesis

- Usually idiopathic
- Involves loss of glomerular negative charge
- Circulating permeability factor
- Secondary forms due to virus, drugs, lymphoma

Clinical issues

- Nephrotic syndrome
- Most common in young children, boys > girls
- 90-95% respond to corticosteroids
- Can present as acute renal insufficiency in adults

Microscopic

- Glomerulus normal by light microscopy except for variable podocyte hypertrophy
- Protein reabsorption droplets in tubules

Minimal change disease

Ancillary tests

- Immunofluorescence negative except for variable focal IgM ± C3
- Electron microscopy has characteristic findings
- Podocyte foot process effacement, swelling, and microvillous transformation
- Slit diaphragms lost
- Normal glomerular basement membrane and no deposits

Top differential diagnoses

- Focal segmental glomerulosclerosis (FSGS)
- Diffuse mesangial hypercellularity (DMH)
- IgA, IgM, or C1q nephropathy

Postinfectious glomerulonephritis

Etiology/pathogenesis

- Streptococcus pyogenes, group A, β-hemolytic
- Acute immune complex disease
- Variety of infections (bacterial, viral, parasitic, mycotic, etc.)
- Staphylococcus notably appear in elderly

Clinical issues

- Hematuria, hypocomplementemia, ± RF, ± cryoglobulins

- Classically described in pediatrics but recently more in elderly
- ~ 90% resolve spontaneously but worse prognosis in elderly

Microscopic

- Diffuse proliferative, mesangial proliferative, focally proliferative
- Diffuse proliferative form most common and often exudative, with neutrophils
- May be superimposed on diabetic nephropathy

Rapidly progressive GN

Rapidly Progressive Glomerulonephritis (RPGN), a subtype of nephritic syndrome, is a pathological diagnosis characterized by extensive formation of glomerular crescents. In RPGN, more than 50% of sampled glomeruli display crescents, which are identifiable in biopsy specimens. If left untreated, RPGN can progress rapidly to **end-stage renal disease within weeks to months**.

This condition is relatively **uncommon**, affecting approximately 10 to 15% of patients diagnosed with glomerulonephritis. RPGN primarily occurs in individuals aged 20 to 50 years.

The types and causes of RPGN are classified based on findings from **immunofluorescence microscopy** and **serologic tests**. Treatment for RPGN typically involves corticosteroids, administered with or without cyclophosphamide or rituximab. In some cases, plasma exchange may also be utilized as part of the therapeutic approach.

IgA-nephropathy

Etiology/pathogenesis

- Genetic factors (> 7 loci by GWAS)
- Abnormal glycosylation of IgA1
- Autoantibodies to galactose deficient IgA1
- Abnormally active IgA response

Clinical issues

- Most common cause of glomerulonephritis worldwide
- Asia > USA/Europe > Africa
- Often asymptomatic hematuria ± proteinuria
- ↑ circulating serum IgA
- Recurs in transplants (30%)

Microscopic

- Usual: Mesangial hypercellularity and ↑ matrix
- Common: Focal, segmental inflammation of glomeruli
- Less common: Crescents ± necrosis
- Interstitial inflammation with eosinophils
- Histologically normal (10%)

IgA-nephropathy

Ancillary tests

- IF: IgA mesangial deposits (100%)
- C3 (90%), IgG, IgM (50%), C1q (10%)
- EM: Amorphous electron-dense deposits in mesangium

- Subepithelial or subendothelial deposits occasionally

Top differential diagnoses

- Henoch-Schönlein purpura
- Postinfectious glomerulonephritis (IgA-dominant)
- IgA nephropathy in cirrhosis of liver

Grading

Oxford classification: Mesangial hypercellularity (M), tubular atrophy/interstitial fibrosis (T), and segmental glomerulosclerosis (S) correlate with outcome

Membranous nephropathy

Etiology/pathogenesis

- Autoantibodies to PLA2R1 on podocyte (70-80%)
- Common disease associations in secondary MGN include: Hepatitis B and C; Carcinoma, lymphoma/leukemia; Systemic lupus erythematosus, rheumatoid arthritis; Drugs (especially NSAIDs); Sarcoidosis

