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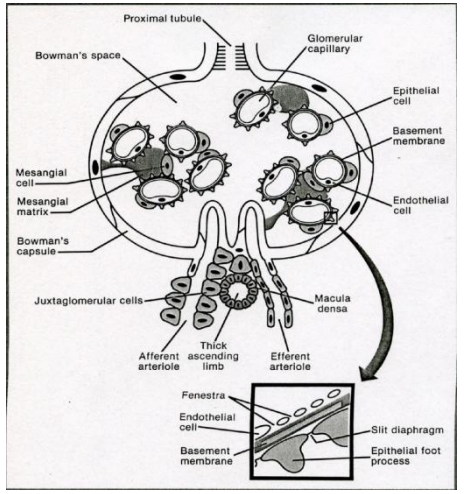
ФЕДЕРАЛЬНОГО АГЕНСТВА ПО ЗДРАВООХРАНЕНИЮ
И СОЦИАЛЬНОМУ РАЗВИТИЮ»

КАФЕДРА ПРОПЕДЕВТИКИ ВНУТРЕННИХ БОЛЕЗНЕЙ

Пропедевтика внутренних болезней

Учебно-методическое пособие
Часть IX



Introduction to Internal Diseases

Manual
Part IX

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Учебно-методическое пособие составлено в соответствии с Государственным образовательным стандартом высшего профессионального образования (2000), Государственными требованиями к минимуму содержания и уровню подготовки выпускника вуза по специальности 040100 «Лечебное дело», типовой и рабочей программами по дисциплине «Пропедевтика внутренних болезней» (2003). В учебно-методическом пособии подробно освещается содержание занятий, даны теоретические и справочные материалы, описываются практические умения в четкой последовательности действий у постели больного. Пособие предназначено для иностранных студентов медицинских вузов.

CONTENTS
PART IX

DIAGNOSTICS OF RENAL DISEASES

Theme 34. MAJOR CLINICAL SYNDROMES IN RENAL DISEASE (RENAL EDEMAS, RENAL HYPERTENSION, RENAL ECLAMPSY, RENAL INSUFFICIENCY, UREMIC COMA). DIFFUSE GLOMERULONEPHRITIS. NEPHROTIC SYNDROME. RENAL AMYLOIDOSIS. PYELONEPHRITIS.

Goal: to get a notion about the main renal diseases, their symptoms and signs, diagnostic meanings of additional diagnostic methods data; instrumental diagnostics of renal diseases; to master skills.

Knowledge objectives:

- to know symptoms and signs of main renal syndromes and diseases, appropriate changes of physical examination data, diagnostic meaning of additional diagnostic methods and their findings in these diseases.

Skill objectives:

- to collect interviewing data, to perform physical examination of patients with renal diseases (inspection, palpation, percussion and auscultation), to interpret data of additional diagnostic methods, to establish diagnosis of main renal diseases.

Subject-matter:

1. complaints of patients with renal disease
2. etiology and pathogenesis of glomerulonephritis
3. renal hypertension: pathogenesis, types, diagnostics
4. uric syndrome: notion, causes, laboratory diagnostics
5. etiology and pathogenesis of acute renal failure
6. etiology and pathogenesis of chronic renal failure
7. diagnostics of renal failure
8. diagnostics of nephrotic syndrome
9. diagnostics of acute glomerulonephritis
10. diagnostics of chronic glomerulonephritis
11. diagnostics of acute and chronic pyelonephritis
12. diagnostics of renal calculi

Equipment required: stethoscope.

EDUCATIONAL MATERIAL

CLINICAL EVALUATION OF RENAL DISORDERS

Urinary disorders may present nonspecifically but usually do so as abnormal clinical or laboratory manifestations suggesting a primary renal abnormality or a systemic disease associated with renal pathology.

Normally, adults void about 4 to 6 times/day, mostly in the daytime, totaling 700 to 2000 mL/day.

Symptoms and Signs

Asymptomatic patients with renal disease may have hypertension or abnormal blood or urine findings. They may have a family history of renal disorders.

In symptomatic patients, fever, weight loss, and malaise are common findings with renal carcinoma, advanced renal failure, and urinary tract infection (UTI). Typically, renal symptoms include changes in micturition, urinary output, or appearance; or pain, edema, and nonspecific symptoms and signs related to renal insufficiency.

Frequent ***micturition*** *(pollakyuria)* without an increase in urine volume is a symptom of reduced bladder filling capacity. Infection, foreign bodies, calculi, or tumors may injure the bladder mucosa or underlying structures, leading to inflammatory infiltration and edema. Mild stretching of the bladder, reduced bladder elasticity, a pelvic mass, or a gravid uterus functionally reduces bladder capacity, resulting in pain and urgency (a compelling need to urinate).

Polyuria (> 2000 mL/day voided) may be caused by increased water intake (eg, compulsive water drinking), osmotic diuresis (eg, glycosuria from uncontrolled diabetes mellitus), decreased vasopressin release due to hypothalamic or posterior pituitary disease, or decreased renal tubular response to ADH from hypercalcemia, K deficiency, or congenital or acquired nephrogenic diabetes insipidus (NDI).

Oliguria (< 500 mL/day voided) tends to be acute and caused by decreased renal perfusion (prerenal factors), ureteral or bladder outlet obstruction (postrenal factors), or primary renal disease. Uremia may occur.

Anuria (< 50 mL/day voided), although rare, may signal acute renal failure, the end stage of chronic progressive renal insufficiency, or, rarely, renal infarction or cortical necrosis. It may also be due to reversible urinary obstruction. Prolonged anuria inevitably results in uremia.

Nocturia (voiding during the night) is an abnormal but nonspecific symptom. It may occur without disease; eg, due to excessive fluid intake in the late evening. It may result from urine retention secondary to bladder neck obstruction (eg, prostatism). Less commonly, nocturia may reflect early renal disease and polyuria from a decrease in concentrating capacity or heart and liver failure without evidence of intrinsic urinary system disease.

Dysuria (painful urination) suggests irritation or inflammation in the bladder neck or urethra, usually due to bacterial infection.

Obstructive symptoms (*hesitancy, straining, decrease in force and caliber of the urinary stream, terminal dribbling*) are commonly due to obstruction distal to the bladder. In men, such obstruction is usually due to prostatic obstruction. Similar symptoms may suggest meatal stenosis in either sex.

Abnormal color or appearance of urine has many causes. Urine may be clear during water diuresis or may be a deep yellow color when maximally concentrated due to chromogens (eg, urobilin). If excretion of food pigments (usually red urine) or drugs (brown, black, blue, green, or red) can be excluded, non-yellow urine suggests the presence of *hematuria*, *hemoglobinuria*, *myoglobinuria*, *pyuria*, *porphyria*, or melanoma. Cloudy urine is commonly due to precipitated amorphous phosphate salts

in an alkaline urine; less frequently, it suggests pyuria due to a UTI. Milky urine may be caused by precipitated phosphates in an alkaline urine. Brick dust urine usually is produced by precipitated urates in an acid urine. Urine microscopy and chemical analysis usually identify the cause.

Hematuria (blood in the urine) can produce red to brown discoloration depending on the amount of blood present and the acidity of the urine. Slight hematuria may cause no discoloration and may be detected only by microscopy or chemical analysis. Hematuria without pain usually is due to renal, vesical, or prostatic disease. In the absence of RBC casts (which usually indicate glomerulonephritis), silent hematuria may be caused by bladder or kidney tumor. Such tumors usually bleed intermittently, and complacency must not occur if the bleeding stops spontaneously. Other causes of asymptomatic hematuria include calculi, polycystic disease, hydronephrosis, and benign prostatic hyperplasia. Hematuria accompanied by excruciating pain (renal colic) suggests passage of a ureteral calculus or a clot from renal bleeding. Hematuria with dysuria is also associated with bladder infections or lithiasis.

Kidney pain usually is felt in the flank or back between the 12th rib and the iliac crest, with occasional radiation to the epigastrium. Stretching of the pain-sensitive renal capsule is the probable cause and may occur in any condition producing parenchymatous swelling (eg, acute glomerulonephritis, pyelonephritis, acute ureteral obstruction). There is often marked tenderness over the kidney in the costovertebral angle formed by the 12th rib and the lumbar spine. Inflammation or acute distention of the renal pelvis or ureter causes pain in the flank and hypochondrium, with radiation into the ipsilateral iliac fossa and often into the upper thigh, testicle, or labium. The pain is intermittent but does not completely remit between waves of colic. Chronic obstruction is usually asymptomatic.

Bladder pain is most commonly caused by bacterial cystitis; it is usually suprapubic and referred to the distal urethra during urination.

Edema usually represents excessive extracellular water and Na due to abnormal renal excretion, but it may also be caused by heart or liver disease. Initially, edema may be evident only by weight gain but later becomes overt. Edema associated with kidney disease is sometimes noted first as facial puffiness (Fig.1) rather than swelling in dependent or lower parts of the body. If fluid retention continues, anasarca (generalized edema) with fluid transudates (effusions) in the pleural and peritoneal cavities may occur (Fig.2); it is most frequently associated with continuous, heavy proteinuria (nephrotic syndrome).

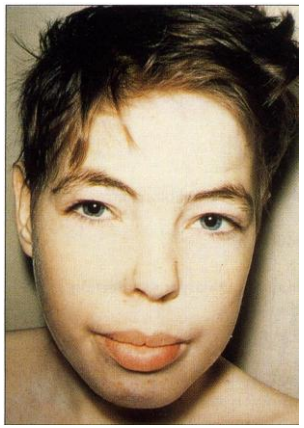


Fig.1. Acute nephritis. The generalized facial puffiness and the erythematous periorbital oedema are typical, and this boy also had ankle oedema and hypertension.

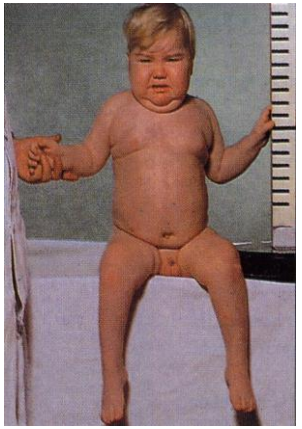


Fig.2. Nephrotic syndrome in a young boy. Note the severe generalized facial and body oedema. The facial oedema gives him a cushingoid appearance, but this picture was taken before he started on steroid therapy. He also had ascites.

Uremia (a toxic condition associated with excessive accumulation in the blood of protein metabolism by-products) occurs when GFR declines to < 10% of normal, with resultant disturbances of multiple organ systems (Fig.3). Weight loss, weakness, fatigue, dyspnea, anorexia, nausea and vomiting, itching, failure to grow, tetany, peripheral neuropathy, pericarditis, and convulsions are the usual symptoms and signs; most can be ameliorated or reversed by dialysis or renal transplantation and appropriate diet.

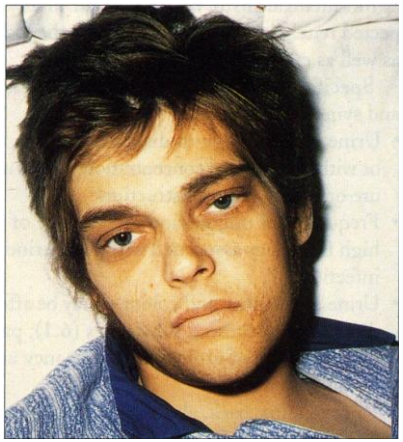


Fig.3. Uremic facies. Note the pale, sallow, yellow-brown appearance of the skin and the anaemic pallor of the sclerae.

Hypertension may be secondary to renal disease (eg, vascular anomalies or occlusion, glomerulonephritis, progressive renal failure). However, <= 5% of adult hypertension is due to renovascular causes (with major renal artery or segmental artery obstruction and demonstrable increased renin secretion from the obstructed side).

Skin changes may include pallor, suggesting anemia, commonly associated with renal disease; excoriations, suggesting pruritus; and infections (eg, carbuncles, cellulitis), which may be due to glomerulonephritis.

Retinal abnormalities on ophthalmoscopy may include hemorrhages, exudates, and papilledema as signs of cerebral edema associated with malignant hypertension or metabolic abnormalities.

Other abnormalities suggesting urinary system disease include stomatitis; ***an ammoniacal breath odor****;* and enlargement of the kidneys, bladder, or prostate on palpation.

INVESTIGATIONS IN RENAL DISEASE

Initial investigations	
Urine stick test:	specific gravity blood protein glucose nitrite pH
Urine microscopy:	red and white cells casts crystals epithelial cells parasites
Midstream urine for culture	
Plasma:	urea creatinine electrolytes: sodium, potassium, chloride, bicarbonate, calcium, phosphate
Haematology:	full blood count
Investigations used selectively	
24-hour urine collection:	creatinine clearance protein excretion
Ultrasound	
Plain X-ray of renal tract:	kidney ureter bladder (KUB)
Intravenous urogram (IVU)	
Specialized investigations	
Further radiology, including CT and MRI	
Isotope scans	
Specialized renal tubule function tests	
Biopsy	
Endoscopy	
Tests for multisystem diseases	

Fig.4. The investigation of patients with suspected renal disease.

LABORATORY FINDINGS (Fig.4).

Blood studies: Hematologic assessment may suggest renal disease. Anemia (particularly normocytic normochromic from a lack of erythropoietin) may be a clue to renal failure.

Serum chemistries often are abnormal in renal dysfunction, but changes are nonspecific In the absence of acute muscle damage, a persistent increase in serum creatinine is highly specific for renal dysfunction.

Urinalysis: Urinalysis is the best guide to intrinsic renal disease and includes microscopic examination of sediment and qualitative evaluation of protein, glucose, ketones. Under standardized conditions, the solute concentration of urine or urine pH may have diagnostic significance. Routine urinalysis in asymptomatic patients is infrequently positive and rarely leads to additional testing or changes in therapy. Routine urinalysis misses about 2% of patients with bacteriuria, and quantitative urine cultures are recommended instead.

A semiquantitative estimation of these formed elements is made by a high-power or low-power field count (eg, 10 to 15 WBCs/high-power field).

Normal urine contains a few cells and other formed elements shed from the entire urinary tract. With disease, these cells are increased and may help localize the site and type of injury. Voided urine in women contains genital tract cells. Urinary system disease is suggested in a male by > 1 WBC, RBC, or epithelial cell/high-power field (400×), ie, > 1000 cells/mL, or in a female by > 4 WBCs/high-power field, ie, > 4000 cells/mL in centrifuged urine.

Excessive WBCs may indicate infection or other inflammatory diseases. In symptomatic patients, the finding of > 10 WBCs/μL strongly suggests significant bacteriuria. Occasional bacteria in a centrifuged urine sediment do not necessarily indicate UTI. However, bacteria in an uncentrifuged fresh urine sample together with urine cultures of > 105 colony-forming units (CFU)/mL of voided urine suggest UTI rather than contamination.

Excessive RBCs may indicate infection, tumor, calculi, or inflammation anywhere in the kidney or urinary tract. When >= 80% of the RBCs are dysmorphic (Fig.5) (wide range of morphologic variation), hematuria is likely to be glomerular in origin. In some clinical conditions, analysis of RBC morphology may be unreliable. For example, isomorphic erythrocyturia can be found in forced diuresis, in glomerulonephritis with gross hematuria, or in renal insufficiency. A mixed morphologic pattern of urinary RBCs may occur in IgA nephritis, a frequent cause of glomerular hematuria. Recent identification of acanthocytes (ring-formed RBCs with one or more protrusions of different shapes and sizes) is a more specific marker of glomerular bleeding. Studies suggest that if 5% of the total urinary RBCs are acanthocytes, then an underlying glomerular disease can be diagnosed with high sensitivity (71%) and specificity (98%).

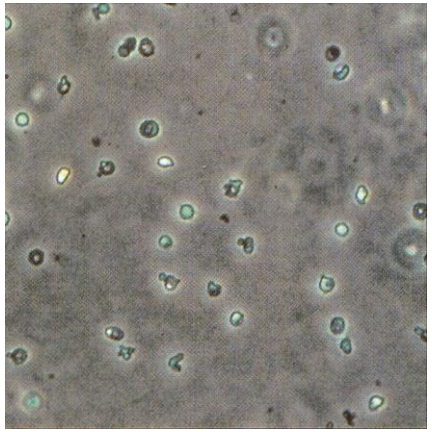


Fig.5. Phase-contrast microscopy of urine sediment, showing a wide range of dysmorphic red cells. In fresh urine, dysmorphic red cells imply glomerular bleeding. In lower urinary tract bleeding, the red cells appear similar to one another (isomorphic). Patients with isomorphic red cells in the urine require further detailed urological investigation, whereas patients with dysmorphic red cells require further investigation for possible renal disease.

