4.0
URINARY SEDIMENT IN NEPHROLOGICAL DIAGNOSIS

During the course of some nephropathies the urinary sediment is very rich and contains a large number of cells and casts with special features or particular associations. Under these circumstances a morphological assessment in combination with a quantitative evaluation may provide useful diagnostic information. In other conditions the changes in the sediment are not so great, but careful examination of the features of the elements present or a patient search for rarer components may be of considerable importance.

In some cases, however, the changes noted are completely non-specific, as they are common to several disorders of the renal parenchyma or urinary tract. The diagnostic value of the sediment is more limited in such cases, though not negligible. It should be remembered, for example, how often a slight or isolated microhematuria reveals a urinary system disorder. Some of these findings will be discussed in the following chapters.

In the last two decades the classification of the nephropathies has been completely revised. For an exact definition of the majority of renal disorders on the basis of the new classifications it is necessary to take into account not only the clinical findings and the results of a few elementary laboratory tests which had to suffice in the past, but also, and sometimes most importantly, the results of many instrumental, immunological and chemical tests and biopsy. Since, in practice, an exhaustive diagnostic protocol is often lengthy and at times unnecessary or impossible for various reasons, it has been considered best, for current diagnostic purposes, to retain the definitions of the main basic nephrological syndromes as widely used by the classical authorities, but also to modify them in the light of present-day requirements.

These syndromes are identified by clinical and laboratory examinations easily carried out even in routine medical practice. We refer to these syndromes constantly, although aware that each includes a number of nephropathies with very different morphological features and clinical courses.

We give a list of these syndromes here, as examination of the urine is indispensable for their identification, and because we shall be using these terms widely from now on.

Table 1   The major clinical syndromes in nephrology. Although first described in texts that are now classics, they are still constantly referred to by present-day nephrologists. In fact there are modern texts on nephrology that describe some nephropathies (especially glomerular diseases) with specific reference to these clinical accounts. Some authors have changed a few terms and their meanings. For example, instead of chronic renal failure they speak of a chronic nephritis syndrome, and the uremic syndrome is sometimes dealt with separately; some syndromes are defined as being specifically related to glomerulonephritis (acute glomerulonephritis, rapidly progressive glomerulonephritis, chronic glomerulonephritis).

These fundamental syndromes have recently been supplemented by two others, which, although not exclusively of nephrological interest, often require the intervention of the nephrologist [14]. They are:

— Arterial hypertension (arbitrarily defined in adults on the basis of blood pressure readings of over 145/95 on at least three separate occasions).

— Nephrolithiasis.

Tab. 1. Major Clinical Syndromes in Nephrology

— **Nephrotic syndrome:**

involves a proteinuria of over 3 g in 24 hours (or according to other definitions 3.5 g/ 24 hours /1.73 m^2). It is often accompanied by hypoalbuminemia, hyperlipidemia, edema, oliguria and lipiduria.

— **Acute nephritis syndrome:**

is characterized by the abrupt onset of hematuria (sometimes with red blood cell casts), accompanied by at least one of the following signs of acutely impaired renal function: reduction of glomerular filtrate, sometimes with hyperazotemia and an increase in blood creatinine; arterial hypertension of recent onset; oliguria; edema.

— **Asymptomatic urinary abnormalities:**

these are indicated by hematuria, leukocyturia, and proteinuria (below the nephrotic range), either occurring singly or in combination, with no signs of renal failure and without arterial hypertension or other obvious indications of urinary system disease.

— **Acute renal failure:**

apart from very rapid onset, this generally implies that the condition is reversible, although this only becomes definite at subsequent examinations. It occurs mostly, though not necessarily, with oliguria or anuria.

— **Chronic renal failure:**

this term is often used to indicate the presence of even moderate functional impairment, which has not yet caused a uremic syndrome. There is also a special, quickly developing type sometimes known as rapidly progressive renal failure.

— **Urinary infections:**

are identified on the basis of significant numbers of bacteria, and a varying number of leukocytes.

— **Obstructions of the urinary tract.**

— **Renal tubule defects, anatomical or functional:**

comprise many heterogeneous renal disorders.

4.1 GLOMERULAR DISEASES

A classification of primary and secondary glomerular diseases, which is more satisfactory than that which could be made in the past, has been achieved by critical, detailed research, largely based on renal biopsy and the use of light, fluorescent and electron microscopy. In primary glomerular diseases the glomeruli are the structures which are initially and principally impaired by a pathological process which, in its most typical form, electively affects the kidneys. The etiology may be unknown («idiopathic» primary glomerulonephritis) or known (e.g. «post-streptococcal» glomerulonephritis).

In secondary glomerular diseases the kidney is affected by a typically multi-system disease, by a hereditary disease, or a disease initially involving other organs. These disorders have proved to be much more common that was once thought. Lupus nephritis, for example, accounts for about 10% of the cases of glomerular diseases that we have diagnosed by renal biopsy.

It is not always easy to distinguish between primary glomerulonephritis of known cause and secondary glomerulonephritis. Some authors, indeed, consider that a third group, associated with specific etiologies, should be identified.

Table 2 Primary and secondary glomerular diseases. In some secondary renal diseases the glomerulus is often the structure most affected, although interstitial, tubular or vascular lesions may be prominent.

Table 3 Specific etiologies which cause glomerulonephritis. The table lists some of the ever-increasing number of causes.

Tab. 2.

I PRIMARY GLOMERULAR DISEASES

II SECONDARY GLOMERULAR DISEASES

- in multi-system diseases (systemic lupus erythematosus, Henoch-Schönlein syndrome, Goodpasture's syndrome, systemic vasculitis, etc.);

- associated with paraproteinemic disorders and amyloidosis (cryoglobulinemia, Waldenström's macroglobulinemia, benign monoclonal gammopathy, multiple myeloma, primary and secondary amyloidosis);

- associated with liver diseases (viral hepatitis B and chronic active hepatitis, cirrhosis);

- associated with hereditary and metabolic disorders (diabetes, Alport's syndrome, Fabry's disease, etc.);

- associated with neoplasia;

- in infectious diseases primarily affecting other organs (bacterial endocarditis, «shunt nephritis», visceral sepsis, etc.).

Tab. 3.

SOME ANTIGENS AND FACTORS ASSOCIATED WITH GLOMERULONEPHRITIS

1) drugs, chemical and toxic agents (penicillamine, penicillin, sulfonamides and other pharmaceutical products, heroin, gold, mercury, etc.);

2) vaccines, bee stings, foreign serum proteins;

3) bacterial, viral, parasitic and fungal.

Table 4 A highly analytical classification of primary glomerular diseases has been made by the combined use of light, fluorescent and electron microscopy. Reference to this classification has now become customary in clinical practice, so that some of the terminology commonly used twenty or thirty years ago is now outmoded.
The basic groups of these disorders are listed in the table. From the results of renal biopsy, however, some 10% of patients with glomerulonephritis cannot be placed in any clearly defined group.
The classification of secondary glomerular diseases has also undergone considerable modification, and for some disorders it is now extremely complex. Numerous kinds of lesions have been described: for example, in the case of lupus glomerulonephritis there are reports of minimal change nephropathy, mesangial proliferative, focal and diffuse proliferative, crescentic and membranous lesions.

Tab. 4. Primary glomerular diseases

— minimal change disease

— focal glomerular sclerosis

— mesangial proliferative glomerulonephritis with diffuse IgM deposits (IgM mesangial nephropathy)

— primary IgA nephropathy (Berger's disease)

— acute glomerulonephritis

— rapidly progressive glomerulonephritis (diffuse crescentic glomerulonephritis)

— membranous glomerulonephritis

— membranoproliferative glomerulonephritis:

> I) with predominantly subendothelial deposits
>
> II) with dense intramembranous deposits
>
> III, IV etc.) other ultrastructure variants with subendothelial, subepithelial and in-tramembranous deposits, and basement membrane alterations

— atypical and unclassifiable lesions

— end-stage kidney

Renal biopsy is often the only form of investigation on which a circumstantial diagnosis of glomerulonephritis can be based. In some cases, however, examination of the urine alone may arouse suspicion of the disease or even lead to a laboratory diagnosis accurate enough to make biopsy unnecessary.

Traditionally the features of the sediment in glomerulonephritis are considered to be:

1) a hematuria which predominates over all other findings; it is not in itself pathognomonic, but acquires greater significance if accompanied by casts, especially red cell casts, and/or by renal epitheliuria and/or by heavy proteinuria.

Of the various kinds of glomerulonephritis it is generally the proliferative forms that produce hematuria. Among the primary glomerular diseases it is acute, rapidly progressive, membranoproliferative and mesangial proliferative glomerulonephritis and primary IgA nephropathy that generally produce sediment of this kind. In the secondary types, many glomerular diseases with glomerular proliferative lesions can also give rise to hematuria. It is less common to find any appreciable microhematuria in glomerular diseases with non-proliferative lesions, such as minimal change disease, focal glomerular sclerosis and membranous glomerulonephritis.

2) a lipuria, free or in cells or casts [71], which may or may not be associated with a varying degree of hematuria. This finding is generally a marker of heavy proteinuria, which can be found in many primary or secondary glomerular diseases.

In minimal change disease, in focal glomerular sclerosis and sometimes in membranous glomerulonephritis, a lipuria may appear unaccompanied by hematuria, or by only very slight hematuria. A quite conspicuous hematuria is generally found concurrently with the nephrotic syndrome in some cases of primary membranoproliferative or rapidly progressive glomerulonephritis and in certain secondary proliferative glomerular diseases.

The quantitative features of the sediment are generally considered to reflect histological activity and, despite occasional anomalous behaviour, regular examination from this point of view is important in following the course of the glomerulonephritis, once the disease has been detected.

Both for the purpose of diagnosis and for subsequent assessment of the course of glomerular diseases the quantitative evaluation of the urinary sediment can be combined with the qualitative examination, which is of particular value in these conditions. Some of the morphological findings of greatest interest will be discussed in the following pages.

In acute glomerulonephritis, particularly in the initial stage of the more severe forms, the morphological findings in the urinary sediment are often so specific as to constitute an important diagnostic feature. In the more typical cases, there is generally a conspicuous hematuria with abnormal and often fragmented red cells. At the same time it is usual to find a large number of polymorphic casts, many of which are red cell casts; tubular epithelial cells are also numerous and many granulocytes can often be found, particularly at the onset of the disease.

317 Cast of erythrocytic origin; the red cells are clearly polymorphic (even at this magnification). The fragmentation and depigmentation of the red cells can be noted (acute glomerulonephritis at the initial stage) (160x).

318-320 More specimens of various cases of acute glomerulonephritis in the early stages. With findings of this sort the hematuria is certainly not from the urinary tract, and severe parenchymal nephropathy can be diagnosed; generally acute or rapidly progressive or membranoproliferative glomerulonephritis is involved, or even a cortical necrosis or a severe post-ischemic or toxic-induced acute renal failure in the very early stage. The last two diseases, however, present very different clinical pictures.
Findings of this type are of immediate prognostic value, since even when diuresis is still unaffected, they indicate that severe impairment is occurring and this can often lead to acute renal failure (100x), (160x), (100x).

321-322 Various kinds of cast (hyaline, waxy and red cell granular) and hematuria with clearly degenerating and polymorphic cells in two cases of acute glomerulonephritis, some time after onset of the disorder. The fragmentation of the erythrocytes is not as marked here as in the previous cases. As has already been pointed out fragmentation is common in acute and severe chronic nephropathies and indicates the parenchymal source of the hematuria, provided there are no clots in the urinary tract (100x), (160x).