Clinical issues

- Nephrotic syndrome
- Insidious onset, ~ 33% progress to end-stage renal disease
- Peak age: 30-50 years

Microscopic

- Diffuse thickening of glomerular capillary wall
- Subepithelial "spikes" in PAS and Jones methenamine silver stains
- Immunofluorescence: Diffuse granular deposits along GBM that stain for IgG, usually C3; IgG4 usually dominant subclass

Membranoproliferative GN

MPGN historically divided into **3 morphologic categories**, all with glomerular C3 deposition, chronic hypocomplementemia, and sometimes C3 nephritic factor:

- MPGN I defined by mesangial hypercellularity, subendothelial deposits, and duplication of GBM
- MPGN II or dense deposit diseasedefined originally by EM feature of hyperdense deposits
- MPGN III defined by prominent subepithelial deposits or diffuse intramembranous GBM deposits

Those with prominent C3 and little or no immunoglobulin deposition were recently separated into the category "C3 glomerulopathy" in which the demonstrable abnormality is dysregulation of alternative pathway of complement

MPGN with immune complexes

Terminology

Glomerular disease characterized by mesangial hypercellularity and duplication of GBM with subendothelial and mesangial immune complex deposits without known cause (infections, autoimmune disease)

Clinical issues

- Older children, adolescents, & young adults
- Nephrotic syndrome: > 50% of patients
- Hematuria: 10-20% with acute nephritic syndrome
- Hypocomplementemia
- 50% have detectable abnormalities in alternative complement pathway

Top differential diagnoses

- Cryoglobulinemic GN
- Chronic Infections
- Lupus erythematosus

MPGN with immune complexes

Microscopic

- Lobular, hypercellular glomerulus with thickened capillary walls & increased mesangial substance
- "Tram tracks" or duplication of GBM on PAS & silver stains
- Crescents in ~ 20% of cases
- Endocapillary hypercellularity ± neutrophils and monocytes
- IF: Classic feature is C3 in capillary walls & mesangium, "railroad track," "lumpy bumpy" granular C3
  - Distinguished from C3 glomerulopathy by prominent Ig &/or C1q & C4
- EM: Amorphous, dense subendothelial and mesangial deposits ± intramembranous or subepithelial deposits
  - 3 types based on predominant location of deposits: Type I, subendothelial; type III (Burkholder), subepithelial deposits; type III (Anders and Strife) complex intramembranous deposits

Focal segmental glomerulosclerosis

Etiology/pathogenesis

- Idiopathic disease with podocytopenia
- Plasma factor & genetic predisposition
- Adaptive structural-functional response to advanced renal disease of any cause, HTN, obesity-related glomerulopathy (ORG), atheroemboli/vasoocclusion, sickle cell anemia, congenital heart disease, drugs (anabolic steroids, calcineurin inhibitors)

Clinical issues

- Common cause of nephrotic syndrome (15-20% of biopsies)
- More common in blacks
- Therapy: Minority respond to steroids(~ 33%); Cyclophosphamide, cyclosporine, plasmapheresis; Under study: Rituximab, abatacept
- Recurs in transplants

FSGS

Microscopic

- Five pathologic variants (Columbia classification)

1. Not otherwise specified (NOS): Random distribution of adhesions

2. Tip: Adhesion at inlet of proximal tubule
3. Perihilar: Adhesion around hilum
4. Cellular: Luminal occlusion by endocapillary hypercellularity
5. Collapsing: Collapse and hypercellularity of podocytes

- Juxtamedullary glomeruli affected early
- Hyaline can accumulate at adhesion
- Foot process effacement and loss by electron microscopy
- IgM & C3 in segmental scars by immunofluorescence

Top differential diagnoses

- Minimal change disease if no segmental scar sampled
- FSGS superimposed on other glomerular diseases

Diagnostic checklist

- Multiple levels may be needed to see segmental lesion
- FSGS is *diagnosis of exclusion* since other diseases can cause segmental glomerular scars

Goodpasture syndrome is an **autoimmune disorder** characterized by the development of autoantibodies against specific proteins in the basement membrane of the **kidneys** and **lungs**. This condition predominantly affects **young adults**, typically between the ages of 20 and 30.