Crystals of various salts (eg, oxalate, phosphate, urate) or drugs (eg, sulfonamides) may be found when their concentrations and urinary pH exceed the limits of their solubility.

Casts (cylindric masses of mucoprotein in which cellular elements, protein, or fat droplets may be entrapped) in urine sediment are most important in distinguishing primary renal disease from diseases of the lower tract.

Proteinuria is simply and rapidly detectable by commercially available dipsticks (Fig.6). This technique is sensitive to as little as 5 to 20 mg/dL of albumin, the predominant protein in most renal diseases, but is less sensitive to globulins and mucoproteins and may be negative in the presence of Bence-Jones proteins.

The major mechanisms producing proteinuria are elevated plasma concentrations of normal or abnormal proteins (overflow proteinuria; eg, Bence-Jones proteinuria); increased tubular cell secretion (Tamm-Horsfall proteinuria); decreased tubular resorption of normal filtered proteins; and an increase of filtered proteins caused by altered glomerular capillary permeability.

In adults, proteinuria is usually found incidentally during a routine physical examination. Proteinuria may be intermittent, orthostatic (occurring only when upright), or constant (persistent). Most patients with intermittent or orthostatic proteinuria do not show any deterioration of renal function, and in about 50% the proteinuria ceases after several years. Constant proteinuria is more serious. Although the course is indolent without other indicators of renal disease (eg, microscopic hematuria), most patients demonstrate proteinuria over many years; many develop an abnormal urine sediment and hypertension; and a few progress to renal failure.

Measurements of protein excretion are useful for diagnosis and follow-up, especially in constant proteinuria. A 24-h measurement of total protein excretion (normal, < 150 mg/day) may be done. Heavy proteinuria *(> 2 g/m^2/day*) is found in patients with glomerulopathy producing the nephrotic syndrome.

Proteinuria usually is minimal, intermittent, or absent in diseases primarily involving the tubulointerstitial area (eg, pyelonephritis).

Exercise proteinuria sometimes occurs in joggers, marathon runners, and boxers. It is accompanied by elevation of catecholamines and may be associated with hemoglobinuria, hematuria, or even myoglobinuria.

For *glucosuria*, testing by dipstick is specific and very sensitive, detecting as little as 100 mg/dL (5.5 mmol/L) of glucose. The most common cause of glucosuria is diabetic hyperglycemia with normal renal glucose transport. However, if glucosuria persists with normal blood glucose concentrations, renal tubular dysfunction should be considered.

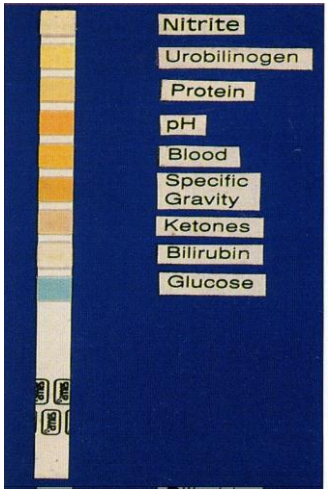


Fig.6. A typical urine test stick, which provides instant measurement of a range of possible abnormalities in the urine.

For *ketonuria*, the dipstick reagent is more sensitive to acetoacetic acid than to acetone. Ketonuria usually is nonspecific, and acetoacetic acid, acetone, and -hydroxybutyric acid are excreted in the urine. Finding any of these three compounds in urine generally is satisfactory for diagnosis of ketonuria. Ketonuria offers clues to the causes of metabolic acidosis. It is present in starvation, in uncontrolled diabetes mellitus, and occasionally in ethanol intoxication. It is not specific for intrinsic urinary system disease.

For *hematuria*, the dipstick reagent is sensitive to free Hb and myoglobin. A positive test in the absence of RBCs on microscopic examination suggests

hemoglobinuria or myoglobinuria--an important etiologic clue in the patient with acute renal failure.

For *nitrituria*, the dipstick test depends on the conversion of nitrate (derived from dietary metabolites) to nitrite by the action of certain bacteria in the urine. Normally no detectable nitrite is present. When bacteriuria is significant, the test will be positive in 80% of cases in which the urine has incubated for >= 4 h in the bladder. Thus, a positive test is a reliable index of significant bacteriuria. However, a negative test does not exclude bacteriuria.

Urinary specific gravity (sp gr) is measured by a urinometer or estimated by a sp gr reagent strip method. Although the correlation with osmolality is not linear, it is satisfactory for clinical use.

Urinary pH is measured by a dipstick impregnated with various dyes that change color when the pH is 5 to 9.

Measurement of renal function

Renal function tests are useful in evaluating the severity of kidney disease and in following its progress.

Serum creatinine can be used as an index of renal function because creatinine production and excretion are reasonably constant in the absence of muscle disease. Serum concentration of creatinine varies inversely with the GFR and therefore is a useful index of the GFR if production (related to muscle mass and age) and metabolism (increased in uremia) are considered. The upper limit of **serum creatinine** concentration in men with normal GFR is **1.2 mg/dL (110 µmol/L);** in women, **1 mg/dL (90 µmol/L**).

Glomerular filtration rate (GFR) reflects amount of plasma ultrafiltrate (i.e. primary urine), resultant from blood during definite time interval (normally **GFR is 115—125 ml/min**). In most cases of renal disease GFR is precise summary index of renal function. More subtle methods of renal function evaluation are based on the use of clearance principle. Clearance (depuration) — is conditional notion, characterized by blood depuration rate; it is defined by plasma volume, which is entirely cleaned with kidneys from that or another substance (creatinine) during 1 min.

Creatinine clearance in men is 140 to 200 L/day (70 ± 14 mL/min/m^2) and in women, 120 to 180 L/day (60 ± 10 mL/min/m^2). The creatinine clearance (Clcreat) can be calculated from the serum creatinine concentration in men as:

$$\mathrm{Cl_{creat}\ (mL/min)} = \frac{(140 - \text{age [yr]})(\text{body wt [kg]})}{(72)\ (\text{serum creatinine [mg/dL]})}$$

In women, the calculated values are multiplied by 0.85.

After loss of 50 to 75% of the normal glomerular filtration surface, a decrease in creatinine clearance is clearly detectable. Thus, a normal creatinine clearance cannot exclude the presence of mild renal disease.

Tests of renal concentrating capacity are simple and diagnostically helpful. The loss of concentrating ability frequently is present long before a depression of GFR is measurable. Renal concentrating capacity is best tested by Zimnitsky test.

Additional special tests of renal tubular function usually require research laboratories and are reserved for patients with specific problems. However, tests that measure plasma phosphate and urate, urinary amino acids, and urine pH are readily available and may prove useful in screening specific clinical problems.

Imaging procedure.

Plain x-ray of the abdomen (kidney, ureter, bladder [KUB] film) can demonstrate the size and location of the kidneys (Fig.7) but has been superseded by ultrasonography (US).

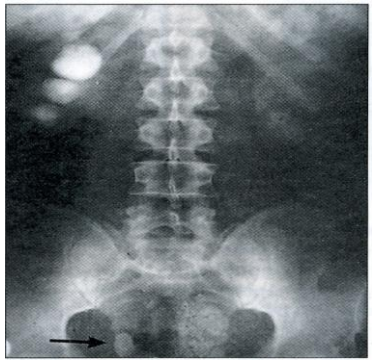


Fig.7. Plain X-ray of the kidney, ureter and bladder (KUB) is a useful initial investigation in many patients. Here it has revealed a rather unusual combination of calculi in both kidneys (more prominent on the right), in the lower right ureter (arrowed) and in a bladder diverticulum.

Because gastrointestinal and urinary diseases tend to mimic each other, KUB film may be helpful in the differential diagnosis. However, the renal outline can be obscured by bowel content, lack of perinephric fat, or a perinephric hematoma or abscess. This difficulty may be overcome by CT. Congenital absence of a kidney may be suggested.. If both kidneys are unusually large, polycystic kidney disease, amyloid disease, or hydronephrosis may be present. If both are small, the end stage of bilateral renal dysplasia or sclerosing disease (eg, glomerulonephritis, tubulointerstitial nephritis, nephroangiosclerosis) must be considered. Normally, the left kidney is 0.5 cm longer than the right.

In 90% of cases, the right kidney is lower than the left because of displacement by the liver. The long axes of the kidneys are oblique to the spine and tend to parallel the borders of the psoas muscles. If both kidneys are parallel to the spine, the possibility of horseshoe kidneys should be considered. If only one kidney is displaced, a tumor or cyst may be present.

Because x-ray film is two-dimensional, a calculus in the urinary tract is practically impossible to diagnose unless it is a staghorn calculus. However, suspicious opaque bodies may be noted in the region of the adrenal, kidney, ureter, bladder, or prostate. Oblique and lateral films and visualization of the urinary tract with

radiocontrast agents, US, or CT are necessary to place the calcification specifically within these organs.

Intravenous urography (IVU; excretory urography) is often used to visualize the kidney and lower urinary tract (Fig.8 & 9).

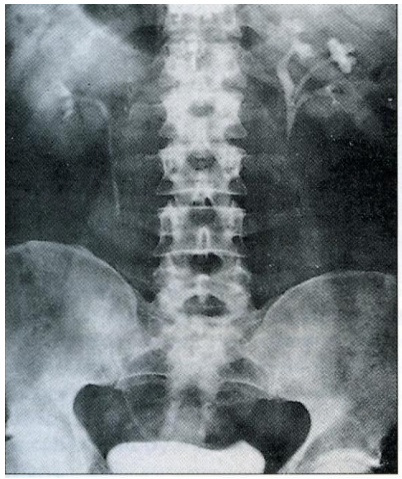


Fig.8. Intravenous urogram showing a normal right kidney and ureter, but marked calyceal clubbing in the left kidney. Note the gross dilatation of the calyces, especially in the middle and upper poles of the kidney.

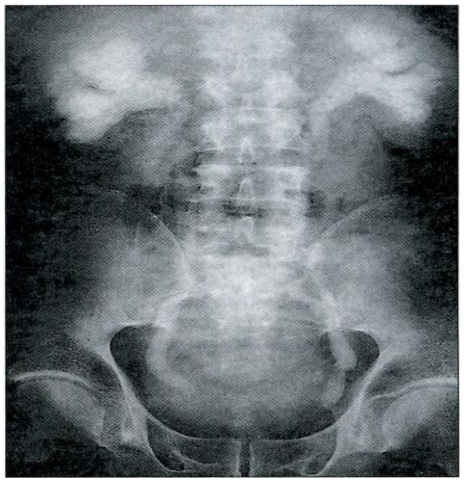


Fig.9. Intravenous urogram showing bilateral hydronephrosis and hydro-ureter with a large bladder. The changes are typical of an elderly patient with chronic urinary retention as a result of prostatic enlargement.

Studies are done by IV infusion of an iodinated benzoic acid derivative. The iodine provides radiopacity, while the benzoic acid is rapidly filtered by the kidney. A contrast agent, after IV injection, becomes concentrated in the renal tubules in <= 5 min, providing a nephrogram. Later, the contrast agent appears in the collecting system, outlining the renal pelvis, the ureters, and finally the bladder. Visualization depends on the concentration of the contrast agent in the kidneys and the urinary collecting system. Therefore, the best radiograms are obtained in patients with a normal GFR.

In *retrograde pyelography* (Fig.10*)*, radiopaque agents similar to those used in IVU are introduced directly into the urinary tract after cystoscopy and catheterization of the ureter. Retrograde pyelography provides more intense opacification of the collecting and voiding system when IVU has been unsuccessful because of poor renal function, a nonvisualized kidney by IVU, upper urinary tract bleeding with normal IVU, or filling defect in the upper urinary tract.

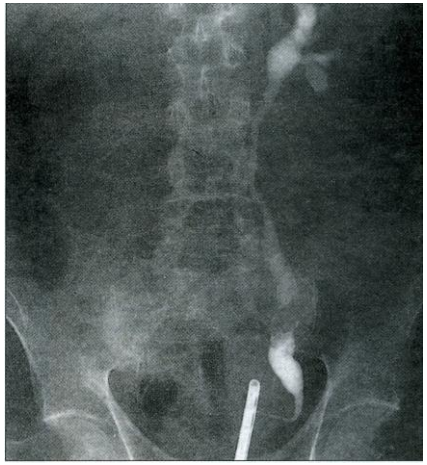


Fig.10. Retrograde pyelogram revealing a large filling defect in the left ureter caused by a transitional cell carcinoma. The technique is particularly useful in defining the nature and site of ureteric obstruction.

In *anterograde pyelography*, radiocontrast agents are introduced into the renal pelvis by radiographic visualization. This procedure may be indicated when retrograde pyelography cannot be done because of inability to catheterize a ureter, severe bladder disease, ectopic or reimplanted ureter, or inability to inject radiocontrast above an obstructed site in a ureter.

CT (Fig.11) is more expensive than US and IVU. However, CT is most useful in evaluating the character and extent of renal masses or determining the cause of a retroperitoneal mass distorting the normal urinary tract (eg, an enlarged abdominal lymph node).

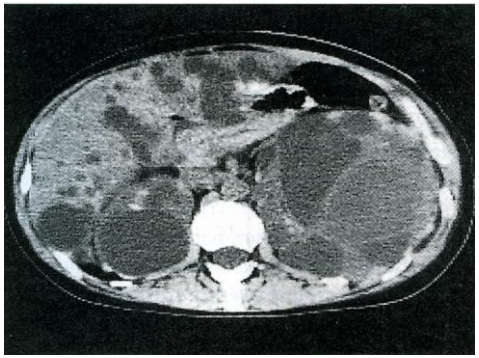


Fig.11. CT scan revealing bilateral congenital polycystic kidneys, larger on the patient's left (to the right of the picture). The liver also contains multiple cysts. The pancreas can be clearly seen in this view, but does not seem to contain any large cysts.

Angiography (Fig.12 & 13) is the most invasive renal imaging procedure and is reserved for special indications. Angiography is best reserved for investigating possible vascular lesions (eg, aneurysm); it may also be useful for suspected renal hypertension; congenital renal anomalies of structure, position, or vascular supply.

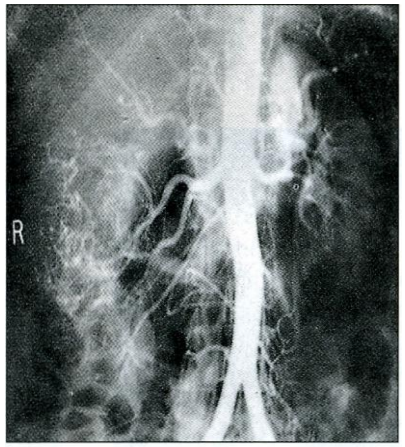


Fig.12. Renal arteriography (aorotography). This "flood" film, in which contrast is allowed to enter both kidneys simultaneously from the aorta, demonstrates a normal arterial circulation in the left kidney and an abnormal tumour circulation in the right kidney. Selective arteriography can also be performed by catheterizing individual renal arteries, and digital substraction imaging (Fig.13) allows further detail assessment.

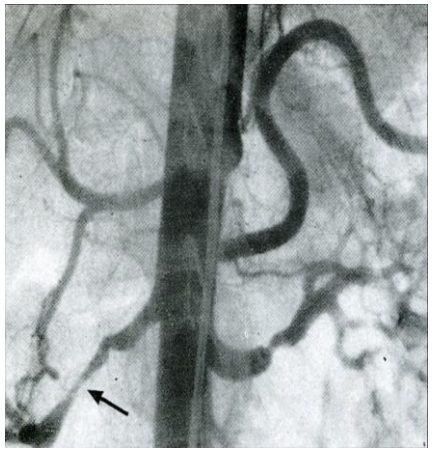


Fig.13. Aortogram (digital subtraction technique) showing bilateral renal artery stenosis. The appearances are typical of stenosis caused by fibromuscular hyperplasia rather than atheroma, and the stenosis is more marked on the right (arrow). The stenoses were successfully treated by balloon angioplasty.

In *venography*, the inferior vena cava is usually visualized for diagnostic purposes by percutaneous puncture of the femoral vein.