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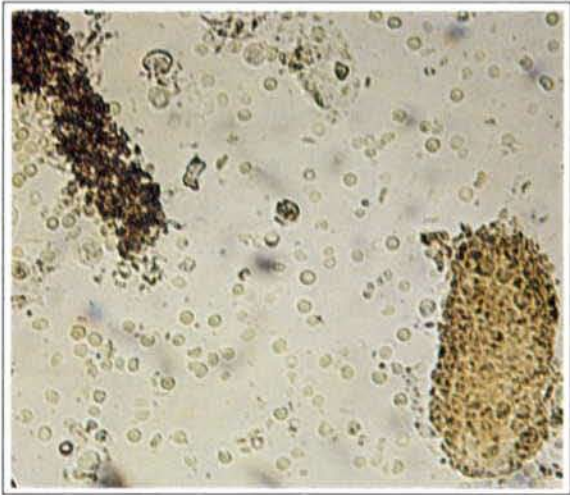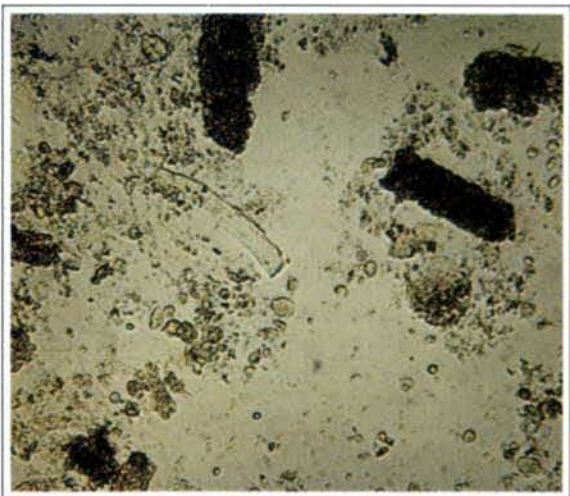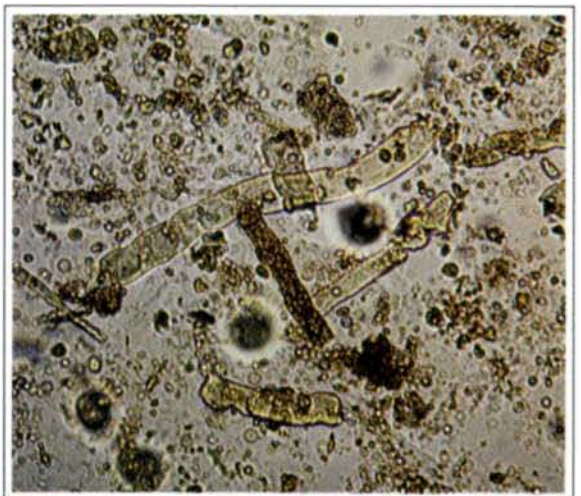
323-324 Polymorphic hematuria; mononuclear cells, at least two probably of tubular origin; granulocyturia (sediment from two cases of acute glomerulonephritis in the initial stages, using ordinary light microscopy and phase contrast, respectively).
At the onset of acute glomerulonephritis with marked exudative phenomena, the predominant nucleated cells may be granulocytes, free or in casts. Granulocyturia may even precede the hematuria and be present as an extremely transitory finding in the first stages, but, in practice, this is very rarely found (400 x), (400 x).
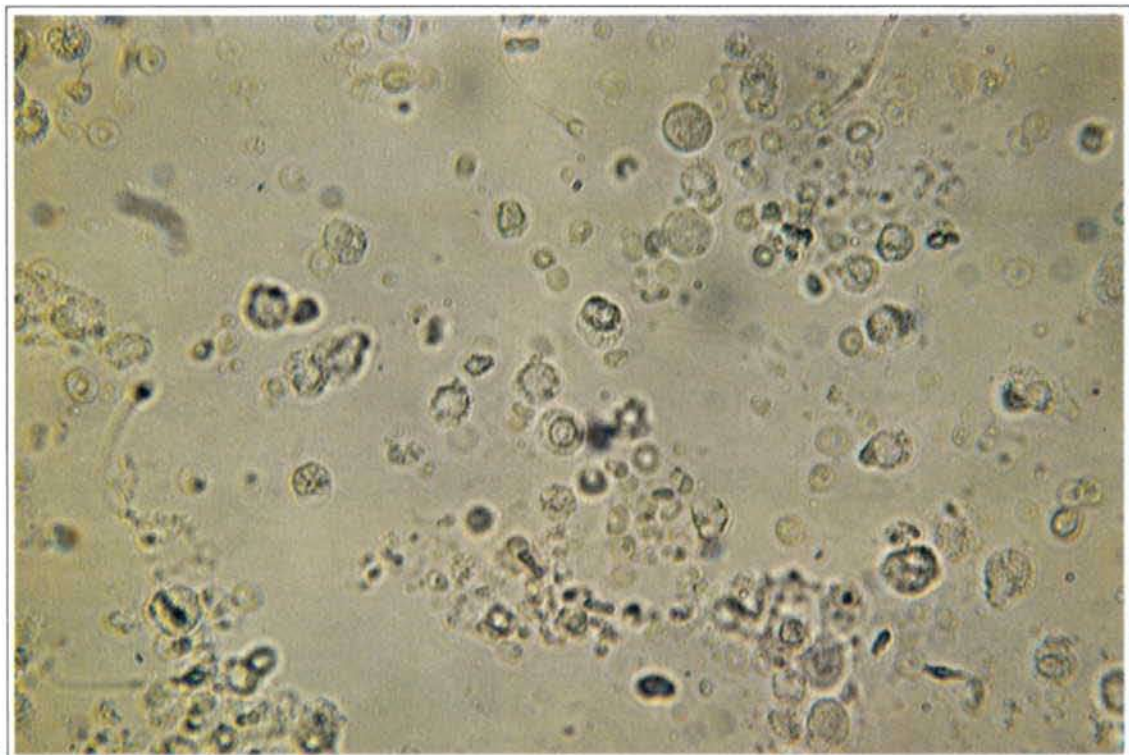
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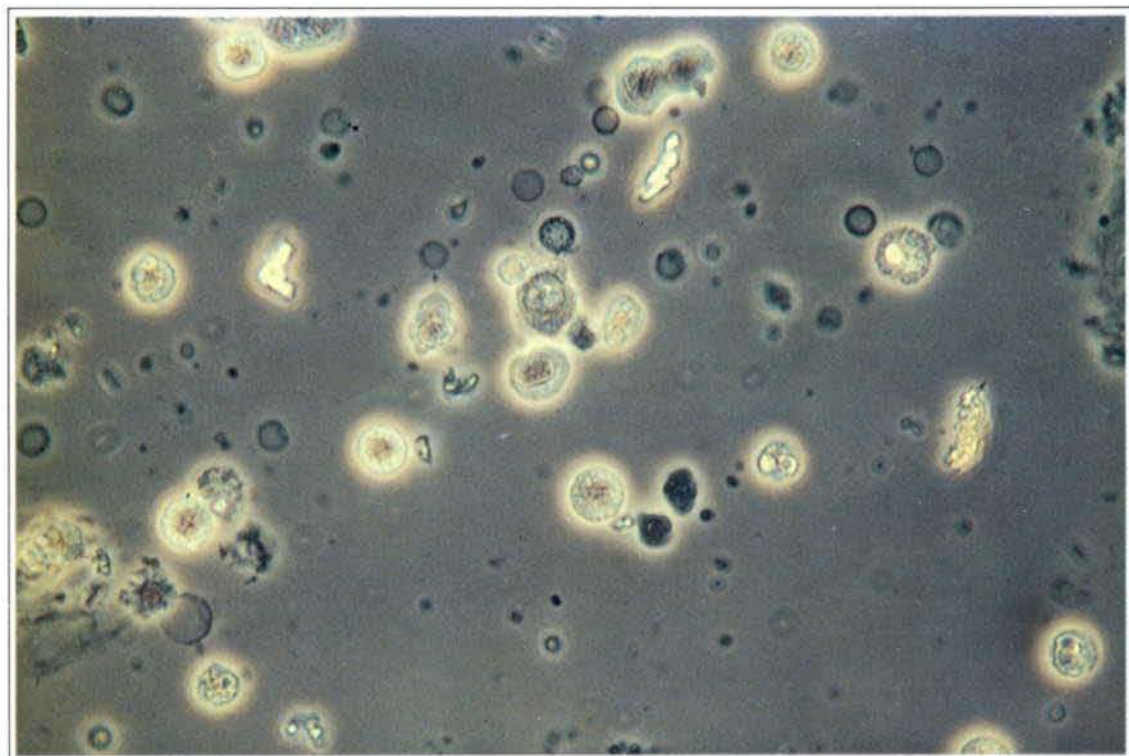
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At various intervals after the onset of acute glomerulonephritis, a series of changes occurs in the sediment. First there is a reduction in the number of granulocytes and a transitory increase in the epitheliuria and mononuclear cells eliminated, then a decrease in the red cell and epithelial casts; later, while fragmentation of the erythrocytes becomes less and less evident, there is a progressive reduction, firstly, in the epitheliuria and mononuclear cells, then in the hematuria and casts.

During recovery, the proteinuria returns to the physiological range in the course of a few months, and the urinary findings generally become non-specific. An occasional, slight microhematuria, generally with abnormal cells, may be the last sign of nephropathy in a patient on the road to recovery.

Acute glomerulonephritis does not always follow such a typical course, and may even produce relatively little sediment with either typically abnormal erythrocytes or mixed cells and only a few casts, even in the initial stage. In these cases the granulocytes and renal epitheliuria are scarce and transitory.

325   Polymorphic microhematuria. Granular cell casts. Mononuclear cells with no special characteristics, probably originating in the renal tubules (acute glomerulonephritis). As this disease develops the number of mononuclear cells, both those of obvious tubular origin and others that are not clearly defined (probably lymphocytes and monocytes) tends, at first, to increase progressively, both in absolute terms and in proportion to the granulocytes. Changes of this type are typical of acute glomerulonephritis. The significance of this lymphomonocyturia in the active phase of glomerulonephritis is not clear at present (160x).

326   Cast in the early stage of becoming waxy. Polymorphic hematuria, clearly abnormal cells with some fragmentation (acute glomerulonephritis) (400x).

327   Slightly polymorphic hematuria. This picture was obtained several weeks after that in 325 and illustrates how, in the course of this acute disorder, there is generally a reduction in the fragmentation of the erythrocytes and their polymorphism, and a decrease in the number of nucleated cells. The sediment clears progressively (400x).

328   Microhematuria. Granular, waxy and hyaline casts with cellular inclusions (severe acute glomerulonephritis in the recovery phase). When the most acute stage is over, red cell casts and epithelial casts become fewer, while the percentage of granular and hyaline casts increases. Waxy casts sometimes appear, but especially if they are small in diameter, they are not an unfavourable sign, as they may indicate renewed functioning of some nephrons. Even when there is improvement in the sediment, considerable care should still be taken, since it has been reported that in acute glomerulonephritis there may be a period of deterioration long after the acute symptoms have cleared up and even when the urinary findings show only slight alterations or appear to have returned to normal (100x).

329   Slight microhematuria; one hyaline cast. Urinary sediment, now clear, three months after the onset of acute glomerulonephritis, initially with acute renal failure (160x).

330   Microhematuria with most cells virtually unchanged. Red blood cell cast. Even in cases such as this, when recovery from acute glomerulonephritis follows a satisfactory course, red blood cell casts may be found for several months. When there are no red cell casts, and if the disorder was initially asymptomatic, a finding of this kind is insufficient for a diagnosis of glomerulonephritis (160x).
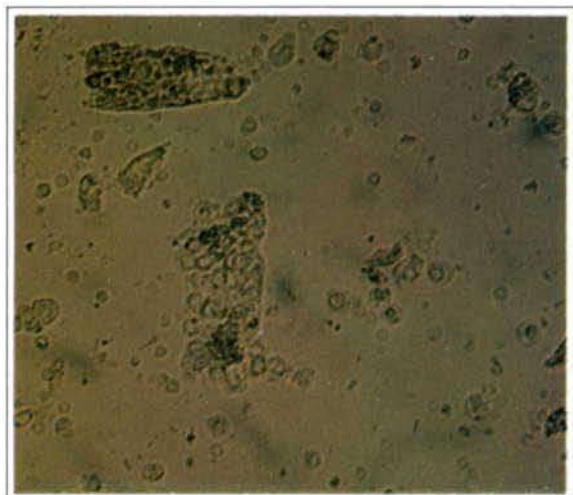
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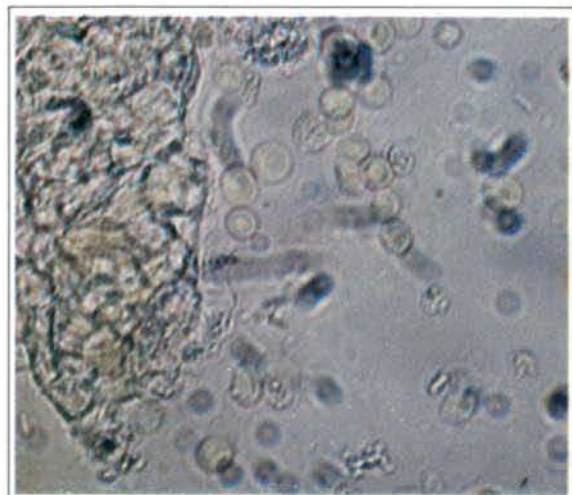
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In primary IgA nephropathy (Berger's disease) there may be transitory and recurrent gross-hematuria, frequently associated with upper respiratory tract or gastrointestinal infection. Generally most of the erythrocytes are abnormal in shape, although fragmentation is rare; especially when there is only slight microhematuria, at least some of the red cells may be of normal appearance. The sediment of this nephropathy usually differs from sediment of acute and membranoproliferative glomerulonephritis in that, even in its most active phases, few renal epithelial cells, mononuclear cells, granulocytes and casts are eliminated in the urine.

In «chronic» glomerulonephritis, when the hematuria (usually here with red cells of obviously abnormal shape) is associated with numerous casts of medium or large diameter in the urine, and renal epitheliuria and/or lipuria, severe lesions should be suspected. These are features of some types of membranoproliferative glomerulonephritis, rapidly progressive glomerulonephritis and secondary proliferative glomerulonephritis.

At least during certain stages, however, all kinds of chronic glomerulonephritis may produce sediment with only slight microhematuria, generally with abnormal red cells.