In Goodpasture syndrome, **autoantibodies primarily target the alpha-3 chain of type IV collagen**, which is found in the basement membranes of the kidneys and the alveolar basement membrane lungs, what leads to their inflammation and damage.

The clinical presentation of Goodpasture syndrome is characterized by a combination of **renal and pulmonary symptoms**. Patients often present with symptoms such as hemoptysis (coughing up blood), dyspnea (shortness of breath), cough, fatigue, and generalized weakness. Renal involvement typically manifests as **hematuria** (blood in the urine), **proteinuria** (protein in the urine), and rapidly progressive glomerulonephritis, leading to **acute kidney injury** or renal failure.

Morphology

On a microscopic level, renal biopsy in Goodpasture syndrome reveals **linear deposits of IgG** and **complement** along the glomerular basement membrane, known as linear IgG staining. Additionally, there may be evidence of **crescentic glomerulonephritis**, characterized by the presence of cellular crescents in the Bowman's space. In the lungs, histological examination may show diffuse alveolar hemorrhage with hemosiderin-laden macrophages.

Differential Diagnosis

Goodpasture syndrome shares clinical features with other forms of rapidly progressive glomerulonephritis and pulmonary-renal syndromes. Conditions such as **granulomatosis with polyangiitis** (formerly known as Wegener's granulomatosis), **microscopic polyangiitis**, and systemic lupus erythematosus (**SLE**) can also present with pulmonary-renal involvement.

Renal amyloidosis is a rare disorder characterized by the **deposition of abnormal protein fibrils**, called amyloid, within the renal parenchyma. These amyloid deposits disrupt normal kidney function, leading to renal impairment and potentially progressive kidney failure.

Amyloidosis can be classified into various types, with the most common being secondary amyloidosis associated with chronic inflammatory conditions such as **rheumatoid arthritis** or **chronic infections**.

Patients may present with symptoms such as **nephrotic syndrome** (characterized by proteinuria, hypoalbuminemia, edema, and hyperlipidemia), **hematuria**, **hypertension**, and **renal insufficiency**. As the disease progresses, symptoms of kidney failure, such as fatigue, weakness, and fluid retention, may develop.

Morphology

On histological examination, renal biopsy in cases of amyloidosis typically reveals **apple-green birefringence under polarized light after staining with Congo red**. This characteristic appearance is due to the alignment of amyloid fibrils. The amyloid deposits are typically found within the glomeruli, tubular basement membranes, interstitium, and blood vessel walls, leading to disruption of normal renal architecture and function. The kidneys may appear enlarged and pale on gross examination.

Differential Diagnosis

The differential diagnosis of renal amyloidosis includes other causes of renal parenchymal disease, such as **diabetic nephropathy**, **membranous nephropathy**, and **focal segmental glomerulosclerosis**.

Acute tubular injury (ATI) is a major cause of **acute renal failure** (ARF), a clinical syndrome characterized by rapid deterioration in renal function and **glomerular filtration rate** (GFR) over a relatively short period of time, ranging from hours to days.

The result is a sudden inability to maintain normal fluid and electrolyte homeostasis.

The acute reduction in renal function can be the result of the impairment of blood flow (so-called **prerenal failure**), obstruction of the urinary collecting system (so-called **postrenal failure**), or a variety of intrinsic renal diseases ranging from glomerulonephritis to interstitial nephritis to ATI.

Acute tubular injury

Etiology/pathogenesis

- Hypovolemia, reduced perfusion pressure (90%)
- Direct toxicity of drugs, exogenous toxins or endogenous substances (10%)

Clinical issues

- Deterioration of glomerular filtration rate occurs over hours to days
- Urinary microscopy reveals muddy brown casts and sloughed epithelium

Microscopic

- Tubular epithelial cells have apical cytoplasmic loss, reduced brush border, open lumens.