Ultrasonography (US), a noninvasive, relatively innocuous technique, is advantageous in that visualization does not depend on function (Fig.14). The kidney can be effectively outlined and the pelvicalyceal echo pattern critically examined by scanning in multiple positions. US is particularly effective in diagnosing polycystic kidney disease, differentiating renal cysts and tumors, detecting hydronephrosis and perirenal fluid collections or intrarenal hemorrhage, estimating renal size and parenchymal thickness, and locating the optimal site for percutaneous renal biopsy or nephrostomy. US is the preferred diagnostic method in a uremic patient when uptake of contrast agent or isotope is impaired. Doppler US may show patency of arteries and veins and the amount and speed of blood flow, which is useful in evaluating kidney transplant patients or selected patients with hypertension.

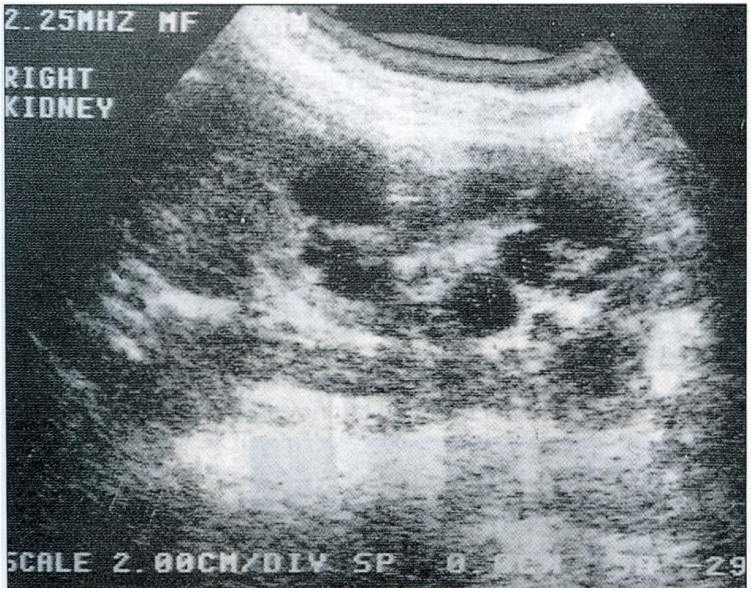


Fig.14. Ultrasound is the preferred initial investigation for kidney size, shape and position. This patient's large kidneys showed the typical appearance of polycystic kidneys. The multiple parenchymal cysts are clearly shown.

The urine-filled bladder is readily outlined by US. Normally, bladder wall contour changes depend on the amount of urine present.

MRI offers information about renal masses that cannot be determined by other techniques. It allows direct imaging in the transverse, coronal, and sagittal planes. Morphologic data are obtained from three-dimensional reconstruction of the tissue. MRI with contrast using gadolinium pentetic acid administered by bolus injection and rapid sequence imaging is increasingly used. This technique provides information about GFR and tubular function.

Morphologic procedures

Renal biopsy is performed to establish a histologic diagnosis, help estimate prognosis and the potential reversibility or progression of the renal lesion, estimate the value of therapeutic modalities, and determine the natural history of renal diseases. The only absolute contraindication to biopsy is uncontrollable bleeding.

For the percutaneous technique the patient is sedated, and the kidney is visualized by radiography or US. With the patient in the prone position, after the overlying skin and muscles of the back are anesthetized, the biopsy needle is inserted and tissue is obtained for light, electron, and immunofluorescent microscopy.

Urine cytology is useful in screening for possible urinary tract neoplasia in high-risk populations (eg, petrochemical workers, patients with painless hematuria from nonrenal causes) and in following patients after resection of bladder tumors.

THE MAJOR RENAL SYNDROMES
URIC SYNDROME
(ASYMTOMATIC PROTEINURIA AND HEMATURIA)

Uric syndrome is the most significant proof of renal disorders, moreover, the greater part of nephrologic disease manifests only by uric syndrome, as they have latent course. The major signs of this syndrome are proteinuria and hematuria (sometimes one of them prevails), at that any clinical signs of disease are not revealed (except macrohematuria, which manifests with changes of urine appearance). During urine investigation in addition to erythrocytes and protein leukocytes and casts may be detected.

ACUTE RENAL FAILURE

Clinical conditions associated with rapid (days to weeks), steadily decreasing renal function (azotemia), with or without oliguria.

Classification and Etiology

Acute renal failure (ARF) can be categorized as prerenal, postrenal, and renal (Fig.15).

COMMON CAUSES OF ACUTE RENAL FAILURE

Pre-renal failure	Intrinsic renal failure	Post-renal failure
Hypovolaemia Low cardiac output Sepsis Trauma	Rhabdomyolysis Haemolysis Drugs or nephrotoxins Glomerulonephritis Interstitial nephritis Multisystem diseases Malignant hypertension Arterial occlusion	Obstructive uropathy

Fig.15. Common causes of acute renal failure.

Prerenal and postrenal causes are potentially reversible if diagnosed and treated early; some renal causes that result in acute glomerular vascular and tubulointerstitial nephropathy also are treatable, such as malignant hypertension, glomerulonephritis, vasculitis, bacterial infections, and drug reactions.

Prerenal azotemia causes about 50 to 80% of ARF cases; inadequate renal perfusion results from extracellular fluid volume depletion or cardiovascular disease.

Postrenal azotemia is responsible for about 5 to 10% of cases; various types of obstruction in the voiding and collecting parts of the urinary system are the cause.

Intrinsic renal causes of ARF are usually associated with prolonged renal ischemia (hemorrhage, surgery) or a nephrotoxin. Acute tubulointerstitial nephritis and acute glomerulonephritis can also present as ARF.

In many patients, no single cause of ARF can be identified. Factors that initiate and those that maintain ARF may differ.

Pathophysiology

Prerenal. Oliguria (urine < 500 mL/day) results from reduced GFR and enhanced Na and water resorption, a normal response to ineffective circulating blood volume.

Postrenal. Bladder outlet obstruction is probably the most common cause of sudden, and often total, cessation of urinary output in adults. Underlying causes include benign prostatic hyperplasia, cancer of the prostate or cervix, and retroperitoneal disorders. To produce azotemia, both urinary outflow tracts or one tract in a patient with a single functional kidney must be obstructed.

Renal. Mechanisms that appear responsible for hypofiltration include a marked decrease in renal blood flow, reduced glomerular permeability, tubular obstruction from cellular and interstitial swelling or blockage from cellular debris, and diffusion of glomerular filtrate across injured tubular epithelium. These factors are interdependent, but all are not necessarily present in every patient; moreover, they vary among patients and sometimes even in the same patient.

Although the general structural integrity of the vessels appears normal, glomerular epithelial cells usually are swollen on scanning electron microscopy.

Symptoms and Signs

Symptoms and signs relate to the loss of excretory function and depend on the degree of renal dysfunction, the rate of renal failure, and the cause. In community-acquired ARF, the only finding may be the passage of cola-colored urine followed by oliguria or anuria. In hospitalized patients, ARF usually relates to some recent traumatic, surgical, or medical event, and symptoms and signs pertain to this event.

A relatively preserved urine output of 1 to 2.4 L/day is common. Oliguria may occur; anuria suggests bilateral renal artery occlusion, obstructive uropathy, acute cortical necrosis, or rapidly progressive glomerulonephritis.

Prerenal azotemia may be suggested by any disorder lowering renal perfusion. Renal artery disorders may be asymptomatic, although partial occlusion rarely causes a bruit.

Postrenal azotemia should be sought in the absence of prerenal factors. A history of difficult voiding or reduced urinary stream, an enlarged kidney, or a palpable bladder suggests urethral or bladder neck obstruction.

Intrinsic renal disease causing acute tubular injury may have three phases.

The prodromal phase varies in duration depending on causative factors (eg, the amount of toxin ingested, the duration and severity of hypotension)

The oliguric phase lasts an average of 10 to 14 days, but it varies from 1 to 2 days to 6 to 8 wk. Urine output typically varies between 50 and 400 mL/day. However, many patients are never oliguric. Nonoliguric patients have a lower mortality, morbidity, and need for dialysis. Serum creatinine typically increases by 1 to 2 mg/dL/day (90 to 180 μmol/L).

In *the postoliguric phase*, urine output gradually returns to normal; however, serum creatinine and urea levels may not fall for several more days. Tubular dysfunction may persist and is manifested by Na wasting, polyuria (possibly massive) unresponsive to vasopressin, or hyperchloremic metabolic acidosis.

Diagnosis

A progressive daily rise in serum creatinine is diagnostic of ARF. Immediately reversible prerenal or postrenal causes must first be excluded. Correction of an underlying hemodynamic abnormality with abatement of ARF confirms a prerenal cause. For postrenal causes, the potential for recovery of renal function is often inversely related to the duration of obstruction. Urinary and serum chemical analyses early in the course of ARF may help distinguish the cause.

Recommended blood tests include creatinine, antistreptolysin-O and complement titers; urine Na and creatinine; and blood and urine cultures. Characteristic laboratory findings are progressive azotemia, acidosis, hyperkalemia, and hyponatremia. Serum K concentration increases slowly. The hematologic picture is that of a normochromic-normocytic anemia with an Hct of 25 to 30%.

The urinary sediment may give valuable etiologic clues. For example, the sediment usually is unremarkable in prerenal azotemia and perhaps in obstructive uropathy, although WBCs, RBCs, and casts (granular and tubular cells) are frequently seen. With primary renal injury, the sediment characteristically contains tubular cells, tubular cell casts, and many brown pigmented granular casts. RBC casts suggest glomerulonephritis.

X-ray of the abdomen can detect 90% of urinary calculi that are radiopaque. Ultrasonography or CT is helpful because a normal or enlarged kidney favors reversibility, whereas small size suggests chronic renal insufficiency.

Renal biopsy may be performed if the diagnosis remains elusive.

Treatment

ARF can often be prevented by proper maintenance of normal fluid balance, blood volume, and BP during and after major surgery; by adequate isotonic NaCl infusions in patients with severe burns; and by prompt transfusion in hemorrhagic hypotension.

Dialysis improves fluid and electrolyte imbalances and allows adequate nutrition.

CHRONIC RENAL FAILURE

The clinical condition resulting from chronic derangement and insufficiency of renal excretory and regulatory function (uremia).

Chronic renal failure (CRF) may result from any major cause of renal dysfunction (Fig.16). The most common cause of end-stage renal disease is diabetic nephropathy, followed by hypertensive nephroangiosclerosis and various primary and secondary glomerulopathies.

MAJOR CAUSES OF END-STAGE CRF

Cause	Percentage of patients
Glomerulonephritis	25
Diabetes mellitus	25
Hypertension	10
Pyelonephritis or reflux nephropathy	10
Polycystic kidneys	10
Interstitial nephritis	5
Obstruction	3
Miscellaneous or unknown	12

Fig.16. Major causes of end-stage chronic renal failure.

The functional effects of CRF can be categorized as diminished renal reserve, renal insufficiency (failure), and uremia. The concept of renal functional adaptation explains why a loss of 75% of renal tissue produces a fall in GFR to only 50% of normal.

Plasma concentrations of creatinine and urea (which are highly dependent on glomerular filtration) begin a nonlinear rise as the GFR diminishes (Fig.17). Changes in creatinine and urea concentrations are minimal early on; when the GFR falls below 6 mL/min/m^2, levels increase rapidly and are usually associated with systemic manifestations (uremia). For substances that are excreted mainly through distal nephron secretion (eg, K), adaptation usually produces a normal plasma concentration until advanced failure occurs.

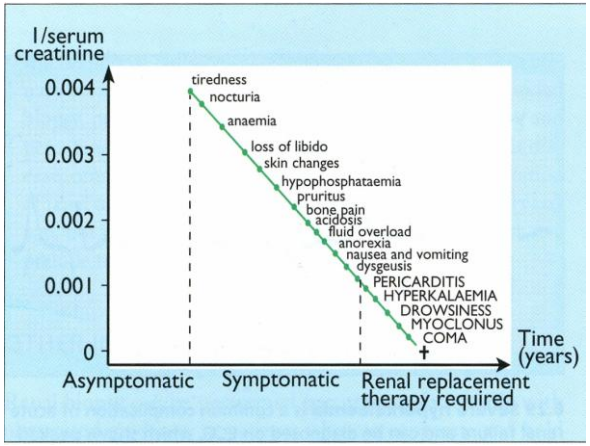


Fig.17. The typical progressive onset of the nonspecific symptoms and signs of chronic renal failure.

Classification of CRF is based on the grade of severity and characteristic clinical manifestations.

• Mild: GFR is 30—50 ml/min.
• Moderate: GFR is 10—30 ml/min.
— anemia;
— hypertension;
— osteodystrophy.
• Grave: GFR is 5—10 ml/min.
— nausea;
— anorexia;
— pruritus.
• Terminal (end-stage): GFR is < 5 ml/min.
— pericarditis;
— pulmonary edema;
— coma.

In end-stage CRF pharmacotherapy is ineffective, long-term dialysis or transplantation should be considered for prolongation of life.

Symptoms and Signs

Patients with mildly diminished renal reserve are asymptomatic, and renal dysfunction can be detected only by laboratory testing. Skin with peculiar greenish tint (urochromes retention) allows to suspect CRF. Anemia pathogenesis as a sign of renal damage is combined:

• influence of uremic toxins on a marrow;
• decrease of RBC's life span in uremia;
• kidneys' inability to produce sufficient supply of erythropoietin, essential for maintenance of marrowy erythropoiesis, in pronounced nephrosclerosis.

A patient with mild to moderate renal insufficiency may have only vague symptoms despite elevated creatinine; nocturia is noted, principally due to a failure to concentrate the urine during the night. Lassitude, fatigue, and decreased mental acuity often are the first manifestations of uremia.

Neuromuscular features include coarse muscular twitches, muscle cramps, and convulsions (usually the result of hypertensive or metabolic encephalopathy).

Anorexia, nausea, vomiting, hiccup, diarrhea, stomatitis, and an unpleasant taste in the mouth are almost uniformly present. Malnutrition leading to generalized tissue wasting is a prominent feature of chronic uremia. Skin is dry with excoriations due to pruritus, tongue is of brownish colour, dry with fetor ammonia In advanced CRF, GI ulceration and bleeding are common. Hypertension is present in > 80% of patients with advanced renal insufficiency and is usually related to hypervolemia and occasionally to activation of the renin-angiotensin-aldosterone system. Cardiomyopathy (hypertensive, ischemic) and renal retention of Na and water may lead to congestive heart failure or dependent edema. Fibrinous pericarditis, usually seen in end-stage uremia, may occur in acute, potentially reversible, uremia (Fig.18). It is manifested by severe retrosternal pain, effusion addition is accompanied by dyspnea and other signs of heart tamponade.

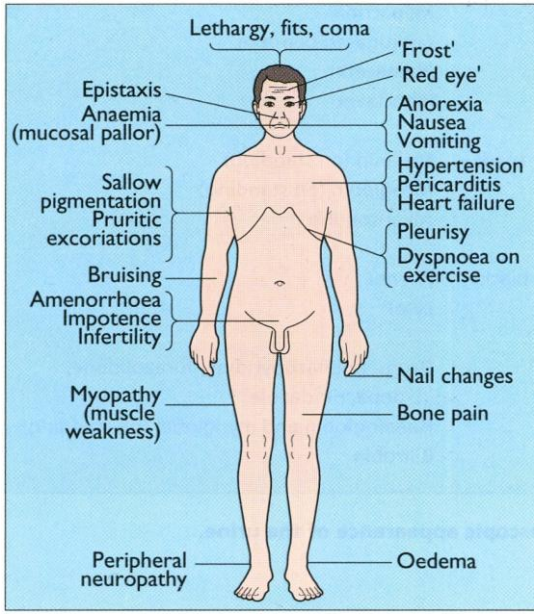


Fig.18. Chronic renal failure: common symptoms and signs.

The skin may appear yellow-brown; occasionally, urea from sweat may crystallize on the skin as uremic frost. Pruritus is especially uncomfortable for some patients.

Abnormalities with lipid metabolism also occur with CRF, on dialysis, and after renal transplantation. The primary finding in CRF and dialysis is hypertriglyceridemia; the total cholesterol level is usually normal.

Diagnosis

The first step is to determine whether the renal failure is acute, chronic, or acute superimposed on chronic. Progression to CRF is common when the serum creatinine concentration is > 1.5 to 2 mg/dL. This may occur even if the underlying disorder is not active. Obtaining a precise diagnosis becomes increasingly difficult as the patient approaches end-stage renal disease. The definitive diagnostic tool is renal biopsy, but it is not recommended when ultrasonography indicates that the kidneys are small and fibrotic.