When there is no heart failure, large numbers of hyaline, granular, or granular cell casts, especially if accompanied with lipuria, are sufficient evidence on which to diagnose glomerulonephritis with heavy proteinuria.

Hyaline and granular casts, often with lipuria but no (or only slight) hematuria, are frequently found in the nephrotic syndromes of some primary glomerular diseases without proliferative lesions, such as «minimal change disease», focal glomerulosclerosis, and membranous glomerulonephritis.

Sediment like this can also be found in some secondary nephropathies with severe proteinuria, as in some cases of amyloidosis, myeloma, or diabetic glomerulosclerosis, and in a few cases of lupus glomerulonephritis (with minimal change nephropathy, membranous or mesangial lesions).

Such findings are rare in proliferative glomerular diseases.

331 Hematuria with abnormal cells, red cell granular casts and fatty casts; lipuria and oval fat bodies (acute glomerulonephritis).
In acute glomerulonephritis, the appearance of lipuria (in casts, cells or free) indicates the onset of a nephrotic syndrome. This patient had originally had oliguria followed by a period of functional and urinary improvement. The acute glomerulonephritis, diagnosed by biopsy, had become severe again as a result of intercurrent sepsis.
The case later proceeded satisfactorily. Sediments of this kind can more often be found in other, much more severe forms of glomerulonephritis (160x).

332 Lipuria in casts. Slight hematuria (minimal change disease) (100x).

333 Lipuria, free and in an oval fat body (focal glomerular sclerosis; nephrotic syndrome) (400x).

334 Many hyaline casts (nephrotic syndrome) (100x).

335 Polymorphic, waxy and granular casts. Abnormal erythrocytes. Mononuclear cells and granulocytes (membranoproliferative glomerulonephritis) (160x).

336 Many polymorphic, granular and waxy casts. Microhematuria with obviously abnormal cells (membranoproliferative lupus glomerulonephritis, with a nephrotic syndrome and renal failure) (100x).
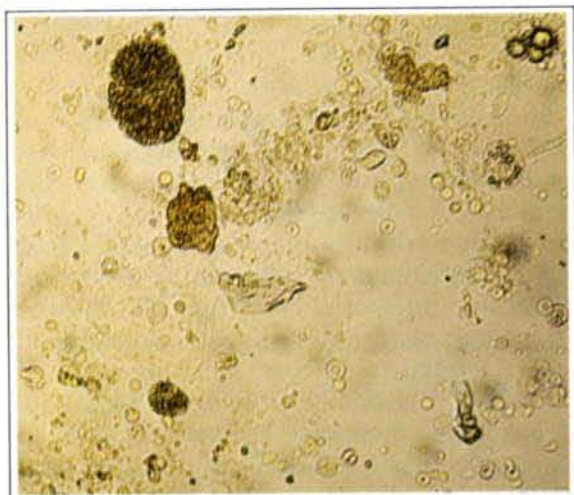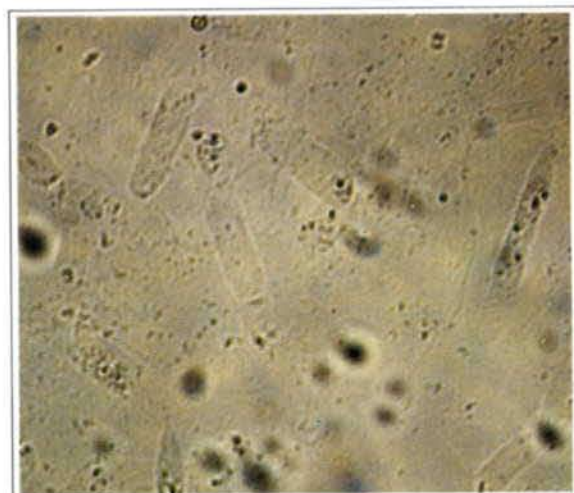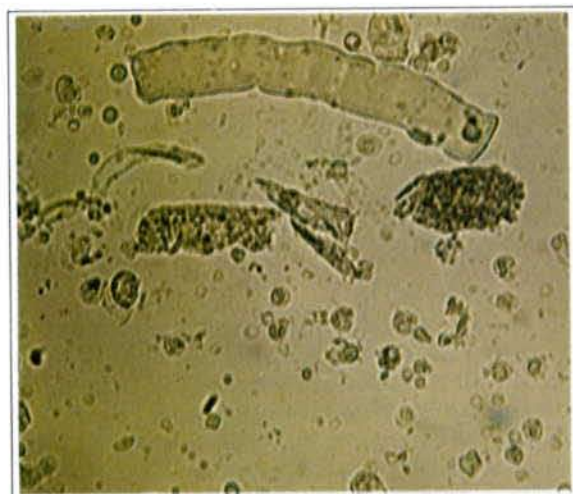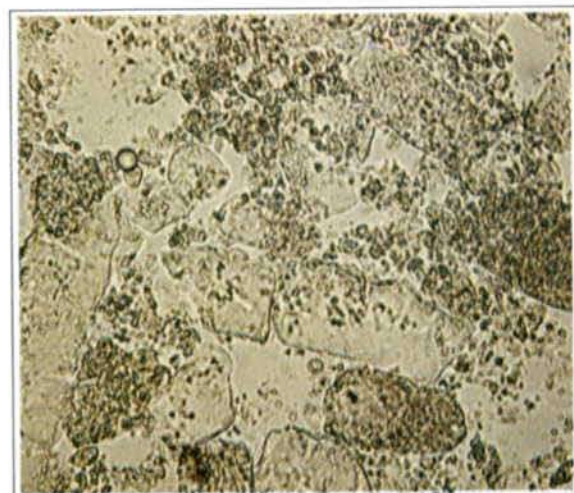
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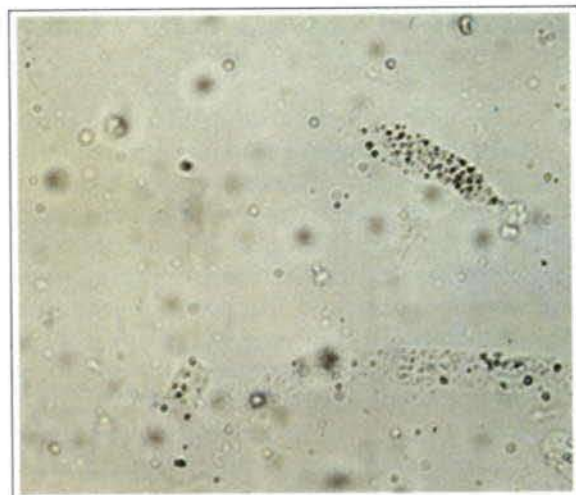
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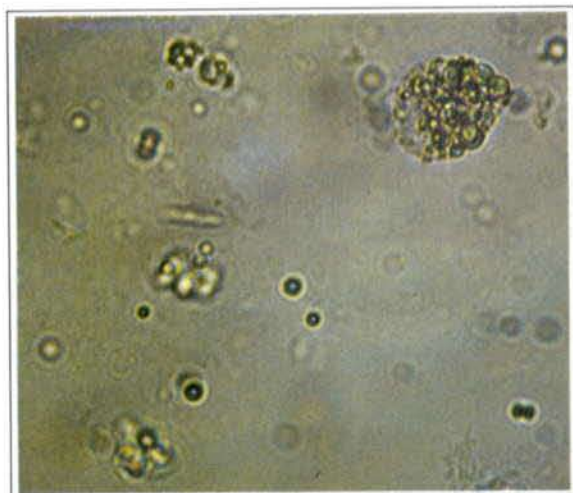
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4.2 INTERSTITIAL NEPHROPATHIES

After being practically ignored in the treatises of the early years of the century, interstitial nephropathies began to be recognized between 1925 and 1940, particularly by pathologists. For a long time, however, only a limited number of nephropathies were included in this class: among them was pyelonephritis, a disorder due to the direct localization of non-specific bacteria in the renal interstitial tissue, the calyces and pelvis.

In the 1950s and 1960s many clinicians and some pathologists failed, however, to recognize the non-specificity of the parenchymal lesions of chronic pyelonephritis: this led them to assume that chronic pyelonephritis was the most, or one of the most, frequent causes of uremia, and renal interstitial lesions of any severity tended to be attributed to it.

Opinion on the matter has now changed greatly, since it has been recognized that interstitial lesions, almost identical to those found in chronic bacterial pyelonephritis, can have toxic, chemical, immunological, vascular or mechanical causes. The importance of this disorder, as a cause of chronic uremia, is now also considered to be less than was thought previously.

Interstitial nephropathies have been re-examined and the number of conditions now known to give rise to such a pathological picture has increased considerably. Since most of the interstitial nephropathies that have been identified so far have very similar morphological features, classification is usually based here chiefly on etiopathogenetic criteria.

Table 5   Interstitial nephropathies. Apart from tubercular and mycotic conditions, most cases of interstitial nephritis have essentially similar lesions. Hence classifications based on a variety of criteria have been suggested. The simplest classification takes into account their etiology and is that largely used in clinical practice. Besides the disorders listed in this table, interstitial lesions, some of which may be very large, can also be seen in some glomerular, vascular and tubular nephropathies, and in congenital malformations of the urinary system.

Tab. 5. Interstitial nephropathies

A) ACUTE
- localized bacterial (acute pyelonephritis), fungal and viral infections
- associated with generalized infections (without bacteria in the kidney)
- drug-induced hypersensitivity
- immunological disorders (LES, cryoglobulinemia, transplant rejection)
- idiopathic.

B) CHRONIC
- bacterial (chronic pyelonephritis; tubercular)
- with urinary tract obstruction
- reflux nephropathy
- drug-induced (analgesic, lithium nephropathy, etc.)
- heavy metal-induced (Pb, Cd, Hg)
- radiation nephritis
- in metabolic disorders (hypokaliemia, hypercalcemia, urate and oxalate nephropathy, etc.)
- immunological (in LES, transplant rejection, etc.)
- in neoplastic disorders
- hereditary diseases
- Balkan nephropathy
- idiopathic

Neutrophil granulocytes are often considered to be the most characteristic feature of the sediment in interstitial nephritis. Though this is true in some cases, it is not a general rule [17]. The leukocytes here essentially indicate granulocyte infiltration in the renal interstitial tissue and the urinary tract, where both these sites are involved at the same time, as in the case of pyelonephritis. Granulocytes are, however, by no means a constant feature in interstitial nephritis. Hence granulocytes are found only in some cases [64,66].

This is also true of pyelonephritis, where concurrent inflammation of the urinary tract makes an abundance of granulocytes in the urine more likely. This occurs, however, only where there are active exudative lesions. When the inflammation of the urinary tract (much of the urinary sediment in this disorder is probably affected by changes at this level) is only slight, and that of the parenchyma consists mainly of a mononuclear infiltrate, there may be few or no leukocytes in the urinary sediment, even when the lesions are progressing.

A small amount of sediment, despite active renal interstitial lesions, is a common feature of many acute and chronic, non-bacterial interstitial nephropathies in which lymphocytes, monocytes and plasma cells predominate and there is no inflammation in the urinary tract. Some cases of acute interstitial nephritis caused by drugs, for example methicillin and beta-lactam antibiotics, follow a different course. Here the renal interstitial infiltrate may be rich in eosinophils and eosinophiluria is frequent [24,32,33].

Marked eosinophiluria may also be found in some cases of cystitis (such as the cystitis in schistosomiasis) and in bladder neoplasms.

337 Chronic pyelonephritis. The interstitial tissue is fibrous with an abundant infiltration of inflammatory cells. The tubules are few in number and atrophied. The glomerulus in the center of this field shows periglomerular fibrosis. Histological findings of this kind are common to chronic pyelonephritis and other types of non-bacterial interstitial nephropathies (100x).