- Necrosis is sparse except in toxins
- Interstitial edema may be prominent, but minimal inflammatory infiltrate
- Casts of necrotic cells, cell debris, and lipofuscin pigment

Top differential diagnoses

- Acute interstitial nephritis
- Autolysis
- Cortical necrosis

Diagnostic checklist

- Important to determine the cause of the ATI
- Casts, pigments, epithelial cytoplasmic changes and nuclear features may provide clues to etiology
- Glomerular neutrophils, monocytes, and sparse thrombi in sepsis
- Ischemia shows little or no overt necrosis in contrast to toxins
- Histologic changes can be subtle despite severe dysfunction

Interstitial nephritis (IN) is an inflammatory condition affecting the renal interstitium, which is the tissue surrounding the kidney tubules. It can be caused by various factors, including **medications**, **infections**, **autoimmune diseases**, and **systemic conditions**. Drug-induced interstitial nephritis is one of the most common causes and can be triggered by antibiotics (such as penicillins, cephalosporins), non-steroidal anti-inflammatory drugs (NSAIDs), proton pump inhibitors (PPIs), and certain diuretics. Infections such as urinary tract infections and viral infections (e.g., HIV, CMV) can also lead to interstitial nephritis. Autoimmune conditions like systemic lupus erythematosus (SLE) and sarcoidosis may involve the kidneys and cause interstitial inflammation.

Common symptoms include acute **kidney injury**, **flank pain**, **fever**, **malaise**, **nausea**, **vomiting**, and urinary abnormalities such as **hematuria** and **leukocyturia**. Some patients may present with features of systemic illness, including rash, arthralgia, or eosinophilia.

Interstitial nephritis

Histological examination of renal biopsy specimens in interstitial nephritis typically reveals inflammatory infiltrates within the **renal interstitium**, composed mainly of **lymphocytes**, **plasma cells**, and occasionally **eosinophils**. Tubulitis, characterized by infiltration of inflammatory cells into the tubular epithelium, may also be observed. The presence of interstitial fibrosis and tubular atrophy may indicate chronicity and irreversible kidney damage. Immunofluorescence studies are usually negative or show nonspecific findings.

The differential diagnosis of interstitial nephritis includes other causes of AKI or CKD, such as **acute tubular necrosis**, **glomerulonephritis**, and **obstructive uropathy**. Distinguishing features on clinical evaluation, laboratory tests, and renal biopsy findings are crucial for accurate diagnosis. Careful consideration of the patient's medical history, medication use, and exposure to potential nephrotoxic agents is essential for identifying the underlying cause of interstitial nephritis and guiding appropriate management strategies.

Pyelonephritis is a bacterial infection of the kidneys, typically caused by **ascending urinary tract infections**. The most common pathogens responsible for pyelonephritis are Escherichia coli, followed by other Gram-negative bacteria such as Proteus, Klebsiella, and Enterobacter species. Pyelonephritis may result from the migration of bacteria from the lower urinary tract (e.g., bladder) into the kidneys, facilitated by factors such as urinary tract obstruction, instrumentation, or vesicoureteral reflux. Additionally, systemic bacteremia can lead to hematogenous spread of bacteria to the kidneys, particularly in immunocompromised individuals.

The **clinical presentation** of pyelonephritis can vary depending on the severity of the infection and the presence of complications. Common symptoms include **fever**, **chills**, **flank pain** (often unilateral), **dysuria**, **urinary frequency**, **urgency**, and **costovertebral angle tenderness** on physical examination. Systemic symptoms such as malaise, nausea, vomiting, and fatigue may also be present. In severe cases, pyelonephritis can lead to sepsis, acute kidney injury, or renal abscess formation.

Histological examination of renal biopsy specimens in pyelonephritis typically reveals **inflammatory changes within the renal parenchyma**, including interstitial inflammation, tubular injury, and neutrophilic infiltrates. The **renal pelvis and calyces may show evidence of acute inflammation**, such as edema and neutrophilic infiltrates. Chronic pyelonephritis is characterized by interstitial fibrosis, tubular atrophy, and lymphocytic infiltrates, often associated with recurrent or persistent infections.