Urea and creatinine are elevated. Plasma Na concentrations may be normal or reduced. The serum K is normal or only moderately elevated (< 6 mmol/L).

Usually, moderate anemia is characteristic. The anemia of CRF is normochromic-normocytic, with an Hct of 20 to 30%. It is usually caused by deficient erythropoietin production due to a reduction of functional renal mass. Other causes include deficiencies of iron, folate, and cyanocobalamin. Urinary volume does not respond readily to variations in water intake. Findings on urinalysis depend on the

nature of the underlying disease, but broad (especially waxy) casts often are prominent in advanced renal insufficiency of any cause.

Treatment

Factors aggravating or producing CRF (eg, Na and water depletion, nephrotoxins, heart failure, infection, hypercalcemia, obstruction) must be treated specifically. However, progression of underlying chronic renal disease generally does not respond to specific treatment. If uremia results from a progressive and untreatable disorder, conservative management is palliative until dialysis or transplantation is required.

Diet should receive meticulous attention as CRF progresses from moderate to end-stage disease. Anorexia requires evaluation of caloric intake. Increased caloric intake should be coupled with reduced dietary protein. Endogenous protein catabolism is minimized by providing sufficient carbohydrate and fat to meet energy requirements and prevent ketosis. A mixed-protein diet, including low-quality protein for variety, improves patient acceptance. The equivalent of daily urinary protein loss should be added. Many uremic symptoms (fatigue, nausea, vomiting, twitching, confusion) markedly lessen when protein catabolism and urea generation are reduced, although a slowing effect on continued GFR reduction is modest. It may be possible to defer dialysis or transplantation for a short time.

Because dietary restrictions may reduce necessary vitamin intake, patients should take a multivitamin preparation containing water-soluble vitamins. Administration of vitamin A or E is unnecessary.

Fluid and electrolyte levels are an important aspect of management. Hyperkalemia is infrequent (except for K-sparing diuretic therapy) until end-stage renal failure, when intake may need to be restricted. More severe hyperkalemia (> 6 mmol/L) warrants urgent treatment if the ECG demonstrates hyperkalemic changes (Fig.19).

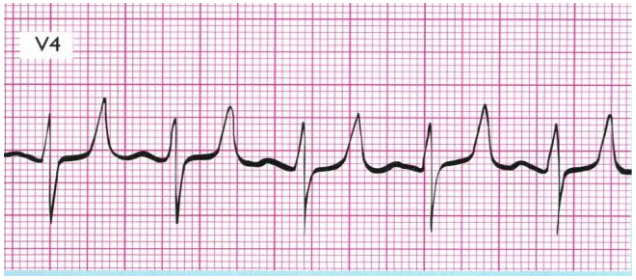


Fig.19. Severe hyperkalaemia is a common complication of acute renal failure and can be diagnosed on ECG, which shows peaked and symmetrical T waves. Hyperkalaemia is an indication for urgent dialysis; other indications include pulmonary oedema, severe acidosis and pericarditis.

Anemia is treated to keep the Hct between 30 and 36%. Anemia slowly responds to recombinant human erythropoietin. Due to increased iron utilization with stimulated erythropoiesis, iron stores must be replaced, usually with parenteral iron.

The bleeding tendency in CRF can be lessened by RBC, platelet, or cryoprecipitate infusions.

Congestive heart failure, most commonly due to Na and fluid retention by the kidney, responds to Na restriction and diuretics.

Moderate or severe hypertension should be treated to avoid its deleterious effect on cardiac and renal function. Pruritus may respond to ultraviolet phototherapy.

Activity need not be restricted, because fatigue and lassitude usually keep it within acceptable limits.

When conventional therapy is no longer effective, long-term dialysis (Fig.20 & 21) or continuous peritoneal dialysis (Fig.22 & 23) or transplantation (Fig.24 & 25) should be considered.

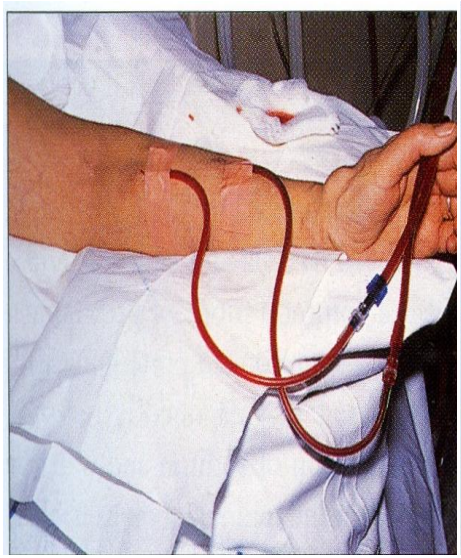


Fig.20. Vascular access for long-term hemodialysis is usually provided through a surgically created arteriovenous fistula. Blood leaves the patient through the distal needle to pass through the dialyser before returning to the patient through the proximal needle. Patients usually become adept at inserting their own needles.

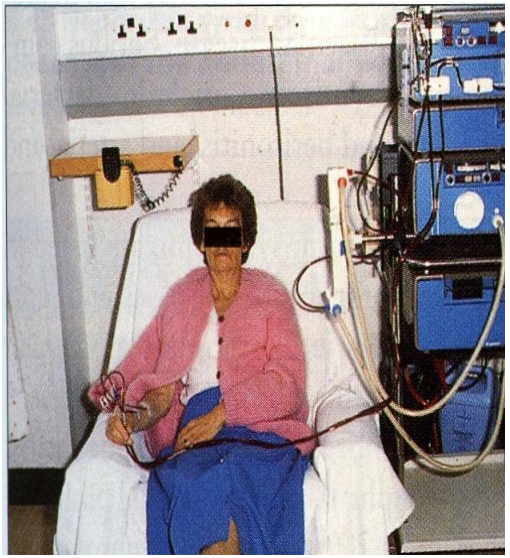


Fig.21. Typical patient with chronic renal failure undergoing hemodialysis in a hospital setting. In some countries, including the UK, many patients carry out this treatment on a long- term basis in a specially converted room at home.

Fig.22. Continuous ambulatory peritoneal dialysis (CAPD) is a simpler and less restricting technique than haemodialysis, and is compatible with a virtually normal lifestyle. Bags need only be connected to the peritoneal catheter four times per day during exchanges of fluid.

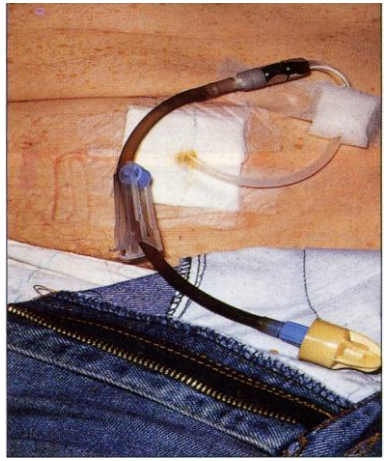


Fig.23. The Tenckhoff peritoneal dialysis catheter remains implanted in the CAPD patient, but it can be simply strapped to the abdominal wall when not in use for fluid exchanges.

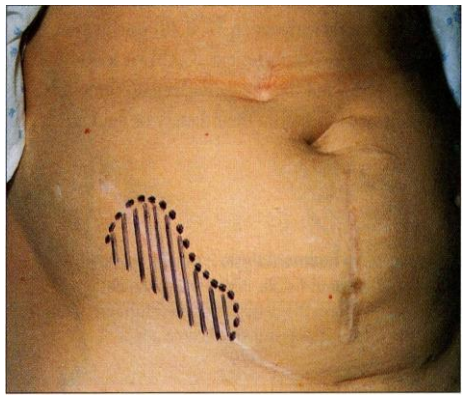


Fig.24. Renal transplant — typical surface markings. The kidney is usually implanted extraperitoneally in either the right or left iliac fossa, and it can be easily palpated.
Percutaneous biopsy is also simple when necessary.

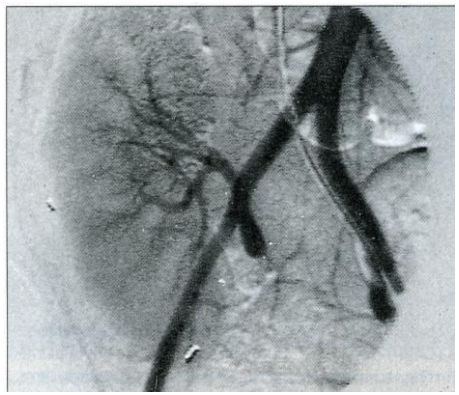


Fig.25. Normal renal transplant in situ. This digital subtraction angiogram shows the normal site for a renal transplant.

NEPHROTIC SYNDROME

The nephrotic syndrome is characterized by the combination of heavy proteinuria, hypoalbuminaemia and oedema (Fig.26, 27 & 28) and is a common mode of presentation in a variety of glomerular diseases.

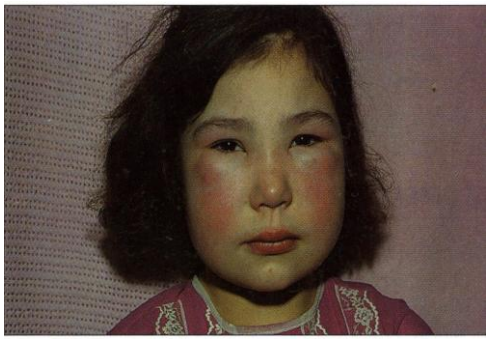


Fig.26. Nephrotic syndrome in childhood. Note the gross facial and periorbital edema, which was associated with gross proteinuria.

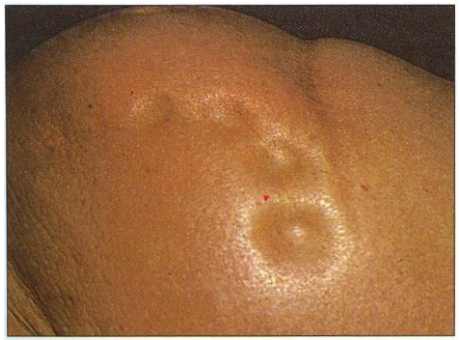


Fig.27. Nephrotic syndrome — gross pitting edema of the abdominal wall, secondary to severe hypoalbuminaemia.

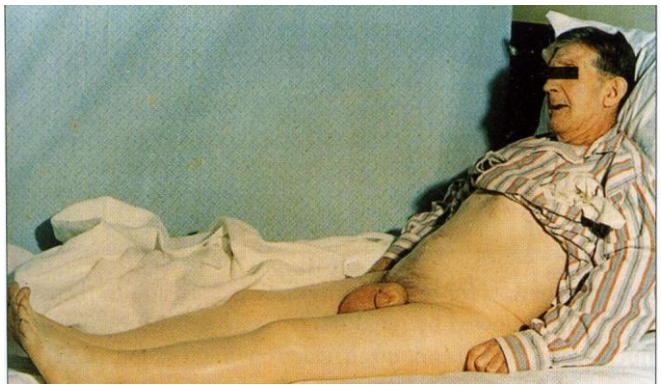


Fig.28. Nephrotic syndrome — a typical adult patient. He is breathless as a result of pulmonary edema and has edema of the ankles, calves, scrotum and penis. He has abdominal swelling as a result of edema of the abdominal wall, and ascites.

Prolonged proteinuria leads to hypoalbuminaemia, decreased plasma oncotic pressure, hypovolaemia, subsequent retention of sodium and water by the kidney caused by activation of the renin—angiotensin—aldosterone axis and accumulation of fluid in the extravascular space. Hypercholesterolemia is frequently present and may be a consequence of increased hepatic synthesis of cholesterol as well as albumin.

Prolonged hypercholesterolaemia may lead to premature corneal arcus (Fig.29) and vascular disease.

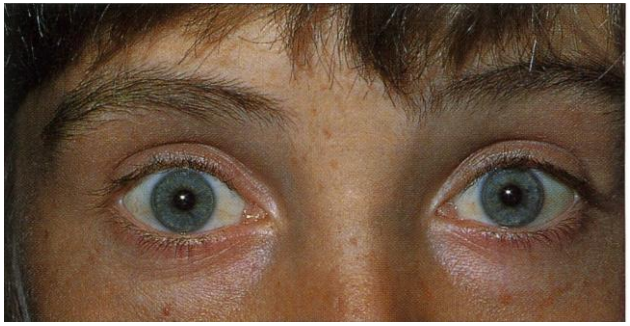


Fig.29. Premature corneal arcus in a 15-year-old boy with chronic nephrotic syndrome. This was associated with hypercholesterolaemia, and is indicative of a risk of premature vascular disease.

Serious complications of the nephrotic syndrome include bacterial infections, particularly cellulitis and peritonitis, and arterial and venous thrombotic episodes.

The major causes of the nephrotic syndrome are listed in Fig.30.

CAUSES OF NEPHROTIC SYNDROME

Glomerulonephritis
Diabetes mellitus
Amyloidosis
Multisystem disease
Drugs: gold, penicillamine, heroin, captopril
Neoplasia
Infection
Heredofamilial disorders

Fig.30. Causes of nephrotic syndrome.

No systemic cause is evident in 80% of cases and renal biopsy in such patients shows a variety of primary glomerular diseases. Almost 20% of cases of nephrotic syndrome are caused by renal involvement from systemic disease (e.g. diabetes meffitus, amyloidosis) and the remainder are caused by drugs, neoplasia or rare heredital disorders.

The nonspecific treatment of the nephrotic syndrome involves fluid and dietary sodium restriction, high protein intake and judicious use of diuretics. A mild degree of ankle edema late in the day while on treatment is desirable, in order to avoid complications from hypovolemia. Infusions of albumin should be reserved for patients

with gross hypovolemia or refractory edema. Renal outcome is dependent on the underlying cause of the nephrotic syndrome. Corticosteroid treatment is of value in patients with minimal change glomerular lesions, and may have a role in some other forms of glomerulonephritis.

ACUTE NEPHRITIC SYNDROME

In the acute nephritic syndrome (acute nephritis) there is an abrupt onset of haematuria and proteinuria accompanied by evidence of salt and water retention and reduced renal function. The clinical features are periorbital puffiness, ankle edema, brown or cola-coloured urine and hypertension. Sometimes the patient or his or her parents may also notice a reduction in urine volume. All patients have hematuria and proteinuria on urinalysis, but the degree of renal impairment is variable. Glomerular bleeding in patients with nephritis can be confirmed by demonstrating red-cell casts in the urinary sediment.

Acute nephritis may result from:

• Infection: poststreptococcal glomerulonephritis, infective endocarditis or shunt nephritis

• Multisystem disease: systemic lupus erythematousus (SLE), vasculitis

• Primary glomerulonephritis.

Evidence of infection or extrarenal involvement should therefore be sought in all patients with acute nephritis. It is important to establish the underlying cause of the nephritic syndrome as soon as possible, as renal outcome can be improved when specific therapy is started promptly.

RENAL HYPERTENSION

Renal disease is the most common cause of secondary hypertension and should be excluded in all young hypertensive patients. Causes of renal-mediated hypertension can be classified into vascular diseases and parenchymal diseases (Fig.31).

CAUSES OF RENAL HYPER-TENSION

Vascular diseases
Atheromatous renal artery stenosis
Fibromuscular renal artery hyperplasia
Renal infarction
Renal vasculitis
Systemic sclerosis

Parenchymal diseases
Glomerulonephritis
Chronic pyelonephritis
Polycystic kidney disease
Multisystem disease
Hydronephrosis

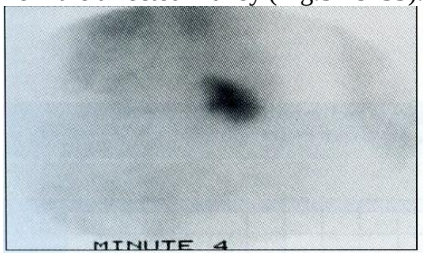
Fig.31 Causes of renal hypertension.

The clinical features associated with hypertension depend on the underlying disease. Renal artery stenosis may be caused by atheroma or fibromuscular hyperplasia.

• Atheromatous renal artery stenosis should be suspected in patients with severe hypertension presenting in middle age or later without other evidence of renal disease; often these patients are heavy smokers and there is evidence of widespread atherosclerosis. This is now a relatively common problem in elderly patients, who may present with acute renal failure, CRF or end-stage renal failure requiring dialysis at presentation

• Fibromuscular hyperplasia is more common in women, appears most often in the third or fourth decades, and is frequently bilateral.