338 Chronic pyelonephritis. Note the dilated tubules with a «colloid» appearance. The tubules are lined with flattened epithelium and contain homogeneous, eosinophilic casts. Mononuclear cells have infiltrated into the interstitial tissue. In cases of this kind granulocyturia is generally slight and may even be absent (250x).
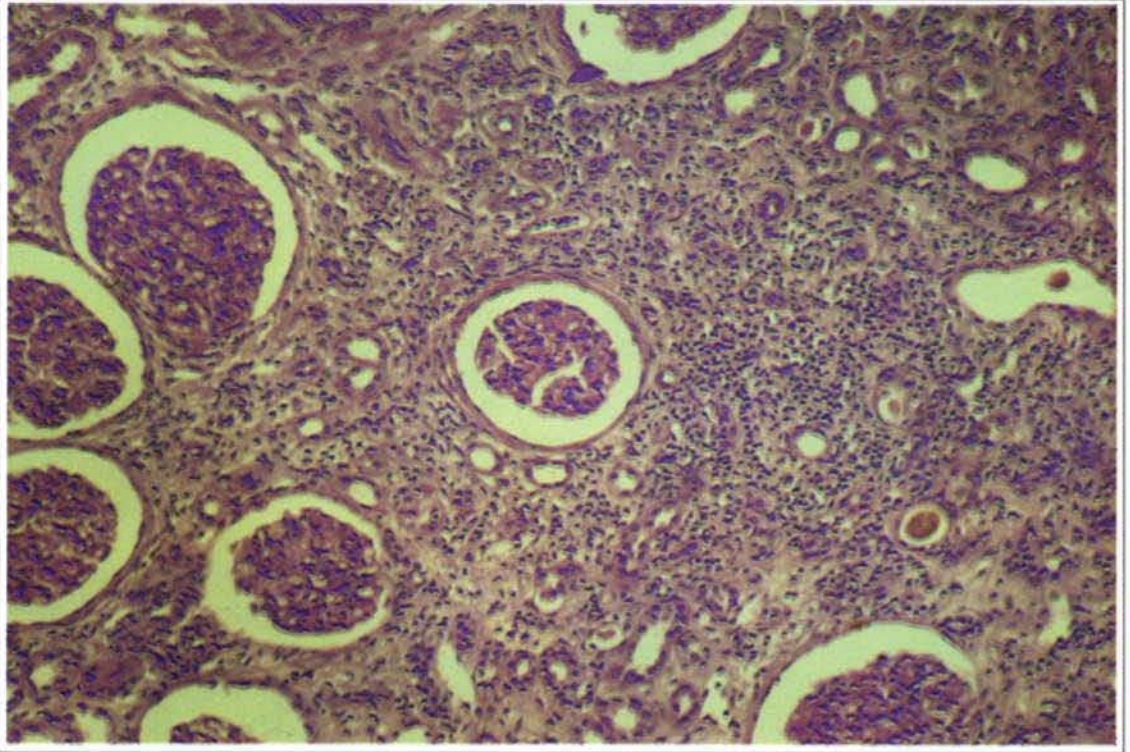
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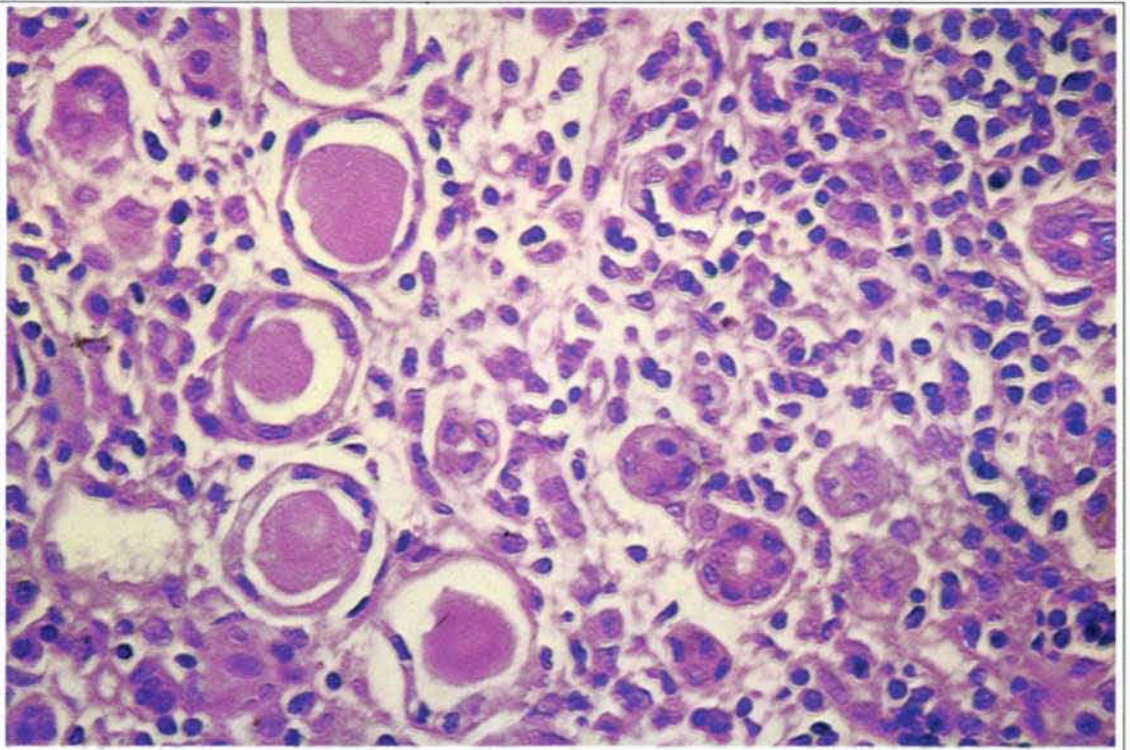
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In urinary infection the possibility that the leukocytes in the urinary sediment may have come from the urinary tract rather than the kidney makes it difficult to distinguish between a limited infection, which affects only the urinary tract, and pyelonephritis. Observation of the Sternheimer-Malbin cells (p. 26) is of no use in this connection, and only the appearance of granulocyte casts or the presence of a few granulocytes within casts indicates that the leukocytes come from the renal parenchyma. Granulocyte casts have, however, no diagnostic value for pyelonephritis and other interstitial nephropathies, since they can also be found in other non-interstitial nephropathies, such as glomerulonephiritis, although the urinary picture is then very different (p. 102).

In spite of this limitation, the presence of granulocyte casts where leukocytes are prevalent and persistently present is an important factor in favour of a diagnosis of interstitial nephritis. The same is true for the consistent association of leukocytes, whether abundant or isolated, with other kinds of cast (hyaline, granular, cellular). Although casts are often found at the parenchymal level, they rarely pass into the urine in interstitial nephropathies, so that they must be sought with particular care, and, if not found, this diagnosis is not necessarily excluded.

339 Chronic pyelonephritis. Few leukocytes. Bacteriuria. There is no relationship between the leukocyte findings and the impairment of the kidney in chronic pyelonephritis. There may be severe parenchymal lesions and yet only scant urinary sediment. Often, as in this case, the finding is completely non-specific (400 x).

340 Acute pyelonephritis associated with urolithiasis. Severe hematuria and leukocytes (400 x).

341 Squamous cells, leukocytes and a cellular cast (chronic pyelonephritis) (400 x).

342 Phase-contrast examination does not always permit recognition of the granulocytes in casts (400x).

343 Moderate leukocyturia (uroculture with negative bacterial count); chronic interstitial nephritis caused by phenacetin (400 x).

344 Leukocyturia. The hyaline casts here suggest that the parenchyma may be involved (chronic pyelonephritis) (400 x).
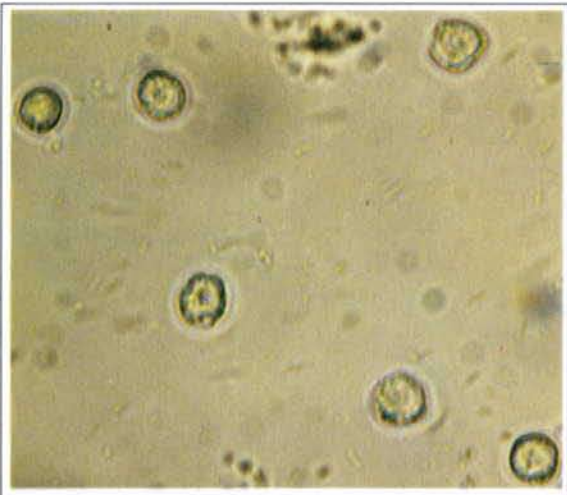
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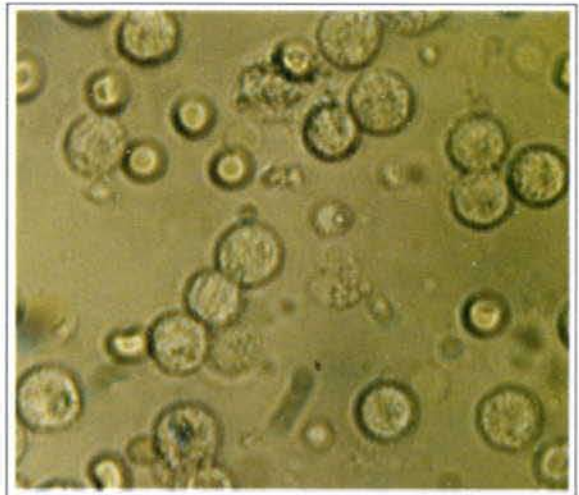
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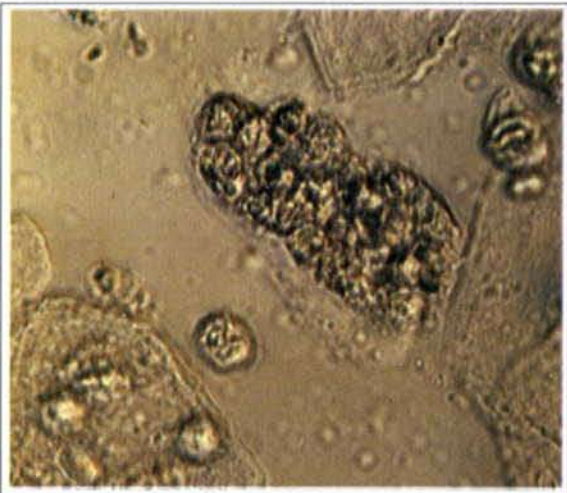
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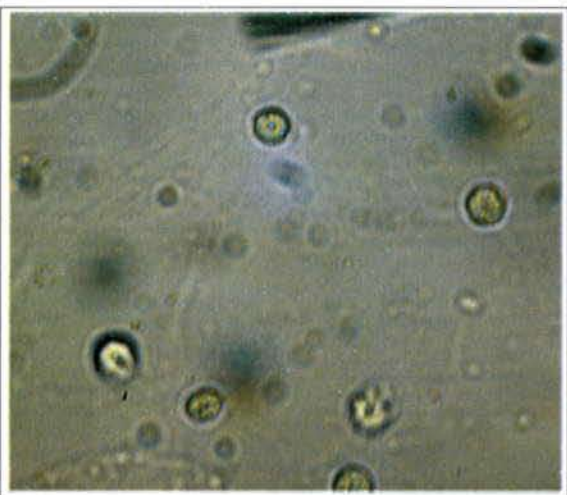
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In interstitial nephritis, hematuria is generally absent or is only slight and less than the leukocyturia; it is a prominent feature or abundant only in a minority of cases, and even then is often only transitory.

Hematuria of parenchymal origin is rather rare, and may be due to associated glomerular lesions. In pyelonephritis it can generally be attributed to a concurrent urologic lesion such as calculus, inflammation of the pelvis, ureters or bladder, rupture of venous plexuses in hydronephrosis, polyposis, etc.

It should be remembered that erythrocytes of «non glomerular» origin are generally better preserved, whereas those from the renal parenchyma are more often of abnormal appearance.

An increase in squamous cells from the urinary tract is considered a sign of inflammation. It is, however, a finding observed mainly, and not constantly, only in acute stages or during relapses.

345   Leukocytes and erythrocytes (polycystic kidney, probably with pyelonephritis as well) (400x).

346   Severe hematuria and pyuria. Well-preserved erythrocytes, more numerous than leukocytes (chronic pyelonephritis, urolithiasis) (400x).