The **differential diagnosis** of pyelonephritis includes other causes of flank pain and urinary symptoms, such as **renal calculi** (kidney stones), **renal infarction**, **renal abscess**, and **acute interstitial nephritis**. Imaging studies such as ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI) may be helpful in distinguishing between these conditions. Laboratory tests including urinalysis and urine culture are essential for confirming the diagnosis of pyelonephritis and identifying the causative organism.

Hydronephrosis is a condition characterized by the **dilation of the renal pelvis** and calyces **due to obstruction of urine flow** within the urinary tract. This obstruction can occur at any level, including the ureteropelvic junction (UPJ), ureterovesical junction (UVJ), or along the ureter. The most common causes of hydronephrosis include **urinary tract stones**, ureteropelvic junction obstruction (UPJO), vesicoureteral reflux (VUR), congenital anomalies, tumors, and strictures. The obstruction leads to the accumulation of urine within the renal collecting system, causing dilation and distension of the renal pelvis and calyces.

The **clinical presentation** of hydronephrosis can vary depending on the severity and duration of obstruction. Patients may present with symptoms such as **flank pain**, **abdominal pain**, **urinary frequency**, **dysuria** and **hematuria**. In severe cases or when associated with infection, patients may develop fever, chills, and signs of sepsis. Chronic or longstanding hydronephrosis can lead to renal impairment, renal insufficiency, or renal failure if left untreated.

On imaging studies such as ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI), hydronephrosis appears as **dilation of the renal pelvis and calyces**, often accompanied by **thinning of the renal parenchyma**. The degree of hydronephrosis can vary from mild to severe, depending on the extent and duration of obstruction. Histological examination of renal biopsy specimens may reveal signs of **chronic interstitial fibrosis** and **tubular atrophy** in cases of longstanding hydronephrosis.

The **differential diagnosis** of hydronephrosis includes other causes of renal enlargement or pelvic dilation, such as **renal cysts**, **renal tumors**, **renal abscesses**, and **polycystic kidney disease**. Additionally, conditions causing extrinsic compression of the urinary tract, such as pelvic masses or retroperitoneal fibrosis, may mimic the appearance of hydronephrosis on imaging studies.

INFORMATIONAL AND METHODOLOGICAL PART

MAIN LITERATURE

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2. Klatt, E. C. Robbins and Cotran Atlas of Pathology : [with Student Consult Online Access] / Edward C. Klatt. - third edition. - Philadelphia : Elsevier, 2015. - 587 p. : il.

3. Robbins Basic pathology / [ed. by] Vinay Kumar, Abul K. Abbas, Jon C. Aster. - 9th ed. - [Philadelphia] : Elsevier ; Saunders. - 910 p. : ill., scheme, tab.

ADDITIONAL LITERATURE

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2. Sobotta. Atlas of human anatomy. [V. 2]. Internal organs / ed. by F. Paulsen, J. Waschke. - 15th ed. - München : Elsevier. Urban & Fischer, 2011. - 259 p. : ill., col. ill.

3. Sobotta. Atlas of human anatomy. [V. 3]. Head, neck, and neuroanatomy / ed. by F. Paulsen, J. Waschke. - 15th ed. - München : Elsevier. Urban & Fischer, 2011. - 370 p. : ill., col. ill.

4. Weir & Abrahams' imaging atlas of human anatomy / ed.: J. D. Spratt [and oth.] ; consultant eds.: J. Weir, P. H. Abrahams. – 5th ed. - [S.l.] : Elsevier, 2017. - xvi, 263 p. : ill.

NORMATIVE LEGAL ACTS AND DOCUMENTS

1. Order of the Ministry of Health of the Republic of Belarus No. 111 of 06/01/1993 "On further improvement of the pathological service of the Republic of Belarus"

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ELECTRONIC DATABASES

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