A bruit may be heard over the flank, and biochemical investigation often reveals evidence of secondary hyperaldosteronism. Screening for unilateral renal artery stenosis is best performed by ultrasound, which may show unequal-sized kidneys, and the diagnosis can be confirmed noninvasively by isotope renogram. The renogram shows delayed perfusion, delayed uptake, and a reduced rate of excretion of isotope from the affected kidney (Fig.32 & 33).



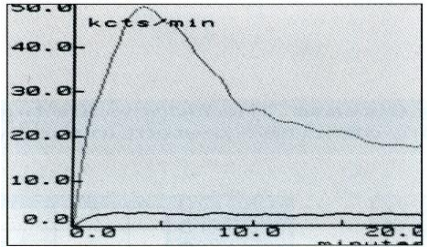


Fig. 32 & 33. ^{99}mTc-renogram in a patient with left renal artery stenosis. The minute 4 static renogram (32) shows the right kidney clearly, but the outline of the left kidney is not seen. The dynamic renogram (33) shows a very low count over the left kidney, which remains more or less constant, whereas the count over the right kidney shows a normal peak and decline. These appearances are typical of unilateral renal artery stenosis.

Identification of renal artery stenosis can then be accomplished by arteriography (Fig.34).

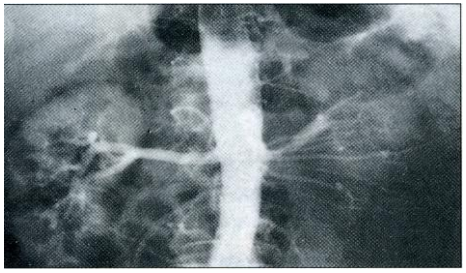


Fig.34. Renal artery stenosis. There is an atheromatous stricture of the left renal artery with slight poststenotic dilatation and a reduction in left renal size.

Hypertension caused by fibromuscular disease is cured in more than 90% of patients after renovascular surgery. In patients with atherosclerotic disease, the failure rate after either surgery or angioplasty is much higher and corrective procedures are often restricted to patients who have severe renal failure or poorly controlled hypertension on medical therapy.

Renal disease may ultimately develop in about one-half of patients with systemic sclerosis, often with the sudden onset of severe hypertension and progression to end-stage renal failure within months. Renal biopsy shows gross intimal thickening and reduction in the lumen of the interlobular arteries. Control of hypertension may be difficult and, if renal failure develops, recovery of renal function is unlikely.

Renoparenchymal hypertension is caused by Na and water retention as a result of pressor system (rennin-angiotensin-aldosterone) activation and depressor system (prostaglandin and kallikrein- kinin) depression.

Causes of hypertension may be bilateral (glomerulonephritis, diabetic nephropathy, tubulointerstitial nephritis, polycystic kidney disease) and unilateral (pyelonephritis, tumour, trauma, solitary kidney cyst, hypoplasia, tuberculosis) renal disorders. In pathogenesis of renoparenchymal hypertension hypervolemia and hypernatriemia due to reduction of functioning nephrons and rennin-angiotensin system activation; increase of total peripheral vascular resistance in the presence of normal or decreased cardiac output play important role. The most frequent cause of renoparenchymal hypertension is glomerulonephritis.

Clinical picture is determined by the level of BP elevation and evidence of heart and vessels damage. Patients present complaints on headache, impaired vision, heart pain, dyspnea. Malignant hypertension is characterized by particular high and steady diastolic BP, pronounced retinopathy (with hemorrhages, papilledema, plasmorrhagia, not seldom with poor sight up to blindness), hypertensive encephalopathy, heart failure.

The main distinctive signs of renoparenchymal hypertension are premature renal disease, urinalysis changes (proteinuria >2g/day, hematuria, casts, leukocytes, high blood level of creatinine), ultrasound signs of renal disorders. Changes in urinalysis usually precede BP elevation.

GLOMERULONEPHRITIS

Glomerular diseases may be classified on a three-tier basis:

• Clinical syndromes

• Histological appearances

• Etiology.

Glomerular disease may lead to a variety of clinical syndromes, including asymptomatic proteinuria, hematuria, acute nephritis, nephrotic syndrome and slowly or rapidly progressive renal failure.

There is a degree of correlation between the histological appearance of the glomeruli (Fig.35) and the clinical presentation (Fig.36).

Diffuse:	all of the glomeruli are uniformly involved
Focal:	some of the glomeruli are involved
Segmental:	only part of the glomerular tufts are involved
Crescentic:	at least 70% of the glomerular tufts are compressed by crescents (proliferation of macrophages and epithelial cells of Bowman's capsule)

Fig.35. Terminology used in the histological description of glomerular lesions.

HISTOLOGICAL / CLINICAL CORRELATION	
Histological type	**Clinical features**
Minimal change glomerulonephritis	Nephrotic syndrome
Focal and segmental glomerulosclerosis	Nephrotic syndrome, progressive renal failure
Membranous glomerulonephritis	Nephrotic syndrome
Mesangiocapillary glomerulonephritis	Haematuria, proteinuria, acute nephritis, progressive renal failure
Mesangial proliferative glomerulo-nephritis	Haematuria, proteinuria
Diffuse endocapillary proliferative glomerulonephritis	Acute nephritis, progressive renal failure

Fig.36. Correlation between histology and clinical picture in primary glomerulopathy.

The histological appearance often provides a valuable guide to prognosis and likely response to therapy.

Investigations in glomerular disease should usually include the renal biopsy, with assessment of light- microscopic (Fig.37) and, often, electron-microscopic (Fig.38) and immunofluorescence-microscopic appearances.

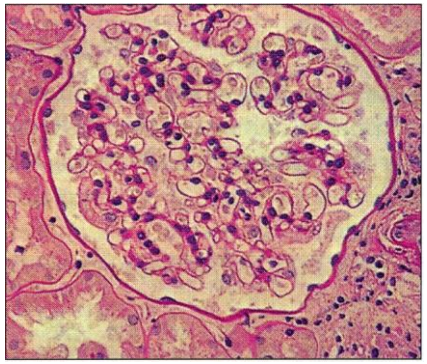


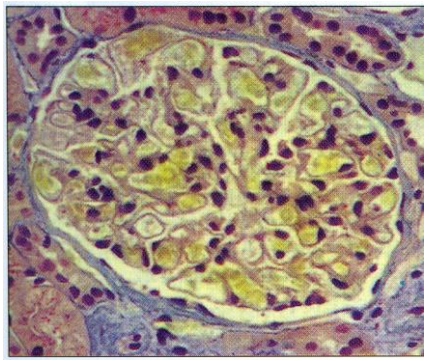
Fig.37 A normal glomerulus.

Fig.38 The ultrastructure of the normal glomerulus as seen on electron microscopy: 1 = capillary lumen; 2 = epithelial cell; 3 = basement membrane; 4=red blood cell; 5=epithelial foot processes; 6=endothelial cell; 7 = mesangial matrix; 8 = mesangial cell.

Due to histological appearance glomerulopathy may be classified in following order.

Minimal change glomerulonephritis (Fig.39 & 40).

The nephrotic syndrome is the clinical presentation in almost all cases of minimal change glomerulonephritis, but occasionally asymptomatic proteinuria may be the only abnormality. Hypertension and haematuria are both rare. The disease is the underlying cause in more than 80% of children and almost 20% of adults with the nephritic



Fig, 39. Minimal change glomerulonephritis showing a normal glomerulus on light microscopy of a renal biopsy.

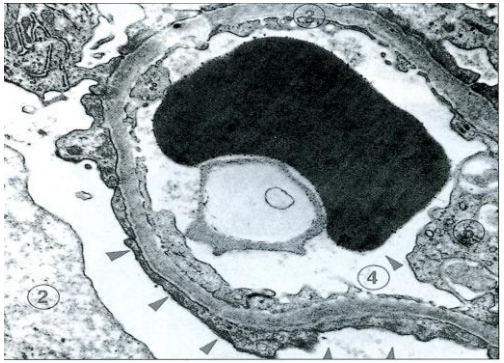


Fig.40. Minimal change glomerulonephritis. Electron micrograph showing fusion of the epithelial foot processes (arrowed) and absence of electron-dense deposits.

syndrome and a biopsy is indicated in all cases.. Renal prognosis in this condition is very good, even though a few patients may develop acute renal failure as a result of overuse of diuretics.

Focal and segmental glomerulosclerosis

Patients with focal and segmental glomerulosclerosis most commonly present with nephrotic syndrome; this disease is the underlying cause in almost 10% of child nephrotics. Autoantibodies and complement studies are normal. Renal biopsy shows segmental areas of sclerosis, initially only in the juxtamedullary glomeruli, without evidence of cellular proliferation or necrosis (Fig.41). Immunofluorescence microscopy often shows deposition of 1gM and C_3 in affected glomeruli.

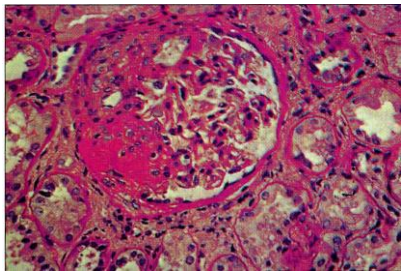


Fig.41. Focal and segmental glomerulosclerosis. The segmental sclerosis is clearly seen on light microscopy of a renal biopsy.

As glomerular involvement is at first focal, early cases may be indistinguishable from minimal change glomerulonephritis even on renal biopsy. This disease may be suspected if the nephrotic syndrome in childhood is resistant to steroid therapy or runs a relapsing and remitting course. In more than 50% of patients renal function declines progressively and 20—40% of patients reach end-stage renal failure after 10 years.

Membranous glomerulonephritis

Membranous glomerulonephritis is the most common cause of adult-onset nephrotic syndrome, but is rare in childhood. Microscopic haematuria is common and hypertension is present in around one-third of patients at presentation. The diagnosis is confirmed by the presence of diffuse uniform thickening of the glomerular capillary wall in all glomeruli (Fig.42), associated with subepithelial electron-dense deposits on electron microscopy (Fig.43) and diffuse granular capillary-loop IgG on immunofluorescence microscopy. Most cases are idiopathic, but it is important to exclude associated infection (syphilis, hepatitis B), neoplasia or drug therapy (gold, penicillamine, captopril).. If untreated, 20% of the idiopathic group remit spontaneously and up to 30% reach end- stage renal failure after 10 years.

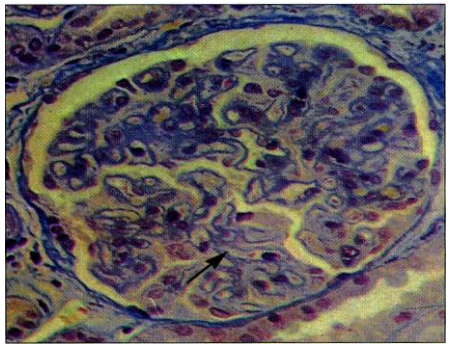


Fig.42 Membranous glomerulo-nephritis. The renal biopsy shows uniform thickening of the capillary basement membranes (arrow).

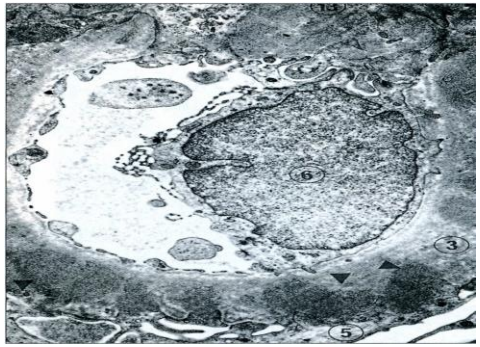


Fig.43. Membranous glomerulo-nephritis. Electron micrograph showing markedly thickened basement membrane with electron-dense deposits (arrowed) representing deposits of antigen—antibody complexes located subepithelially, that is beneath the fused epithelial cell foot processes.

Mesangiocapillary glomerulonephritis

The mode of presentation of mesangiocapillary glomerulonephritis is variable: 20% of patients have the acute nephritic syndrome, whereas all of the remaining patients have proteinuria; 50% have hypertension, 50% have renal failure and 30% have haematuria. The disease mainly affects school-age children and young adults and is more common in females. Its frequency is falling in the developed world. Serum C3 levels are reduced transiently in Type 1 and are persistently low in Type 2 (Fig.46). These are differentiated from each other on renal biopsy. The histological feature common to both types of disease is a combination of mesangial cell proliferation and thickening of the glomerular capillary wall on light microscopy (Fig.44). In the subendothellal type (Type 1) there is interposition of gial matrix between the endothelial cells and glomerular basement membrane, subendothelial deposits on electron microscopy (Fig.45) and granular deposition of IgG and C3 on immunofiuorescence microscopy.

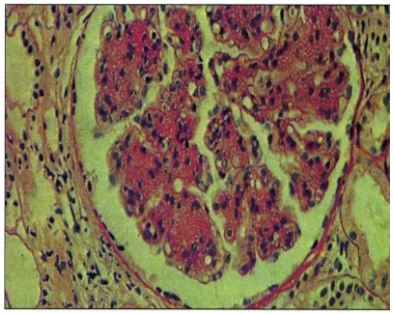


Fig.44. Mesangiocapillary glomerulonephritis. Light microscopy showing an increase in mesangial cells and matrix and patchy thickening of the basement membrane. This glomerulus also shows marked lobulation of the glomerular tufts.

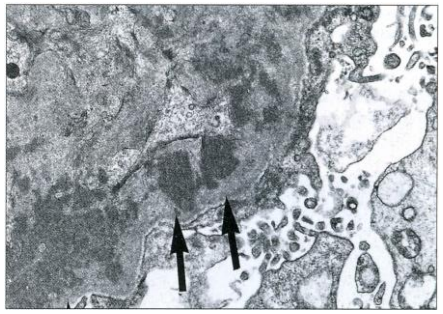


Fig.45. Mesangiocapillary glomerulonephritis. Electron micrograph showing subendothelial electron-dense deposits (arrowed) in a patient with Type 1 mesangiocapillary glomerulonephritis (Magnification x13200).

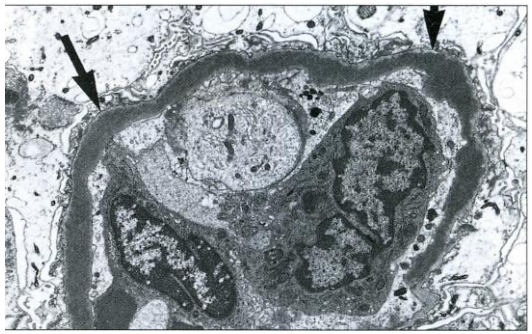


Fig.46. Mesangiocapillary glomerulonephritis. Electron micrograph from a patient with Type 2 mesangiocapillary glomerulonephritis (dense-deposit disease) showing linear dense intramembranous deposits (arrows) (Magnification x5200).

There is no specific therapy for this form of glomerulonephritis and the renal prognosis is relatively poor: more than 50% of patients reach end-stage renal failure after 10 years.

Mesangial proliferative glomerulonepliritis

Recurrent macroscopic haematuria, often within 2 days of an upper respiratory tract infection, was the most common mode of presentation of this disorder; however, as a result of routine urinalysis many patients are now detected with microscopic haematuria or asymptomatic proteinuria, or both. Peak incidence is in young adults, and men are more commonly affected. Renal failure at presentation is uncommon.

Autoantibodies and complement studies are usually normal. Renal biopsy shows increased mesangial cells and mesangial matrix (Fig.47).

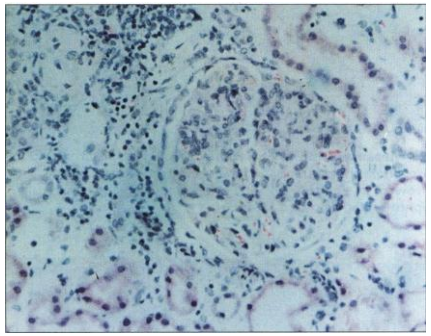


Fig.47 Mesangial proliferative glomerulonephritis. Light microscopy of a glomerulus from a patient with microscopic haematuria and asymptomatic proteinuria showing an increase in mesangial cells and matrix.