347   Leukocytes more numerous than erythrocytes, mostly depigmented (active stage of chronic pyelonephritis) (250x).

348   Squamous cells, slight leukocyturia, microhematuria (chronic pyelonephritis in renal failure) (250x).

349   Leukocyturia. A hyaline cast (chronic pyelonephritis) (400x).

350   Leukocyturia and microhematuria, magnesium ammonium phosphate crystal (chronic cystitis; hypertrophy of the prostate with urinary stasis (400x).
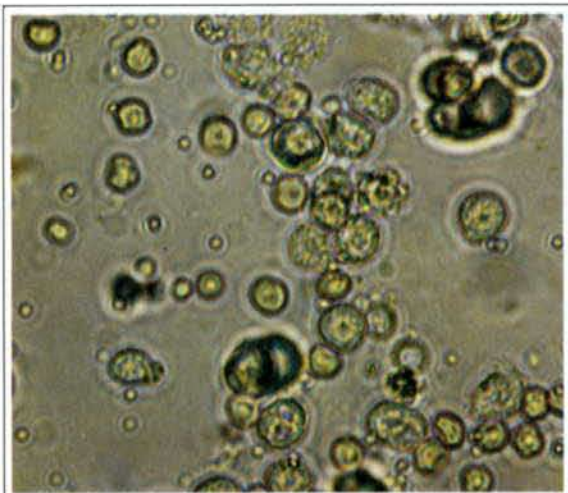
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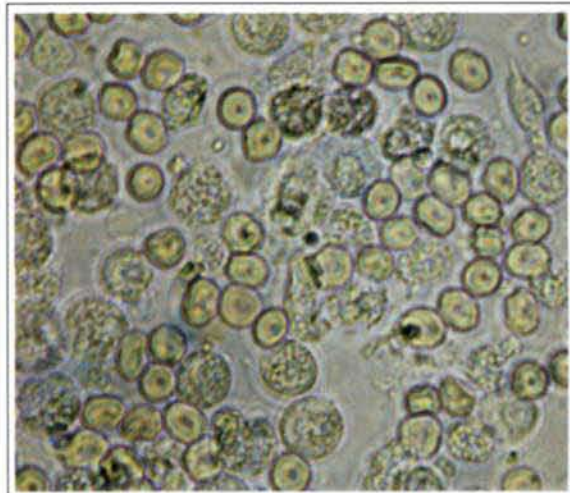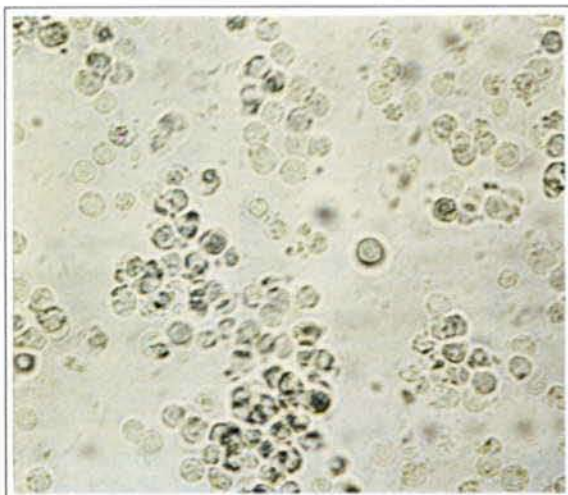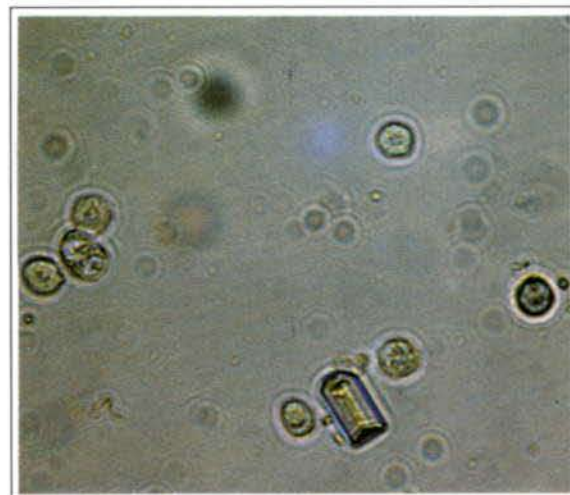
4.3 ESSENTIAL ARTERIAL HYPERTENSION

Almost all diseases of the kidney may cause arterial hypertension, and the characteristics of the urinary sediment that indicate such a nephropathy are obviously important. Many authors insist that urinary findings in «non-renal» arterial hypertension are often negative (that is in essential hypertension, although endocrine, renovascular and other forms of hypertension behave in a similar way). In fact, secondary renal functional and structural lesions are almost always present in patients with long-standing benign essential hypertension but often escape notice in routine diagnostic tests.

In borderline essential hypertension which, provided there are no renal atherosclerotic lesions, is accompanied by a proteinuria within the normal range or only in slight traces, the urinary sediment is normal or shows only barely significant microhematuria or sporadic hyaline casts. Findings of this kind are more obvious in some cases of mild hypertension, in which their appearance or increase indicates a definite deterioration. In severe essential hypertension, especially in the accelerated forms, proteinuria may become conspicuous, and the sediment is often rich in erythrocytes and polymorphic casts, and sometimes also red cell casts.

351 Slight hematuria in a patient who had had essential arterial hypertension (180/120 mm Hg) for at least 5 years. Slight proteinuria. Creatinine clearance within the normal range. A finding of this kind may be indicative of the initial stage of secondary renal impairment (400x).

352 Hyaline casts, microhematuria. Proteinuria within the physiological range (40 mg/day). Essential hypertension. Previous urinary findings had always been normal. A situation of this kind raises doubts about the efficacy of hypotensive treatment. Its anomalous character is confirmed by the fact that it may disappear after a few months of careful treatment of arterial hypertension. Similar behaviour is sometimes found in cases with slight proteinuria (400x).

353 Microhematuria, hyaline cell casts. Arterial hypertension defined as essential, after 5 years of irregular treatment. Blood pressure recently deteriorated, with values of up to 220/140 mm Hg. If the diagnosis of essential hypertension is correct, the appearance of secondary renal anatomical lesions should be suspected in such a case (160x).

354 Microhematuria. Malignant stage of essential hypertension (250/150 mm Hg). In these conditions the sediment may become indistinguishable from that found in chronic glomerulonephritis. A finding of this kind is often accompanied by functional impairment (400x).

355 Hematuria, hyaline cast. Heavy proteinuria. Malignant stage of hypertension, probably essential. Gross hematuria can be found in 10-20% of cases of malignant hypertension (160x).

356 Many hyaline casts (long-standing arterial hypertension; heart failure) (100x).
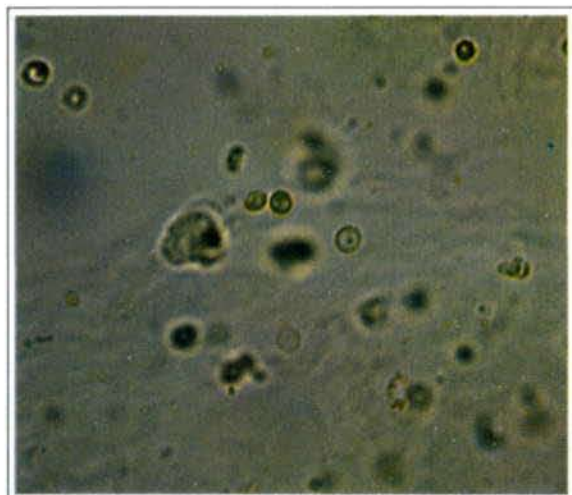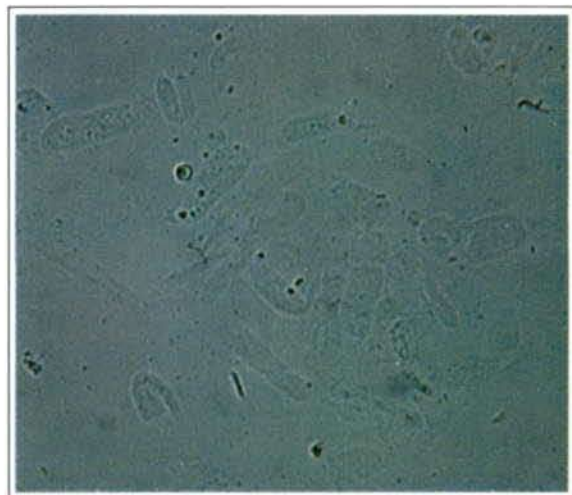
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The interpretation of urinary findings in hypertensive patients may often be difficult. It is now recognized that chronic glomerulonephritis may be asymptomatic for some time initially, and in such cases arterial hypertension may constitute the first sign of the nephropathy. Some patients with primary IgA nephropathy (Berger's disease) may have, even over long periods, normal urinary findings, or only slight hematuria together with arterial hypertension, which can then be classified as essential.

Chronic interstitial nephropathies and cystic diseases of the kidneys may also sometimes proceed for a long time with normal or only slightly altered urinary findings, in which case arterial hypertension, when present, becomes the first obvious sign of the nephropathy. It is understandable that in cases of this kind a hurried assessment of the urinary findings could lead to mistaken diagnoses.

357 Isolated hyaline casts from a patient with severe arterial hypertension (220/130 mm Hg) treated irregularly for years, with signs of left ventricular hypertrophy and hypertensive retinopathy.
Findings of this kind do not, however, exclude the presence of renal lesions, with functional impairment (polyuria and reduction in creatinine clearance; unilateral chronic nephropathy with renal atrophy) (100x).

358 Quite normal red cells in urine collected in the course of a renal colic (mild arterial hypertension). The relationship between calculi and arterial hypertension is quite often difficult to define clearly. Sometimes it is a mere coincidence (400x).

359 Leukocyturia; bacteriuria produced by contamination (cultural examination of the urine was negative here). Arterial hypertension. An intravenous pyelogram showed up the pyelocaliceal alterations typical of a chronic interstitial nephritis of analgesic origin and enabled a previous diagnosis of essential hypertension to be corrected (400x).

360 Slight microhematuria and leukocyturia. Slight proteinuria. Arterial hypertension (190/115). Polycystic kidneys (160x).

361 Arterial hypertension of up to 180/110 mm Hg for two years. Right kidney cut off by a calculus in the ureter. Arterial pressure returned to normal after nephrectomy had been carried out because of pyonephrosis. When the patient entered hospital, the urinary findings were just within the normal range, because of the total exclusion of the damaged kidney (400x).

362 Severe arterial hypertension. Biopsy diagnosis of Berger's glomerulonephritis. This sediment, observed over a prolonged period between two episodes of macrohematuria, contained a few quite normal erythrocytes and gave no clear indication of glomerulonephritis (400x).
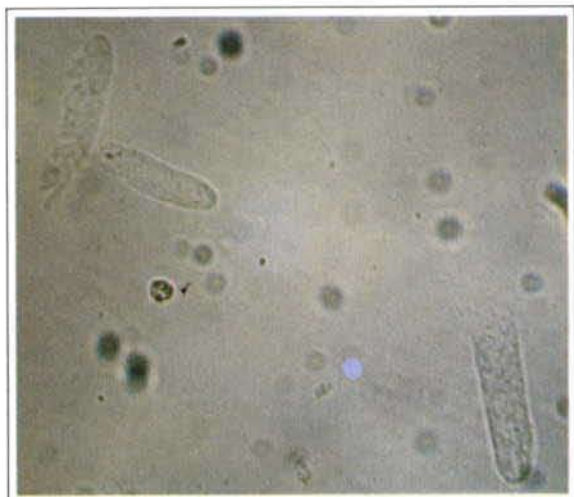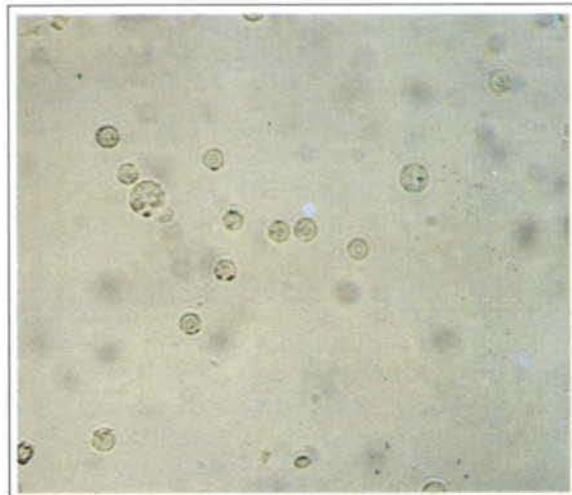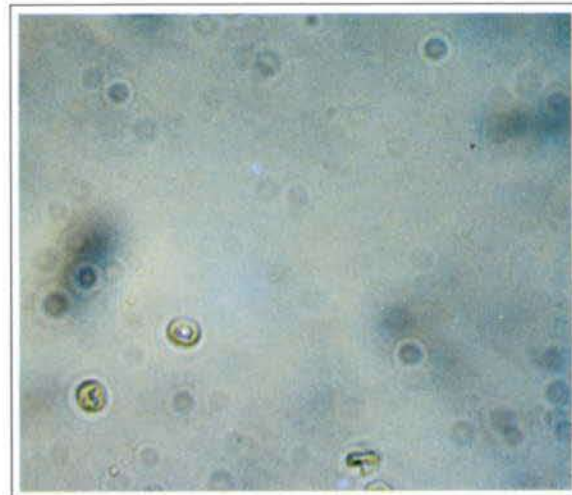
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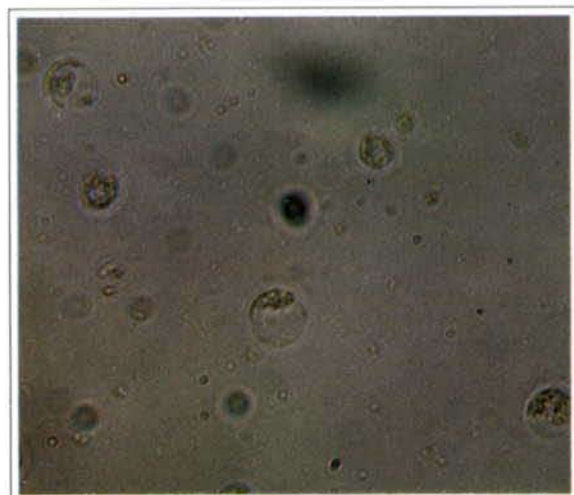
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4.4 HEMATURIA

Hematuria, as demonstrated clinically and in the laboratory, is often a guide to diagnosis. For example, microhematuria together with moderately severe proteinuria (at least 1 g/24 hours) and/or casts, is suggestive of a nephropathy that is usually of glomerular origin. Recent excretion of clots is typical of a lesion of the urinary tract.

However, it is often very difficult to differentiate a microhematuria, accompanied by a proteinuria within or slightly above the normal range, resulting from a nephropathy (generally glomerulonephritis), from that of a urologic disorder, for example a microlithiasis.