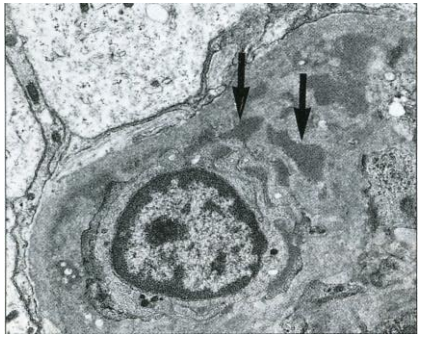


Fig.48 Mesangial proliferative glomerulonephritis. Electron micrograph showing electron-dense deposits distributed within the mesangium (arrows) (Magnification x13 200).

These light- microscopic appearances are associated with the presence of mesangial deposits on electron microscopy (Fig.48) and commonly with mesangial deposition of IgA on immunofluorescence microscopy, so-called IgA nephropathy (Berger's disease). There is no specific treatment for IgA nephropathy, but the overall prognosis is good. Only 5—10% of patients with IgA nephropathy reach end-stage renal failure after 10 years.

Diffuse endocapillary proliferative glomerulonephritis

Patients with diffuse endocapillary proliferative glomerulonephritis usually present with acute nephritis, although not all features may be evident. The condition is more frequent in children and young adults. In some patients, the onset of renal disease is associated with an extrarenal infection 10—14 days earlier, but most cases are idiopathic.

Classically, this disease is preceded by ***a nephritogenic group A streptococcal infection***, usually of the throat or skin. However, the frequency of isolating streptococcus from the presumed site of infection, or demonstrating a rise in antibody titre to streptococcal antigens (*anti-streptolysin 0 titre*), is relatively low. Autoantibodies are negative and serum C3 levels are usually transiently decreased. Renal biopsy is characterized by hypercellularity in all of the glomeruli (Fig.49), not infrequently associated with crescent formation (Fig.50).

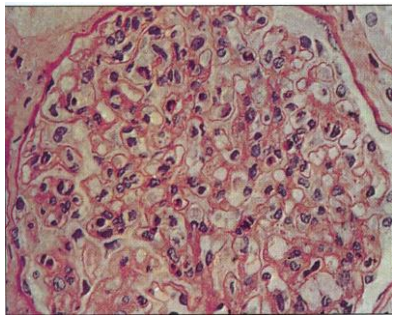


Fig.49. Diffuse endocapillary proliferative glomerulonephritis. The glomerulus shows increased cellularity, caused by endothelial and mesangial cell proliferation and polymorph infiltration

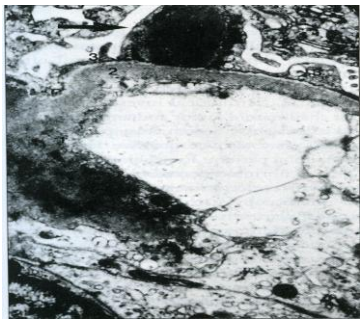


Fig.50 Diffuse endocapillary proliferative glomerulonephritis. The electron micrograph shows a large subepithelial electron-dense deposit (arrowed)

Electron microscopy in the acute stage shows large subepithelial electron-dense deposits and immunofluorescence microscopy shows granular staining of IgG and C_3 within the glomeruli. The prognosis in poststreptococcal glomerulonephritis is generally good, and the only specific treatment recommended is a 7-day course of penicillin. Complete recovery is common, and less than 5% of patients reach end-stage renal failure after 10 years. The latter is more likely in adult patients with persistent hypertension or nephrotic syndrome, and in patients with rapid progressive renal failure. The long-term outcome for the larger idiopathic group is less well defined, but is again generally good if there is early regression of features of renal disease.

ACUTE DIFFUSE GLOMERULONEPHRITIS

Acute immune renal inflammation with predominant glomerular affection and clinically manifested by acute nephritic syndrome.

Etiology and Pathogenesis.

The most frequent cause is streptococcal infection (tonsillitis, scarlet fever, erysipelatous inflammation, pneumonia). Except β-hemolytic A group streptococcus (12^{th} culture of this streptococcus, called nephritogenic due to its affinity to basement membrane), acute glomerulonephritis may occur under other antigenic influences (vaccination, serum and medications introduction). In some cases cooling may play role of nephritogenic factor.

Blood immune complexes formation and their precipitation on glomerular basement membrane with damage of the latter causes complex autoimmune inflammatory process with increased vascular permeability and other changes, conditioning disease signs.

Clinical manifestations.

There is typical cyclic course of acute glomarulonephritis, characterized by stormy onset and development of classical signs, such as hematuria (cloudy urine in

the form of “meat slops”) with proteinuria, edemas with oliguria and weight gain due to liquid retention, hypertension and rapid amelioration after increase of diuresis, disappearance of edemas and BP normalization.

In the height of disease due to large Na and water retention pronounced hypervolemia develops, which may cause acute left-sided heart failure with dyspnea, asthma (cardiac asthma), pulmonary edema; sometimes decrease of GFR and azotemia are established.

Except cyclic course of acute glomerulonephritis, terminating, as a rule by complete recovery, acute glomerulonephritis with protracted course and prevalence of nephrotic syndrome clinical and laboratory signs, not rarely transforming to chronic glomerulonephritis, and latent (low-grade) form of acute glomerulonephritis, beginning gradually (with moderate face puffiness and moderate changes in urine) and also frequently transforming to chronic glomerulonephritis, are distinguished.

It is necessary to bear in mind possibility of dangerous complications development in the height of disease: acute heart failure with cardiogenic pulmonary edema, eclampsy with typical convulsive syndrome, cerebral hemorrhage, ARF with anuria, azotemia, hyperkaliemia, uremic pulmonary edema and transient blindness.

Treatment

In stormy course of disease strict bed rest in the hospital and dietotherapy (vegetable and milk diet) with maximal exception of salt and restriction of water (according to diuresis) and animal protein intake. Diuretic and antihypertensive medications are administered. Glucocorticoids administration is possible in presence of nephrotic syndrome.

CHRONIC GLOMERULONEPHRITIS

Chronic immune renal inflammation, in outcome of which CRF usually develops. As stated above, term “glomerulonephritis” means predominant involvement of renal glomeruli in inflammatory process, but that or another degree of tubulointerstitial structures changes are also detected. If latter prevail, one says about tubulointerstitial nephritis (acute or chronic). In majority of cases chronic glomerulonephritis has latent onset, at that urinal abnormality and other clinical signs of disease are disclosed occasionally (check-up of adolescents, students, pregnant women, etc.).

Classification

Modern approach in classification — division of glomerulonephritis due to histological changes on biopsy (see above). But clinical evaluation of disease is very important as usual. In Russian Federation E.M.Tareev's classification of chronic glomerulonephritis (1958, 1972) is spread:

• *clinical forms*: latent (chronic glomerulonephritis with isolated uric syndrome), hematuric, hypertensive, nephrotic, combined (nephritic syndrome in combination with hypertension).

• *phases*: exacerbation and remission.

Etiology

Above all it is necessary to mention infection (streptococcus, hepatitis viruses B and C, measles, rubella, herpes simplex viruses, cytomegalovirus), parasitic invasions

(schistosomiasis, malaria), and also medications (gold medications, penicillamine, vaccines, serum), alcohol, organic vehicles, mercury-containing substances, lead, cadmium and other metals as etiologic factors of chronic glomerulonephritis. The latter as well as antibiotics and nonopioid analgetics cause severe damage of tubulointerstitial apparatus of kidney with development of clinical picture of tubulointerstitial nephritis.

Pathogenesis

In the base of chronic glomerulonephritis pathogenesis are the mechanisms, similar to those in acute glomerulonephritis. In overwhelming number of cases immune complex, containing different antigens, antibodies to them and complement, is formed in blood (circulating immune complex), and only in a little amount of patients immune complex is formed in situ (on glomerular basement membrane), because in this case there is formation of antibodies to basement membrane itself. After immune complex formation known immune inflammatory reactions appear, leading to glomerular morphologic changes, peculiarities of them allow to mark out definite histological types of chronic glomerulonephritis.

Clinical manifestations

Clinical picture of the most spread form – latent - is revealed by only changes in urine (disclosure of protein and erythrocytes in a little amount). If hematuria is prominent (> 20—30 RBCs in a field of view, macrohematuria episodes are frequent) hematuric glomerulonephritis is diagnosed. Nephrotic variant is characterized by prominent proteinuria (>3,5 g/day) with oliguria and different evidence of edema (from mild puffiness of face to anasarca with presence of effusion in pleural peritoneal and pericardial cavities); hypoproteinemia (hypoalbuminemia) and hyperlipidemia (hypercholesterolemia) are also characteristic. In hypertensive variant of chronic glomerulonephritis hypertension with respective changes of fundus, left ventricular hypertrophy is leading syndrome, at that urine changes are minimal. The most striking clinical variant of chronic glomerulonephritis is combined, clinical picture of which includes simultaneously two major renal syndromes: nephrotic and hypertensive. This combination makes last variant the most severe in its course and prognosis.

RENAL AMYLOIDOSIS

The most common mode of presentation of amyloidosis in the kidney is the nephrotic syndrome associated with renal failure. Even in advanced renal failure, the kidneys may remain relatively large because of the deposition of amyloid. Clinically evident renal disease is more frequent in primary than secondary amyloidosis. Congestive cardiomyopathy, hepatosplenomegaly, peripheral neuropathy and malabsorption may result from systemic deposition of amyloid.

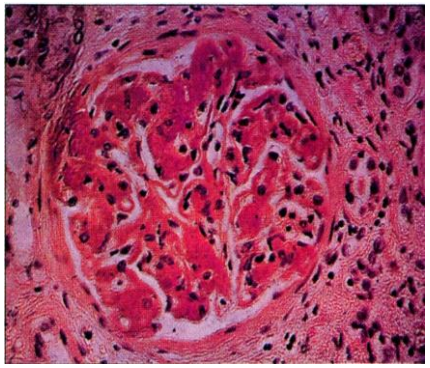


Fig.51 Renal amyloidosis. The glomerulus shows amyloid deposition, stained by Congo Red, in the glomerular capillaries (x330).

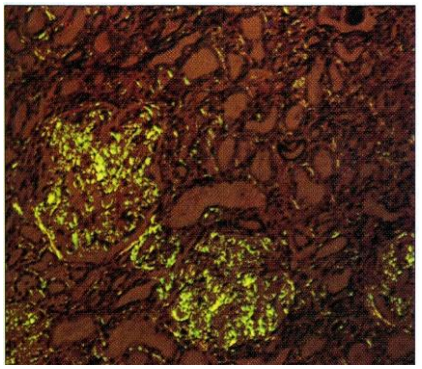


Fig.52 Renal amyloidosis. This Congo Red stained renal biopsy has been examined by polarized light to show the apple-green birefringence caused by amyloid deposition within the glomeruli and around the tubules (x198).

At the ultrastructural level, amyloid consists of protein fibrils and a glycoprotein known as amyloid P component. Two forms of fibril protein are found: amyloid light-chain (AL) proteins are found in myeloma-associated and primary amyloidosis, and amyloid A (AA) fibril proteins are found in amyloidosis secondary to chronic infections, rheumatoid arthritis or familial Mediterranean fever. Rectal or renal biopsy confirms the diagnosis. Renal biopsy sections stained with Congo Red show pink-red deposition within the glomeruli and blood vessel walls (Fig.51), which under polarized light exhibits apple-green hirefringence (Fig.52). Electron microscopy of the amyloid deposits shows a characteristic arrangement of fibrils, and immunofluorescence microscopy for immunoglobulin and complement is negative. Monoclonal antibodies can be used to differentiate amyloid light-chain and amyloid A proteins.

There is no specific treatment for amyloidosis, although renal function may stabilize after chemotherapy in patients with myeloma-associated amyloidosis, or coichicine in patients with familial Mediterranean fever. The prognosis for renal function in most cases is poor, and more than 50% of patients with biopsy- proven amyloidosis reach end-stage renal failure within 1 year.

HYPERTENSIVE NEPHROPATHY

(Damage of target organ in hypertensive disease)

In hypertensive nephropathy, renal failure results from inadequately treated hypertension in the absence of primary renal disease. Long-standing moderate hypertension in itself can lead to hyaline thickening of the intrarenal arterial walls, patchy ischemic atrophy and glomerulosclerosis. Patients with benign hypertensive nephrosclerosis usually present with CRF’ and mild proteinuria, without hematuria or other evidence of glomerulonephritis. Renal impairment often stabilizes if adequate, long-term control of hypertension is achieved.

Accelerated nephrosclerosis is a dramatic complication of malignant hypertension, which commonly caused progressive or acute renal failure before effective antihypertensive drugs were available. The two essential clinical features are the presence of severe hypertension and grade IV retinopathy. Cardiac failure, hypertensive encephalopathy, renal failure, secondary hyperaldosteronism and microangiopathic haemolytic anaemia may accompany the onset of malignant hypertension. The malignant phase may complicate essential and all forms of secondary hypertension. Renal biopsy may be required to determine whether there is underlying renal disease or whether renal failure is a direct consequence of severe hypertension. The histological features of malignant hypertension are fibrinoid necrosis of the afferent arterioles, and endarteritis of the interlobular and arcuate arteries that results in ischaemic atrophy or infarction distal to the abnormal vessels (Fig.53).

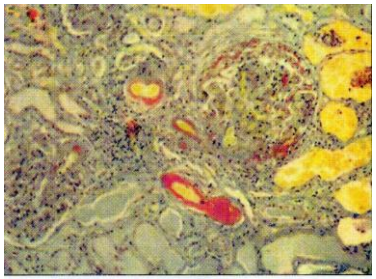


Fig.53 Malignant hypertension. The renal biopsy shows fibrinoid necrosis in the arterial and glomerular capillaries and haemorrhage into the renal tubules

High blood pressure should be lowered gradually, to lessen the risk of a sudden drop in blood pressure either precipitating cerebral infarction or worsening renal function. In many patients, renal function may recover or at least stabilize once blood pressure is controlled and the prognosis depends on whether or not there are cardiac or cerebral complications.

DIABETIC NEPHROPATHY

Renal disease is evident in around 40% of patients 20 years after developing insulin-dependent diabetes mellitus (IDDM) and, until recently, was a major cause of death in diabetic patients. The aetiology of diabetic nephropathy is multifactorial; both metabolic and genetic factors appear to be important, as more than 40% of patients with IDDM do not develop microvasculopathy in spite of the presence of long-term hyperglycaemia. Renal involvement in IDDM usually evolves through a number of stages.

• Stage I: at diagnosis, the glomerular filtration rate is increased, because of poor metabolic control

• Stage II: with improved glycaemic control, renal function remains within the normal range, and urinary albumin excretion (UAE) is normal

• Stage III: within the first 10 years after onset of diabetes, a proportion of patients develop microalbuminuria, defined as a persistent elevation in the urinary albumin excretion rate to greater than 20 pg/mm but without evidence of proteinuria on urinalysis

• Stage IV: most patients with microalbuminuria progress to overt nephropathy, which is characterized by the onset of clinical proteinuria and hypertension and is usually associated with retinopathy; the nephrotic syndrome commonly develops at this stage

• Stage V: renal impairment from stage IV almost invariably progresses to end-stage renal failure.

The evolution of renal disease in noninsulin-dependent diabetes mellitus (NIDDM) is less well defined, because of difficulty in ascertaining the exact time of onset of diabetes in this group.

In patients with suggestive clinical features and associated retinopathy, diabetic retinopathy is usually assumed without performing a renal biopsy. The latter is performed only if renal disease unrelated to diabetes is suspected. The most common feature on renal biopsy is diffuse glomerulosclerosis (Fig.54), which may be associated with the classic lesions of diabetic nephropathy (Fig.55). Electron microscopy in diabetic nephropathy shows thickening of the glomerular membrane in all patients. It is important to exclude other urological diseases associated with diabetes, such as renal papillary necrosis, UTI, perinephric abscess or pyonephrosis and neurogenic bladder.

Progression of renal failure in patients with overt proteinuria can be retarded by achieving good control of hypertension, but the benefits of good glycaemic control and low-protein diets in this group remain to be confirmed. The efficacy of maintenance of normal blood pressure levels and optimal glycaemic control are currently undergoing assessment in patients with microalbuminuria. Early aggressive control of blood pressure, using angiotensin-converting enzyme inhibitors, has demonstrated a reduction in microalbuminuria in patients with incipient nephropathy, and a decrease in proteinuria and improvement in renal function in patients with clinical nephropathy in preliminary trials. These therapeutic strategies, introduced at an early stage of diabetic nephropathy, may help prevent progression of renal failure in future.

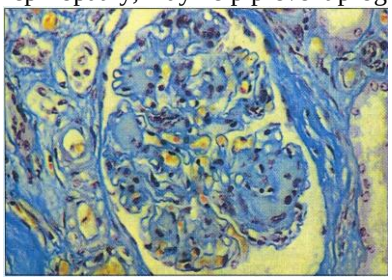


Fig.54 Diffuse glomeruloscierosis is the most common glomerular lesion in diabetic nephropathy. There is generalized thickening of the capillary walls throughout the glomerular lobules.

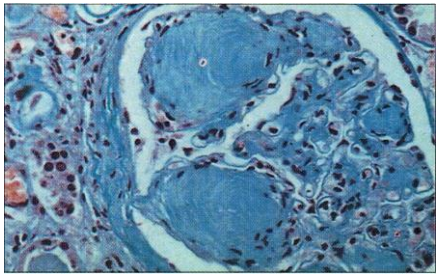


Fig.55 Kimmelstiel-Wilson nodules are the classic lesions of diabetic nephropathy. Their presence is virtually diagnostic of diabetes mellitus. Note the nodular intercapillary glomerulosclerosis.

TUBULOINTERSTITIAL DISEASES

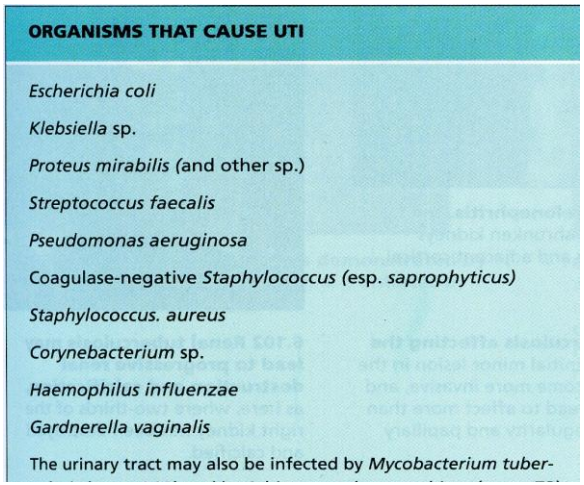
The generic term tubulointerstitial diseases refers to all diseases of the interstitium and tubules with little or no evidence of concomitant glomerular disease.

URINARY TRACT INFECTION

UTI is defined as the presence of microorganisms within the urinary tract with or without symptoms or signs of inflammation. Symptomatic urinary infection is a very common problem.

Bacteriuria is considered significant if the numbers of bacteria in urine voided per urethra exceed 100 000 colony-forming units/ml in a properly collected specimen.

The organisms that commonly cause UTI are listed in Fig.56, and E. coli is numerically most important.



ORGANISMS THAT CAUSE UTI

Escherichia coli

Klebsiella sp.

Proteus mirabilis (and other sp.)

Streptococcus faecalis

Pseudomonas aeruginosa

Coagulase-negative *Staphylococcus* (esp. *saprophyticus)*

Staphylococcus. aureus

Corynebacterium sp.

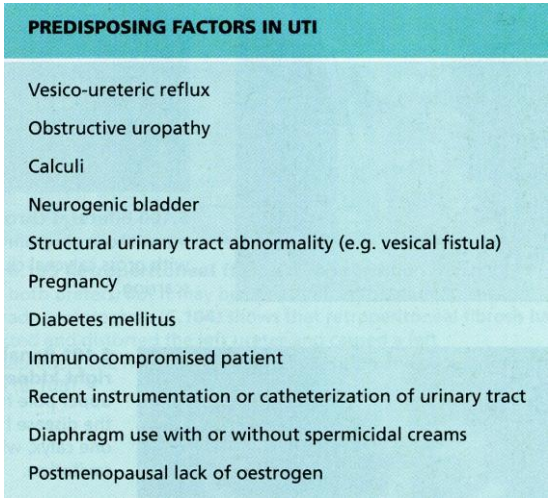
Haemophilus influenzae

Gardnerella vaginalis

The urinary tract may also be infected by *Mycobacterium tuber-*

Fig.56. Organisms that commonly cause urinary tract infection.

The organisms are thought usually to come from the patient's bowel, probably by direct spread from the anus, to colonize the urethra and then ascend to the bladder and kidney. Women are thought to be more likely to have UTIs because of the short length of the urethra. An important local defence against ascending infection is the hydrokinetic effect of passage of urine from the bladder. The clinical relevance of this is the increased incidence of UTIs in prostatic obstruction in men or in the presence of urinary stasis associated with a urinary diverticulum or urinary tract dilatation, Predisposing factors for urinary infection are listed in Fig.57.



PREDISPOSING FACTORS IN UTI

Vesico-ureteric reflux

Obstructive uropathy

Calculi

Neurogenic bladder

Structural urinary tract abnormality (e.g. vesical fistula)

Pregnancy

Diabetes mellitus

Immunocompromised patient

Recent instrumentation or catheterization of urinary tract

Diaphragm use with or without spermicidal creams

Postmenopausal lack of oestrogen

Fig.57. Predisposing factors in urinary tract infection.

UTI is important because of its frequency and its association with reflux nephropathy.

UTI is usually adequately treated with a course of antibiotics but long-term prophylaxis may be required in patients with structural abnormalities or recurrent infections.

ACUTE PYELONEPHRITIS

Clinical picture of acute pyelonephritis is characterized by high fever of continuous or hectic type, chills, and profuse sweats. Muscular tension in lumbar region and of anterior abdominal wall, tenderness to simultaneous, both-sided palpation of kidneys area are marked. Leukocyturia follows bacteriuria, leukocytosis, left shift of leukogramm with increase of band neutrophils, young forms appearance, their toxic granulosity, ESR acceleration are marked in blood.

CHRONIC PYELONEPHRITIS (RE FLUX NEPHROPATHY)

Chronic interstitial nephritis that is thought to result from bacterial infection of the kidney has been termed chronic pyelonephritis. It may occur in patients with predisposing urological abnormalities (vesico-ureteric refiux, obstruction or neurogenic bladder) or in patients with apparently normal urinary tracts. The pathogenesis of pyelonephritic renal scarring in children is attributed to both parenchymal damage and impaired renal growth, which result from intrarenal reflux of infected urine. A history of recurrent UTI during childhood and evidence of vesico-ureteric reflux are therefore risk factors for the development of focal cortical scars.

Among clinical manifestations hypertension appears first of all, simultaneously with changes in urine. Not seldom disease is detected in CRF stage, presenting with fatigue, nausea, anorexia, weight loss, polyuria, nocturia. Usually gradual decrease of renal concentrating capacity and GFR precede those.

Proteinuria in chronic pyelonephritis not exceed 2 g/day. Detection of leukocytes increased amount in daily urine is important for diagnosis.

During micturating cystography, reflux of contrast from the bladder may be limited to the ureter (grade I), reach the kidney but not distend the calyces (grade II) or reach the kidney and cause calyceal distension (grade III) (Fig.58). Vesicoureteric reflux is present in 85% of patients with coarse scarred kidneys and 35% of children with symptomatic UTIs.

Reimplantation of the ureters to correct reflux and long-term antibiotic prophylaxis to prevent infection have been the main interventions utilized to try to prevent development of chronic pyelonephritis in children, but studies have shown no proven benefit from operative treatment of reflux when compared with antibiotic prophylaxis alone. Further renal scarring is unlikely after 7 years of age, so children with vesico-ureteric refiux and UTIs are often treated with prophylactic antibiotics until they reach this age and are encouraged to keep up a liberal fluid intake and practise double voiding.

Chronic pyelonephritis may be unilateral or bilateral and the characteristic appearance on IVU is clubbing of the calyces wit overlying cortical scars, most commonly in the upper poles be ultimately generalized (Fig.59).

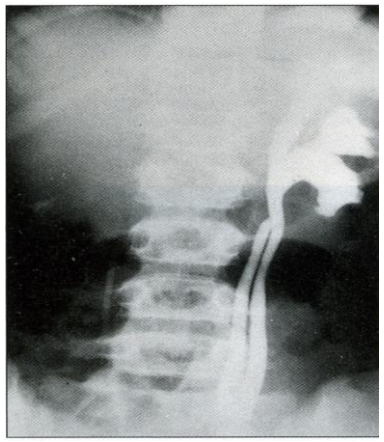


Fig.58 Unilateral grade Ill vesico-ureteric reflux with left bifid ureters, demonstrated by micturating cystogram.

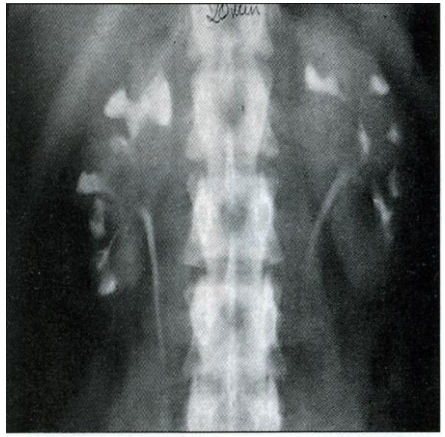


Fig.59 Bilateral chronic pyelonephritis. The intravenous urogram shows shrunken kidneys with gross calyceal clubbing and adjacent cortical scarring.

Scarring of the renal outline may also be demonstrated by DMSA isotope scan, an unilateral scarring is not uncommon. Chronic pyelonephritis may be detected during the investigation of patients with nonspecific ill health, recurrent UTIs, hypertension or CRF. End-stage renal failure may develop in patient with bilateral renal scarring, even when hypertension is treated and further UTI prevented.

Renal tuberculosis is uncommon, but should be considered in all patients with sterile pyuria.

RENAL CALCULI

Renal calculi are relatively common, affecting 1—5% of the population; they are more common in warm, dry countries and are composed of a mixture of chemicals, most commonly calcium oxalate alone or in combination with hydroxyapatite or calcium phosphate. Rarely, they may contain only uric acid or cystine. (Uric acid stones are radiolucent). About 20—40% of patients with calcium-containing stones have hypercalciuria (Fig.60) and a small number have hypercalcaemia.

CAUSES OF HYPERCALCIURIA

- Hyperparathyroidism
- Immobilization
- Bone metastases
- Sarcoidosis
- Distal renal tubular acidosis

Fig.60. Causes of hypercalciuria.

In the others, a search should be made for a cause of increased calcium absorption, for example vitamin D intoxication or renal tubular acidosis.

Clinical presentation is often dramatic, with the sudden onset of acute colicky pain resulting from impaction of the stone in the kidney, the ureter, bladder or urethra. There may also be hematuria and obstruction to urine flow. Passage of the stone produces instant relief, but if it obstructs either ureter or urethra it may cause progressive dull back pain. Infection is common and may produce a pyonephrosis when combined with obstruction.

The diagnosis is usually suggested clinically and is confirmed by a plain X-ray of the abdomen (Fig.61, 62, 63), an IVU (Fig.64), ultrasound or retrograde pyelography.

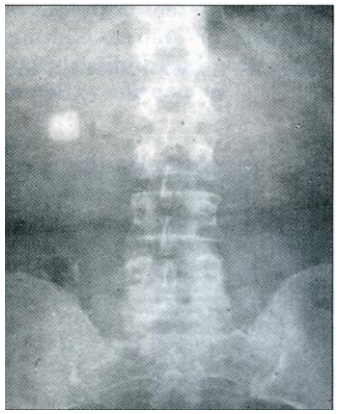


Fig.61. A single calculus in the renal pelvis is demonstrated on this plain (KUB) Xray. The X-ray was performed to investigate an episode of renal colic.

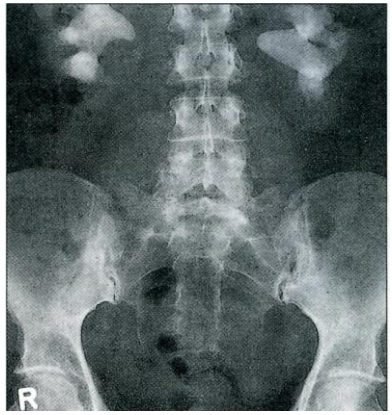
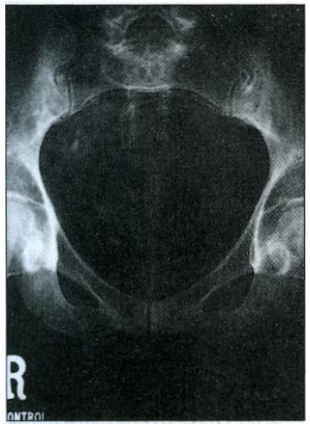


Fig.62. Large bilateral staghorn calculi are shown on this plain (KUB) X-ray. The patient presented with recurrent urinary infections.



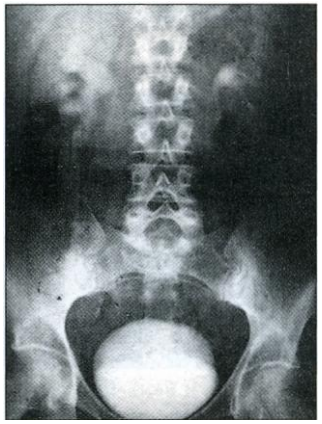


Fig.63 &64. Two small stones in the ureter are seen in 63. Stones of this size may sometimes pass without symptoms or with only a transient effect, but in this patient they caused ureteric obstruction, as can be seen in the intravenous urogram (64).

Urine should be cultured and examined microscopically for blood. Treatment of the pain is the overriding necessity and an antispasmodic may be of value. UTI requires an appropriate antibiotic. Stones less than 5 mm in diameter will usually pass spontaneously. Surgical intervention or lithotripsy may be required for larger stones. In extracorporeal shock wave lithotripsy (ESWL) a shock wave is generated by piezoelectric crystals outside the body and focused on the renal stone(s). Such shocks are administered as short pulses up to 500—2000 times. The stone disintegrates

sufficiently for the particles to be passed down the ureter. Stones of any size may be treated.

Occasionally staghorn calculi may need to be disintegrated percutaneously before ESWL, as may stones in the lower calyces. Uric acid and cystine stones tend to be harder and more difficult to break down. Ureteric stones in the upper two-thirds of the ureter may also be treated with ESWL. The success rate of ESWL is about 60—70%.

Bladder stones may grow to a massive size before presentation and need to be removed surgically. They may arise from stones formed in the kidneys that have migrated, from foreign bodies in the bladder (e.g. sutures) or from the same biochemical abnormalities as in renal stones.

CONTROL QUESTIONS

1. Complaints of patients with renal disease
2. Etiology and pathogenesis of glomerulonephritis
3. Renal hypertension: pathogenesis, types, diagnostics
4. Uric syndrome: notion, causes, laboratory diagnostics
5. Etiology and pathogenesis of acute renal failure
6. Etiology and pathogenesis of chronic renal failure, classification.
7. Diagnostics of renal failure
8. Diagnostics of nephrotic syndrome
9. Diagnostics of acute glomerulonephritis
10. Diagnostics of chronic glomerulonephritis
11. Diagnostics of acute and chronic pyelonephritis
12. Diagnostics of renal calculi

THEME 35. WRITING EXAMINATION CASE REPORT

Goal: to summarize student's skills of patient examination in a form of completing examination case reports with establishing of clinical diagnosis on the base of physical examination data, instrumental and laboratory investigations findings.

Knowledge objectives:

- to know symptoms and signs of main internal diseases, appropriate changes of physical examination data, diagnostic meaning of additional diagnostic methods and their findings in these diseases.

Skill objectives:

- to collect interviewing data, to perform physical examination of patients with the main internal diseases (inspection, palpation, percussion and auscultation), to interpret

data of additional diagnostic methods, to establish diagnosis of main internal diseases, to complete examination case report.

Subject-matter:
1. complaints of patients with the main internal disease
2. etiology and pathogenesis of the main internal diseases
3. diagnostics of the main internal diseases
4. parts and order of medical case report

Equipment required: stethoscope.

EDUCATIONAL MATERIAL

Examination case report is the crown of the introduction to the internal diseases course, reflecting student's knowledge and their practical applications.

The major parts of case are:

I. Medical history
II. Data of physical examination
III. Data of additional (laboratory and instrumental) diagnostic methods
IV. Wording of clinical diagnosis of the main and accompanying diseases
V. Substantiation of the main clinical diagnosis
VI. Pathogenesis of symptoms and signs.

The latter two parts of the report have crucial meaning, reflecting clinical thinking and understanding of clinical case by an examiner.

THEME 36. STUDENTS' CASE REPORT ANALYSIS

Goal: to analyze common and particular mistakes in completing of examination case reports, to improve understanding of diagnostic importance of different diagnostic methods (including physical examination) in establishing of clinical diagnosis.