The morphology of the erythrocytes can sometimes be a guide to diagnosis. They are quite normal in cases of «urologic» lesions, but badly deteriorated with morphological changes in some nephropathies (p. 10). In other cases an indication may come from other elements in the sediment; for example, when there are casts, especially red cell casts, glomerulonephritis is very probably involved (p. 78), but persistent leukocyturia, together with but exceeding the hematuria, is indicative of an inflammatory process, frequently an infection.

It may also prove very useful to examine the features of the hematuria over a period of time, since it is subject to very rapid variations in some urologic lesions.

During the last few years the traditional attribution of intermittent and transitory hematuria to bleeding from the urinary tract (e.g. calculus, a tubercular lesion or a neoplasm) has had to be re-examined, because a relapsing hematuria, which clears up rapidly, is often found in primary IgA glomerulonephritis. Named after Berger, who first described it, it is frequently a focal proliferative glomerular disease. Moreover, in this disease, notwithstanding the pseudo-urologic behavior of the transitory hematuria, which is often macroscopic and quickly resolved, its disappearance is not generally so rapid as that of hemorrhagic lesions in the urinary tract, where the urinary findings may return to normal in a few hours. This is why the practice of checking the urine at short intervals, sometimes several times a day, is still justified in cases of intermittent hematuria. In Berger's glomerulonephritis red cell casts may also be found, though they may easily be missed as they are intermittent and generally very few in number.

363-364 Microhematuria, cells in poor condition (400x), (400x).

365 Microhematuria with abnormal cells (glomerulonephritis) (400x).

366 Severe hematuria. Quite normal erythrocytes (vesical bleeding) (400x).

367 Clot (400x).

368 Partly lysed erythrocytes (from a clot) (100x).
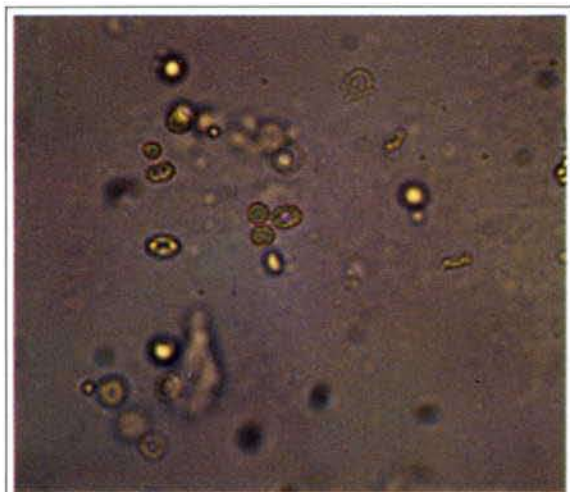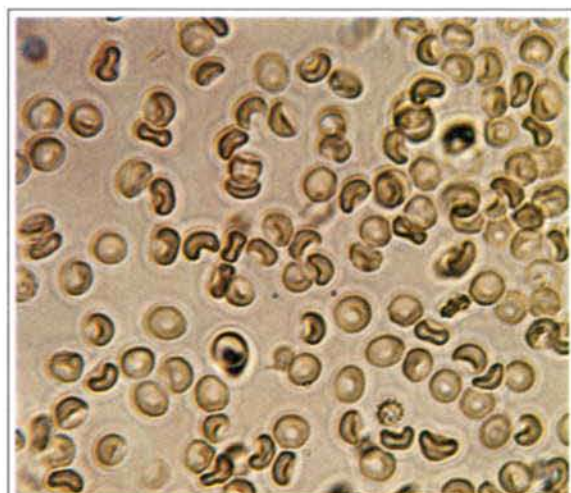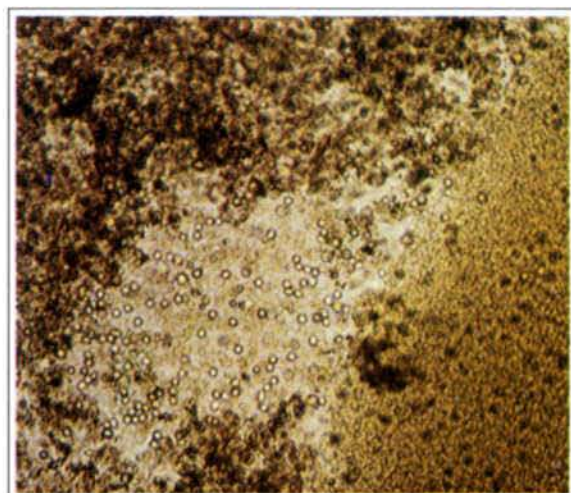
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Non-specific hematuria is very often found. In such cases, which are among the most frequent in nephrological practice, the only sign of abnormality may be in the urinary sediment, examination of which is practically the only means of keeping check on the course of a disorder that has not yet been properly diagnosed. As it has already been pointed out, especially in the case of slight microhematuria, morphological study of the erythrocytes may be insufficient to provide reliable diagnostic evidence (p. 18). In some of these cases only renal biopsy gives a really positive diagnosis. When the microhematuria is an isolated finding of only a few cells, it is not, however, unusual for the biopsy sample to appear normal, or with only «minor» not easily classifiable changes.

369   Microhematuria. Cast with blood cells. A finding of this kind confirms the renal origin of the erythrocytes and thus has a precise diagnostic value. Such casts are rare and it may be necessary to look for them when the urinary sediment has been «enriched», preferably during episodes of intercurrent infection (100x).

370   Finding similar to the above (160x).

371   Finding similar to the above (160x).

372   Erythrocytes of mainly normal appearance. Granular red cell cast (Berger's glomerulonephritis) (400x).

373   Microhematuria, abundant mucus. A finding of this kind is suggestive but not pathognomonic of a haemorrhagic lesion in the lower urinary tract (400x).

374   Leukocytes, microhematuria, well-preserved erythrocytes in a thread of mucus. A «urologic» picture (prostatitis) (400x).

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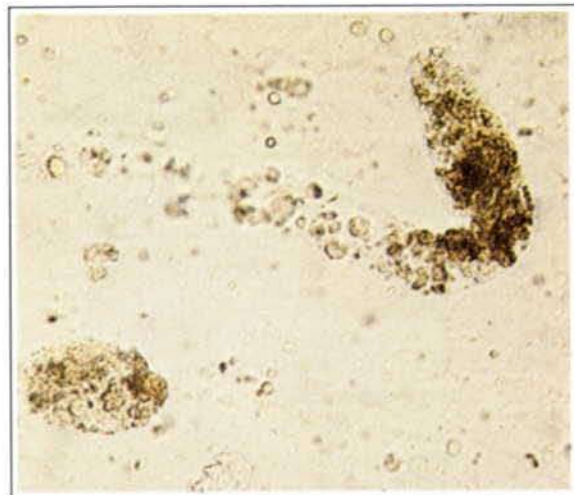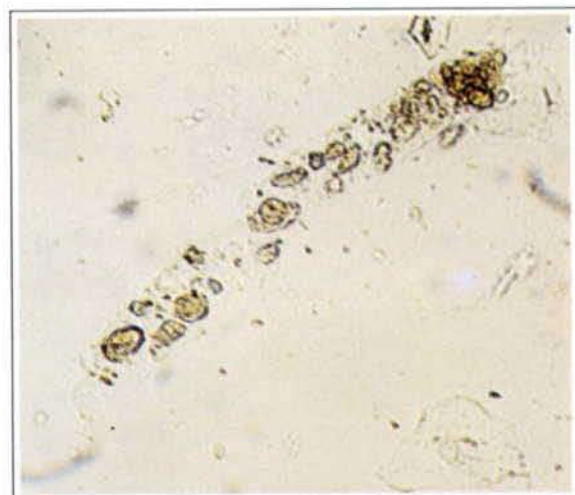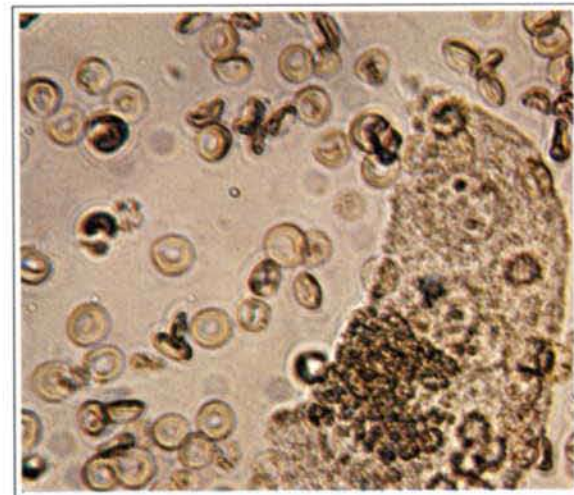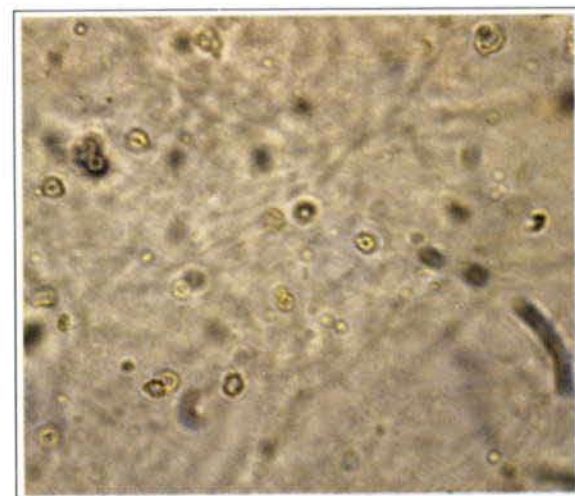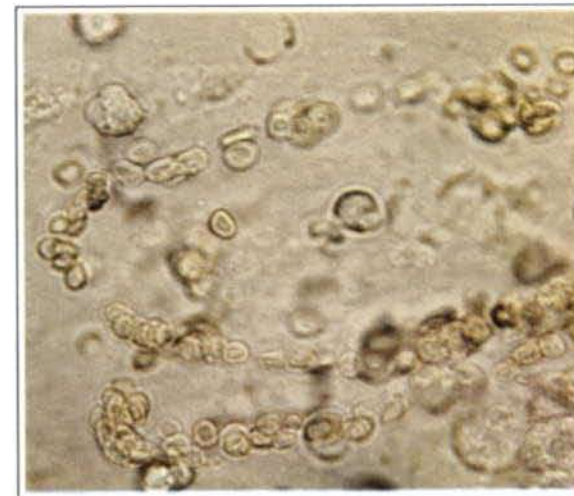
4.5 LEUKOCYTURIA

An increase in leukocyturia that exceeds the physiological range generally indicates inflammation of the urinary tract or the renal parenchyma, unless it is due to contamination from vaginal secretion or smegma.

It is often hard to attach any precise significance to this finding when the leukocyturia is slight or only an isolated finding, but as it may be the only sign of bacterial or other inflammation in the parenchyma or the urinary tract, its importance should not be under estimated. When found together with bacteriuria it is an indication of infection in the urinary tract.

Leukocyturia in alkaline urine containing urease-producing bacteria (e.g. *Proteus*) may indicate a bladder outlet obstruction that is as yet asymptomatic; in a patient with a radio-opaque urinary calculus it should suggest the presence of an infection-induced urinary stone (triple phosphate stone). However, slight leukocyturia with a negative urinary culture is not a rare finding even in urate and oxalate urolithiasis, and is probably produced by the chronic inflammatory action of the calculus on the mucous membrane. It used to be thought that a non-bacterial leukocyturia was indicative of a tubercular lesion, but interstitial nephropathies of toxic, mechanical, obstructive, ischemic or immunological origin, in the absence of infection, may produce a non-bacterial leukocyturia. In these circumstances the acidity or alkalinity of the urine depends on whether or not the acidifying capacity of the kidneys has been impaired, and on the patient's diet.

In glomerulonephritis the presence of neutrophils in the urine is generally associated with pronounced hematuria and renal epitheliuria, and suggests the occurrence of exudative phenomena in the glomerulus.

At the onset of acute glomerulonephritis a large number of leukocytes may be observed in a few cases; they may even be more numerous than the other constituents of the sediment.

375 Granulocyturia, bacteriuria (cystitis) (400 x).

376 Slight leukocyturia, with relatively normal cells. Non-specific finding (250 x).

377 Three leukocytes and an ammonium magnesium phosphate crystal. If found in freshly voided urine, such crystals suggest an infection with urease-producing bacteria and, often, bladder outlet obstruction (400 x).