Knowledge objectives:

- to know symptoms and signs of main internal diseases, appropriate changes of physical examination data, diagnostic meaning of additional diagnostic methods and their findings in these diseases.

Skill objectives:

- to collect interviewing data, to perform physical examination of patients with the main internal diseases (inspection, palpation, percussion and auscultation), to interpret

data of additional diagnostic methods, to establish diagnosis of main internal diseases, to complete examination case report.

Subject-matter:
1. complaints of patients with the main internal disease
2. etiology and pathogenesis of the main internal diseases
3. diagnostics of the main internal diseases
4. parts and order of medical case report

EDUCATIONAL MATERIAL

Analyzing students' case reports it is very important to pay attention on the most wide-spread mistakes in the interpretation of main symptoms and signs of the major internal diseases and also to demonstrate formation of the major syndromes as the collection of symptoms and signs revealed in the course of physical examination of patient with appropriate administering of additional diagnostic investigations.

THEME 37. CONTROL SUMMING-UP

Goal: to check-up knowledge of educational material of the Introduction tj the Internal Disease course.

Knowledge objectives:

- to know educational materials to themes 1-34.

Subject-matter:
1. complaints of patients with the main internal disease
2. etiology and pathogenesis of the main internal diseases
3. diagnostics of the main internal diseases

EDUCATIONAL MATERIAL

Classes include control tests according to themes 1-34. The basic variant of control test is given below.

FINAL TEST
for the III year students.

Correct answer is only one. Choose correct answer.

1. Central cyanosis is characterized by:
A. diffuse character, greyish tint, "warm" cyanosis;
B. distal location, "cold" cyanosis;
C. distal location, icteric tint, "warm" cyanosis;
D. diffuse character, greyish tint, "cold" cyanosis.

2. Anamnesis is referred to
A. laboratory diagnostic methods;
B. subjective diagnostic methods;
C. physical diagnostic methods;
D. instrumental diagnostic methods.

3. Jaundice is caused by increase of blood level of
A. reduced hemoglobin;
B. oxygenated hemoglobin;
C. urea;
D. glucose;
E. bilirubin.

4. General inspection is referred to
A. laboratory diagnostic methods;
B. subjective diagnostic methods;
C. physical diagnostic methods;
D. instrumental diagnostic methods.

5. In what joint motions should be produced in the course of heavy (loud) percussion?
A. wrist;
B. metacarpophalangeal;
C. proximal interphalangeal;
D. brachial;
E. cubital.

6. Cyanosis is caused by increase of blood level of
A. urea;
B. reduced hemoglobin;
C. cholesterol;
D. bilirubin;
E. protein.

7. Forced knee-elbow [Bozeman's] position relieves condition of patient with:
A. dry pericarditis;
B. hypertensive disease;
C. crupous pneumonia;
D. exudative pericarditis;
E. hepatitis.

8. Musset's sign is
A. jugular veins collapse during atrial diastole
B. “carotid dance”
C. diffuse apical impulse

D. rhythmical, synchronous with carotid pulse head jiggles
E. rhythmical, synchronous with heart beats head jiggles from the right to the left

9. Choose cause of organic dysphagia development
A.changes in the liver;
B. spasm of esophageal cardial part;
C. organic changes in esophagus (tumour, stricture);
D. changes of chest shape (trauma);
E. disorders of intestinal reabsorption.

10. Peripheral cyanosis is manifestation of
A. renal failure;
B. hepatic insufficiency;
C. heart failure;
D. malabsorbtrion syndrome;
E. adrenal insufficiency.

11. Pathologic bronchial breath sound – infiltrative variant – is heard in:
A. bronchitis in exacerbation period;
B. dry pleuritis;
C. crupous pneumonia in hepatization stage;
D. exudative pleuritis (below liquid level);
E. emphysema.

12. Pathologic bronchial breath sound – amphoric variant – is heard in:
A. emptying lung abscess;
B. emphysema;
C. crupous pneumonia;
D. chronic bronchitis;
E. dry pleuritis.

13. S_1 is enhanced in:
A. mitral incompetence;
B. tricuspid incompetence;
C. aortic incompetence;
D. mitral stenosis;
E. aortic stenosis

14. «Quail rhythm» appears due to:
A. S_1 doubling;
B. S_2 doubling;
C. S_3 enhancing;.
D. mitral valve opening snap appearance;
E. S_4 enhancing.

15. Pathologic bronchial breath sound – compressive variant – is heard in:
A. pulmonary consolidation syndrome;
B. pleural effusion syndrome;
C. pulmonary cavity syndrome;
D. bronchial obstruction syndrome;
E. hyperinflated lung syndrome.

16. From what BP level (nowadays) hypertension is detected?
A. 140 / 90 mm Hg.
B. 130 / 85 mm Hg.
C. 120 / 80 mm Hg.
D. 160 / 95 mm Hg.
E. 110 / 75 mm Hg.

17. «Rotten egg» belching is characteristic of:
A. GI hemorrhage;
B gastric ulcer perforation;
C. pylorostenosis;
D. gastric ulcer malignisation;
E. gastric ulcer penetration.

18.Tactile fremitus increases in:
A. pneumothorax;
B. chronic bronchitis;
C. emphysema;
D. crupous pneumonia
E. asthma.

19. Pasternatsky's sign is:
A.tenderness to percussion in the lumbar region;
B. presence of dense edemas in infraorbital areas;
C. skin waxen pallor;
D. tenderness to bimanual kidneys palpation;
E. nocturia.

20. Tactile fremitus decreases down to absence in:
A. bronchitis;
B. exudative pleuritis (above liquid projection area);
C. crupous pneumonia;
D. lung abscess after burst;
E. focal pneumonia.

21. Rusty sputum is characteristic of:
A. exudative pleuritis;

B. bronchitis;
C. crupous pneumonia;
D. lung abscess;
E. asthma.

22. «Coffee ground» vomit mass is characteristic of:
A. chronic gastritis;
B. chronic pancreatitis;
C. slow type of gastric hemorrhage;
D. intestinal disorders;
E. chronic esophagitis.

23. Icteric colouring first of all appears at the
A. frenum of the tongue
B. soft palate
C. facial skin
D. sclera
E. hand palm.

24. Orthopnoe relieves patient condition due to:
A. bronchi dilation;
B. blood deposition in the abdominal organs and low extremities;
C. improvement of cerebral blood supply;
D. BP level changes;
E. decrease of capillary permeability.

25. Coarse crackles are originated in:
A. alveoli
B. pleura
C. pericardium
D. bronchi
E. intestine.

26. In severe mitral incompetence S_1 at the apex is:
A. diminished;
B. enhanced;
C. not changed
D. splitted;
E. doubled.

27. What heart chambers are first of all hypertrophied in mitral stenosis?
A. left atrium, right ventricle;
B. left atrium, left ventricle;
C. right atrium, right ventricle;

D. both ventricles;
E. both atria.

28. S_2 accentuation at the aorta appears in:
A. hypertensive disease
B. myocardial infarction
C. myocarditis
D. pericarditis
E. endocarditis.

29. Orthopnoe forced position relieves condition of patients with:
A. renal failure
B. hepatic insufficiency
C. adrenal insufficiency
D. cerebral circulatory insufficiency
E. heart failure.

30. In typical angina attack pain is located:
A. in the hypogastrium
B. at the apex
C. in the masogastrium
D. in the epigastrium
E. beneath sternum.

31. Apical impulse shift to the left and downward, lateral to the left midclavicular line (to the VI-VII intercostals spaces) develops in:
A. aortic incompetence.
B. mitral stenosis.
C. mitral incompetence
D. tricuspid incompetence
E. aortic stenosis.

32. Sinus tachycardia is sinus rhythm with heart rate:
A. > 85/min
B. > 60/ min
C. >75/ min
D. > 90/ min
E. > 70/ min.

33. What does “facies mitrale” mean?
A. erythematous exanthema on cheeks and dorsum of nose
B. facial pallor
C. cyanotic malar flush
D. hyperemia of the left cheek

E. puffiness of face.

34. Where the points of electrodes attachment are situated on I standard lead recording?
A. right arm – left arm
B. right arm – left leg
C. left arm – left leg
D. right arm – right leg
E. right leg – left leg

35. Typical manifestation of heart failure is:
A. dizziness
B. shortness of breath
C. chest pain
D. flashing in the eyes
E. BP elevation.

36. What is the value of α angle normal electrical heart axis position?
A. from +30º up to 0°
Б. from 0° up to -30º
B. from +70° up to +90º
Г. from +90° up to +120º.
Д. from+30° up to + 70º.

37. When do atria and ventricles contract in their own independent rhythm?
A. in III degree a-v block
B. in atrial fibrillation
C. in paroxysmal tachycardia
D. in ventricular ectopic beat
E. in idioventricular rhythm

38. ECG “monophase curve” in myocardial infarction reflects:
A. myocardial ischemia
B. myocardial necrosis
C. myocardial scarring
D. there is no correct answer
E. myocardial injury.

39. Q-wave appearance on ECG in myocardial infarction reflects:
A. subendocardial ischemia
B. myocardial necrosis
C. myocardial injury
D. subepicardial ischemia
E. intramural ischemia.

40. What is the name of scientist, who proposed term «hypertensive disease"?
A.Kurashov S.V.
B. Einthoven W.
C. Lang G.Ph..
D. Botkin S.P.
E. Samoilov A.Ph.

41. The upper level of leukocytes normal amount after Nechiporenko urine analysis is
A. 15000 inв 1 ml of urine
B. 20000 in 1 ml of urine
C. 4000 in 1 ml of urine
D. 8000 in 1 ml of urine
E. 10000 in 1 ml of urine.

42. Curshmann spirals in sputum are detected in:
A. lung abscess
B. crupous pneumonia
C. chronic bronchitis
D. asthma
E. bronchiectasis.

43. Elastic fibers in sputum are detected in:
A. dry pleuritis
B. crupous pneumonia
C. asthma
D. emphysema
E. lung abscess.

44. Indicate referent time interval of white ring appearance after deposition of urine on the nitric acid during quantitative definition of proteinuria after Roberts-Stolnikov-Brandberg:
A.between 1^{st} and 2^{nd} min
B. between 2^{nd} and 3^{d} min.
C. .between 3d and 4^{th} min
D. between 5^{th} and 6^{th} min.
E. between 6^{th} and 7^{th} min.

45. Choose the normal results of S.S. Zimnitsky test.
A. DD>ND; relative density variation – 17,.
B. DD <ND; relative density variation – 4,
C. DD <ND; relative density variation -2,
D. DD <ND; relative density variation – 9,
E. DD <ND; relative density variation – 18.

46. Fine crackles are heard in
A. asthma
B. chronic bronchitis
C. emphysema
D. pneumonia
E. pluritis.

47. Cardiac asthma is:
A. acute manifestation of the right atrium insufficiensy.
B. acute manifestation of the left heart chambers insufficiency.
C. acute manifestation of the right ventricular insufficiency
D. manifestation of acute adrenal insufficiency.

48. What definition of Caer's sign is correct?
A. Significant increase of algesthesia at inhalation during palpation with the thumb of the right hand. in the gallbladder point
B. Significant increase of pain at inhalation during deep dipping of physician's right hand fingers in the gallbladder region
C. Tenderness while percussion with ulnar side of the hand on the right costal arch during patient's breath holding at inhalation
D. Tenderness during pressing between the peduncles of the right sternocleidomastoid muscle at the upper edge of the clavicle
E. Tenderness during slight percussion with the edge of the hand in the right hypochondrium

49. What duration of angina attack may be suspicious of myocardial infarction development?
A. 5 min
B. 2 min
C. 8 min
D. 15 min
E. 10 min.

50. All among listed below signs are components of nephrotic syndrome, except
A. massive proteinuria (> 3,5 g/day)
B. hypoalbuminemia
C. hyperlipidemia
D. edemas
E. macrohematuria.

THEME 38. EXAM CHECK-UP OF PRACTICAL SKILLS

Goal: to check-up practical skills of patients' physical examination.

Knowledge objectives:
- to know educational materials to themes 1-12.

Skill objectives:
- to perform inspection, auscultation, percussion and palpation of patients.

Equipment required: stethoscope.

EDUCATIONAL MATERIAL

Classes include work-up with patients on bedside. Physical examination skills given below will be assessed.

1. Patient interview
2. General inspection
3. Inspection of the chest
4. Palpation of the chest
5. Comparative percussion of the lungs
6. Topographic percussion of the lungs
7. Lungs auscultation
8. Inspection of the precordium
9. Palpation of the precordium
10. Percussion of the relative and superficial cardiac dullness
11. Auscultation of the heart
12. Veins and arteries examination
13. Examination of arterial and venous pulses
14. Defining of blood pressure after N.S.Korotkov method
15. Inspection of the abdomen and oral cavity
16. Percussion of the abdomen
17. Superficial abdominal palpation
18. Methodic deep sliding abdominal palpation after V.P. Obraztsov and N.D. Strazhesko
19. Ausculatation of the abdomen
20. Inspection of the liver and spleen areas
21. Liver and gall-bladder palpation
22. Liver percussion
23. Spleen percussion
24. Spleen palpation
25. Inspection of lumbar and suprapubic regions

26. Kidneys and bladder percussion
27. Palpation of kidneys, bladder and ureteral algesic points
28. Palpation of thyroid gland
29. Palpation of lymph nodes
30. Defining of pitting edema

REFERENCES

1. Основы семиотики заболеваний внутренних органов. Атлас./ А.В.Струтынский, А.П.Баранов, Г.Е.Ротберг, Ю.П.Гапоненков.- М.; РГМУ, 1997, 222 с.
2. Пропедевтика внутренних болезней. /Под редакцией В.Х.Василенко, А.Л.Гребенева, Н.Д.Михайловой.- М., Медицина, 1974, 528с.
3. Симптомы внутренних болезней./М.Затурофф.- М.; Практика,1997, 439с.
4. A Guide to physical examination. Third Edition./B. Bates, R. A. Hoekelman.- J.B. Lippincott Company, Philadelphia, 1995, 539p.
5. Cecil essentials of medicine. Third edition/ T.E.Andreoli, J.C.Bennett, C.J.Carpenter et al. – W.B.Saunders Company, Philadelphia, 1996, 921p.
6. Forbes C.D. Color Atlas and text of clinical medicine / C.D. Forbes, W.F. Jackson. - 2nd ed. - London: Mosby-Wolfe, 1997. - 534 p.: ill.
7. Пропедевтика внутренних болезней Учебно-методическое пособие. Часть I. Introduction to Internal Diseases. Manual Part I. /В.Н.ослопов, А.Р.Садыкова, И.В.Карамышева. Казань, 2005, 65 с.
8. Пропедевтика внутренних болезней Учебно-методическое пособие. Часть II. Introduction to Internal Diseases. Manual Part II. /В.Н.ослопов, А.Р.Садыкова, И.В.Карамышева. Казань, 2005, 86 с.
9. Пропедевтика внутренних болезней Учебно-методическое пособие. Часть III. Introduction to Internal Diseases. Manual Part III. /В.Н.ослопов, А.Р.Садыкова, Л.А.Ануфриева. Казань, 2005, 77с.
10. Пропедевтика внутренних болезней Учебно-методическое пособие. Часть IV. Introduction to Internal Diseases. Manual Part IV. /В.Н.ослопов, А.Р.Садыкова, Л.А.Ануфриева. Казань, 2005, 103 с.
11. Пропедевтика внутренних болезней Учебно-методическое пособие. Часть V. Introduction to Internal Diseases. Manual Part V. /В.Н.ослопов, А.Р.Садыкова, И.В.Карамышева. Казань, 2006, 101 с.

12. Пропедевтика внутренних болезней Учебно-методическое пособие. Часть VI. Introduction to Internal Diseases. Manual Part VI. /В.Н.ослопов, А.Р.Садыкова, И.В.Карамышева. Казань, 2006, 75 с.
13. Пропедевтика внутренних болезней Учебно-методическое пособие. Часть VII. Introduction to Internal Diseases. Manual Part VII. /В.Н.ослопов, А.Р.Садыкова, И.В.Карамышева. Казань, 2006, 75 с.
14. Пропедевтика внутренних болезней Учебно-методическое пособие. Часть VIII. Introduction to Internal Diseases. Manual Part VIII. /В.Н.ослопов, А.Р.Садыкова, И.В.Карамышева. Казань, 2007, 112 с.