378 Granulocyturia, probable leukocyte cast (chronic pyelonephritis) (160 x).

379 Leukorrhea (100 x).

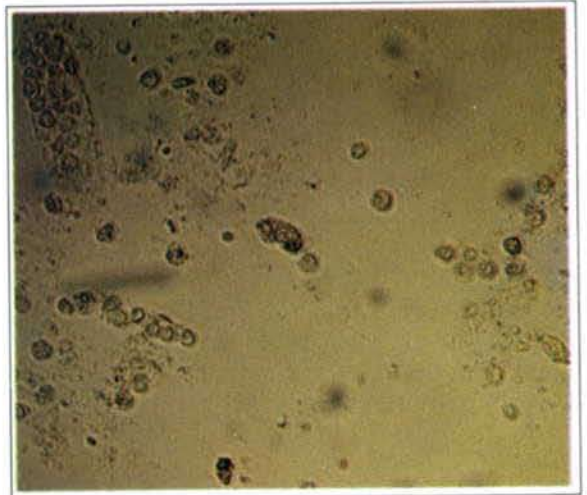380 Leukocytes, free and in threads of mucus (prostatitis) (100 x).
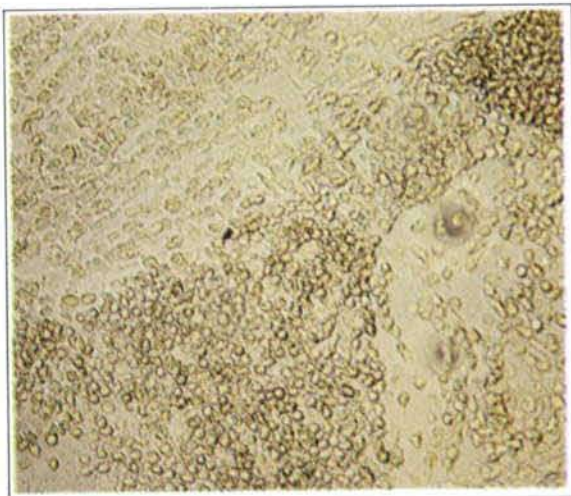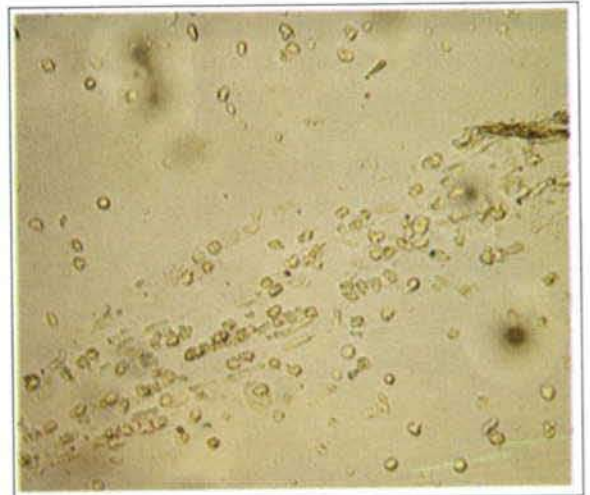
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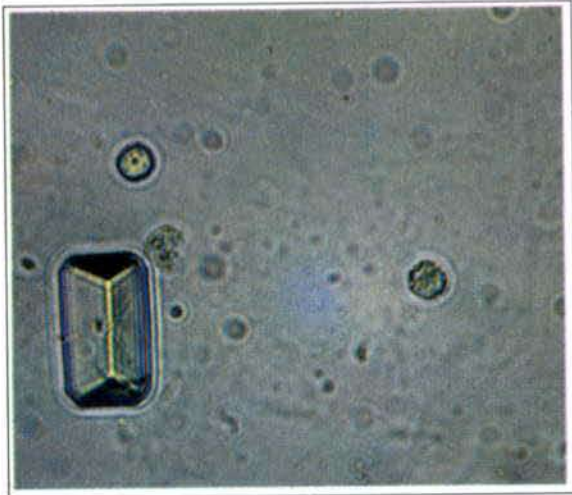
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4.6 BACTERIURIA

The presence of bacteria in routine tests is almost always due to improper storage of the sample to be examined. If urine is examined immediately after voiding, bacteria can generally be observed only in cases with counts of at least 100000 organisms/ml and hence the finding has unquestionable practical significance. Examination of the sediment must, however, be accompanied by bacterial count; the same is true of analysis for nitrites, sometimes claimed to be a method that can be substituted for bacterial counts.

It has been stated that antibody-coated bacteria, which can be detected by immunoflorescence (the Thomas test), can be considered to be of renal parenchymal origin as they are not found in bacteriuria arising from the urinary tract.

Interest in this test is, however, limited as there might also be positive findings in cases of prostatitis and cystitis, or because of vaginal bacteria. At least in males, however, if this test is positive it generally indicates that the disorder is not simply an infection of the lower urinary tract, but involves the kidney, the prostate or else an infection «invading» the bladder walls [61].

The many cases of chronic pyelonephritis among chronic uremic nephropathies, and the increasing availability of antibacterial drugs had led to the hope that, with systematic screening and the treatment of bacteriuria, the frequency of uremia could be reduced.

In fact, it has been found that the situation cannot be resolved in such a simple way, and it has had to be recognized that the nature of the bacteriuria and its relationship with chronic pyelonephritis has not so far been clarified.

The observation of true bacteriuria is still, however, of unquestionable practical significance, and, when it is found together with leukocyturia, a definite diagnosis of urinary infection can be made.

The possible significance of isolated bacteria in the urine is more difficult to assess. In the adult, if the urinary tract is initially normal, even a prolonged follow-up period will not generally reveal parenchymal lesions, and the disorder is, therefore, generally considered to be benign. However, since urinary infection may intensify any nephro-urologic lesions, significant bacteriuria in a nephropathic subject or in a patient with urinary tract disorder, should not be ignored.

In children, and in young children in particular, a bacteriuria should be investigated very carefully as it is so often accompanied by cysto-ureteral reflux and renal lesions [28].

It should also be mentioned that urinary infection may contribute to the development of urolithiasis, and that in pregnancy it is accompanied by a high morbidity rate. Chronic bacteriuria and frequent relapses or reinfection may lead to the discovery of an asymptomatic lesion in the uropoietic tract.
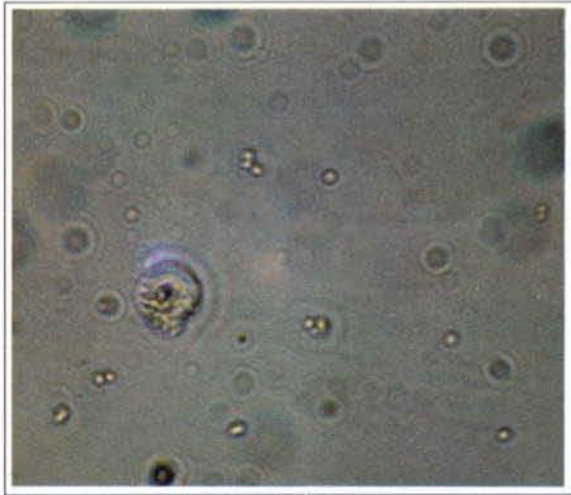
381   Abundant bacteriuria (160x).

382   The same field in phase-contrast (160x).

383   Bacteriuria (400x).

384   The same field in phase-contrast (400x).

385   Antibody-coated bacteria. Thomas test (400x).

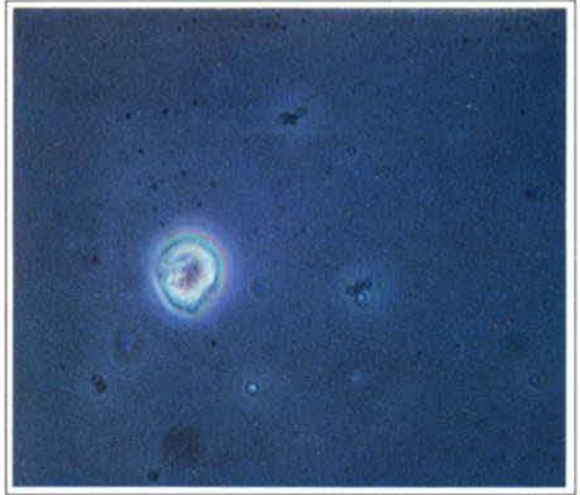386   Antibody-coated bacteria. Thomas test (400x).
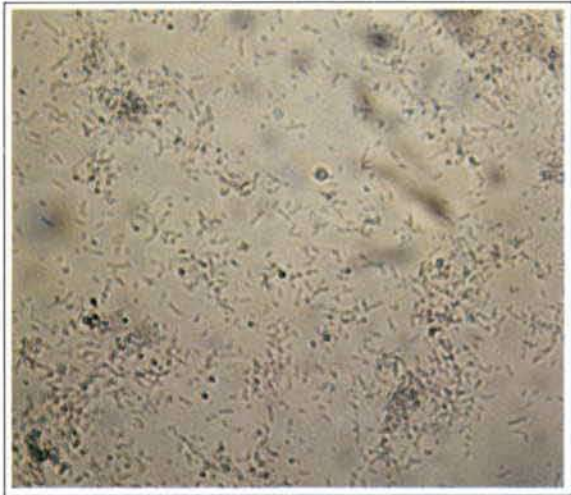
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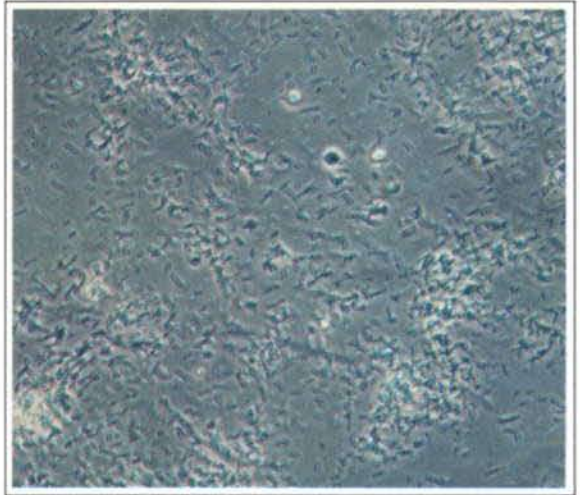
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4.7 ACUTE RENAL FAILURE

Acute renal failure may be caused by several types of nephropathy: glomerular, vascular, interstitial or tubular. Some characteristics of the sediments found in acute glomerulonephritis and in some vascular and interstitial nephropathies have been mentioned in the preceding chapters.

In post-ischemic, pigment or toxin-induced acute renal failure («acute tubular necrosis»), the urinary sediment can also provide information of great interest. At the very onset of vasomotor nephropathy in shock, when the oliguria is rapidly reversible by suitable therapy, the sediment is generally normal; at most, hyaline casts, which are mainly small in diameter, and a few granular casts will be found.

During the initial stage of more severe renal failure, renal epithelial cells will generally be observed free or in inclusion casts; «shock casts», containing medium and small granules that are rounded or oval in shape, are a particularly characteristic feature [63].

These constituents, which may be accompanied much later by a few granular-waxy casts of large diameter, are found almost exclusively during the acute hypovolemic stage and disappear rapidly if this is overcome and the excretory function of the kidney is regained adequately. Microhematuria and leukocyturia are never found in this early phase.

387-388 Oval shock casts (250x), (250x).
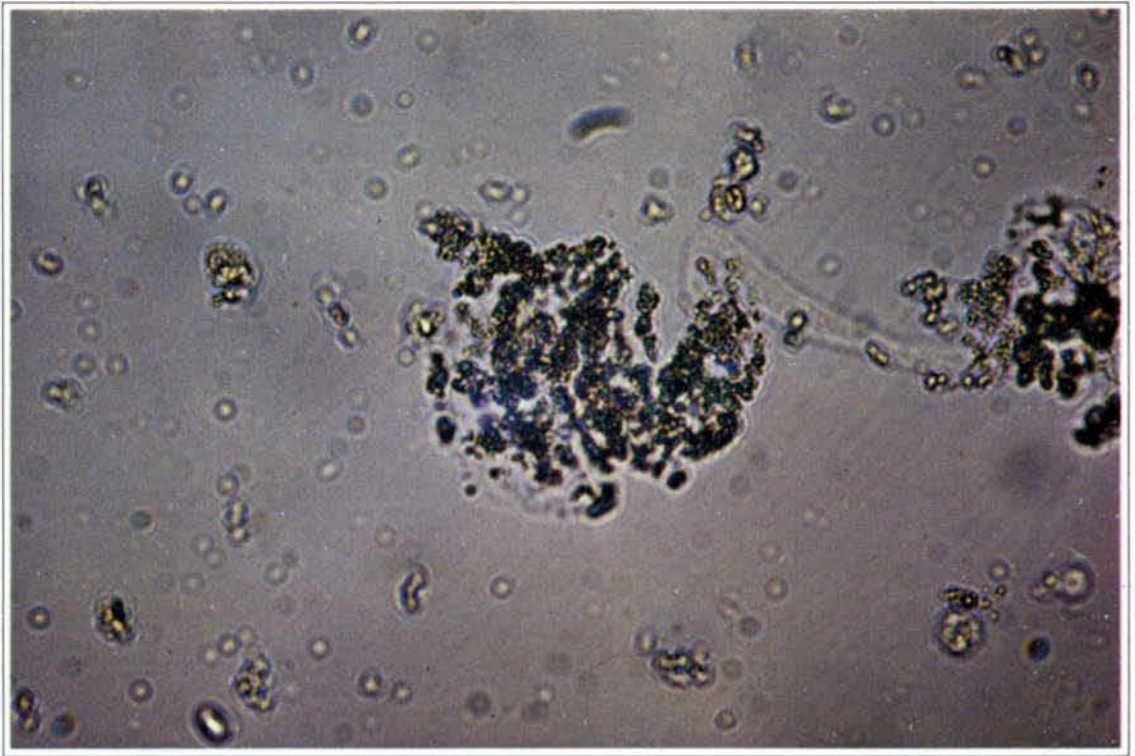
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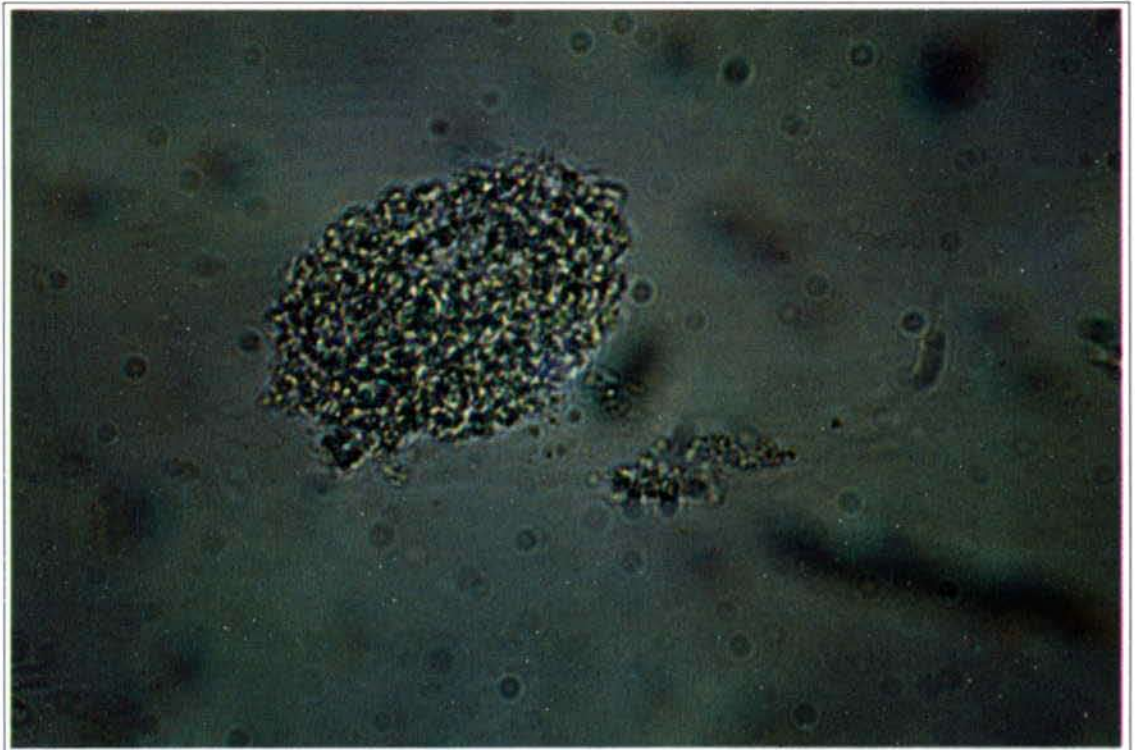
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389-390 Finely granular casts; scattered granular material, no hematuria (acute post-ischemic renal failure, in the very early oliguric stage) (250x), (250x).
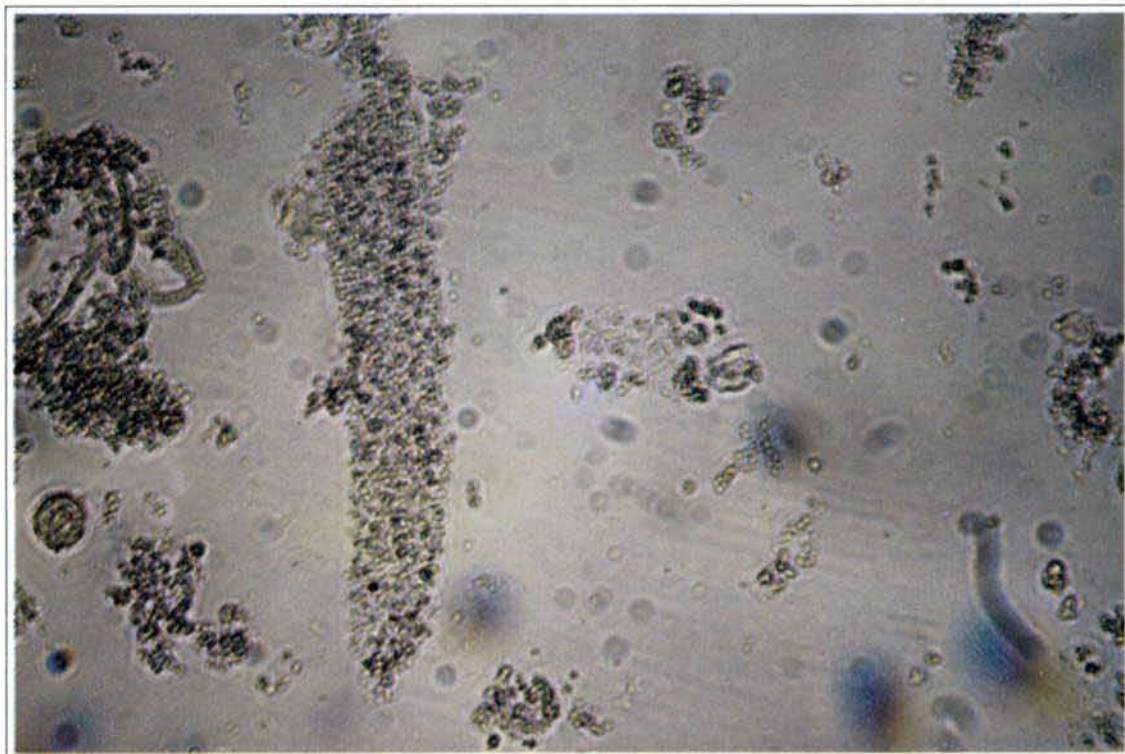
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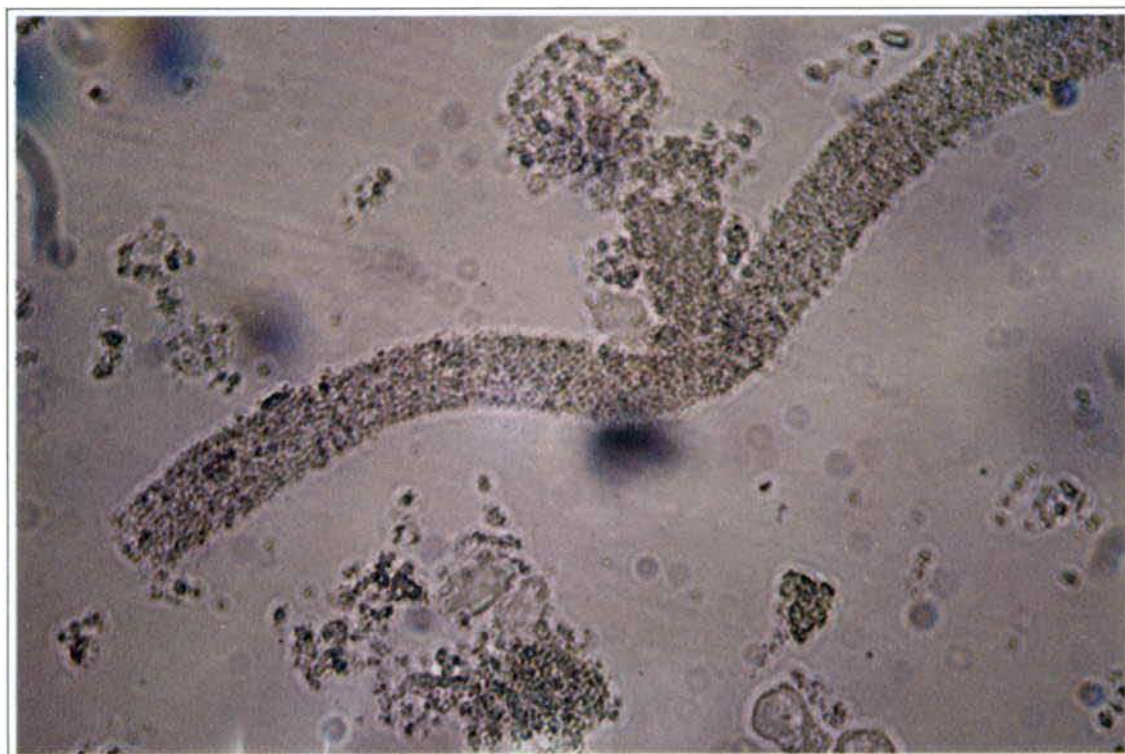
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In post-ischaemic, pigment or toxin-induced acute renal failure («acute tubular necrosis»), hematuria may be a prominent feature of the sediment for a very short time, together with polymorphic casts; an abundance of red cell casts is suggestive of cortical necrosis. Epitheliuria, generally with degenerating cells, may be important initially.

Leukocyturia is generally infrequent, unless there is also a catheter-induced infection [40]. In cases of jaundice, the casts and cells are generally pigmented. When hemolysis has taken place, pigmented casts of hemoglobin origin are usually found.

In acute renal failure there is often very little sediment.

The polyuric phase is generally preceded by the excretion of large casts. The administration of «loop» diuretics has, however, a considerable modifying effect on the sediment under these conditions, and casts are far less frequent. When urine flow is restablished, the amount of sediment is generally negligible, unless infection intervenes.

391-392   Granular casts, granular epithelial casts, and hematuria with abnormal cells in cases of acute renal failure caused by acute pancreatitis.
Findings of this kind in a case of acute, shock-induced renal failure suggest that the pancreas is involved (250x), (250x).

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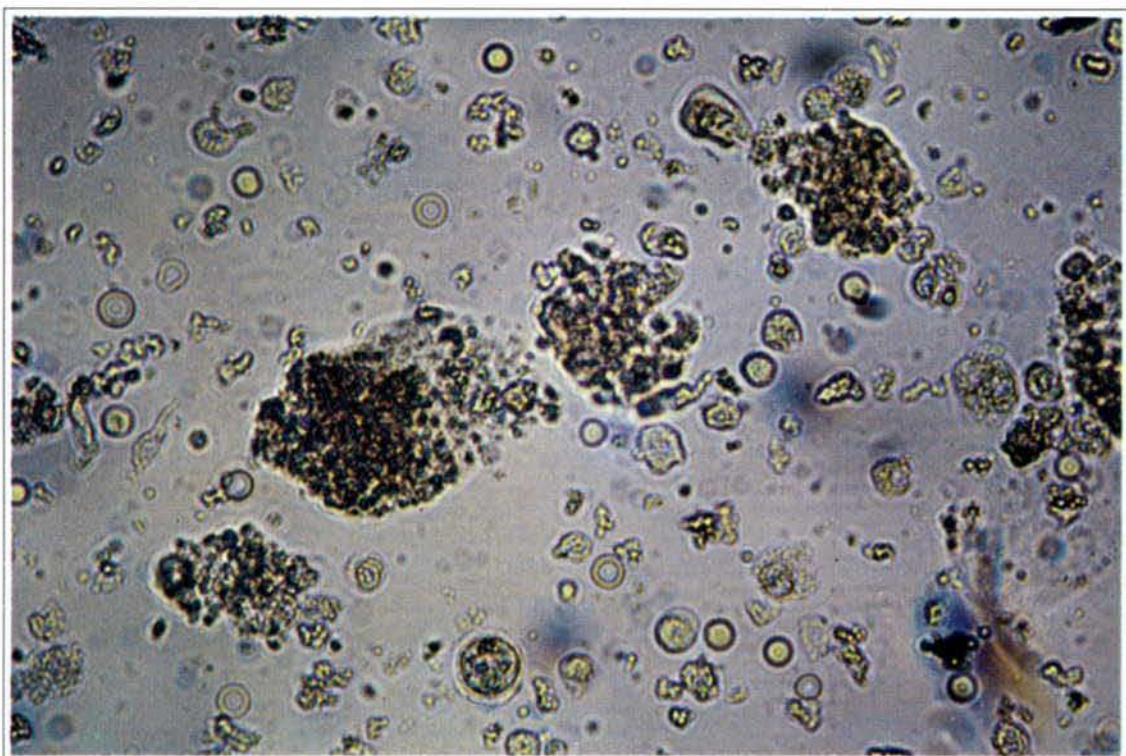
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4.8 CHRONIC RENAL FAILURE

There are many nephropathies which may cause chronic renal failure. Glomerulonephritis has been found in 30% of our patients on dialysis; chronic interstitial nephritis is next in order of frequency (18%), then nephroangiosclerosis (12%) and polycystic kidney disease (8%).

In nephropathies leading rapidly to chronic renal failure the most typical features of the urinary sediment are very clear.

Severe leukocyturia is found, for example, in some cases of severe chronic pyelonephritis involving antibiotic-resistant bacteria and in analgesic nephropathy with recent papillary lesions, particularly if the drug has been taken without interruption. In cases of malignant hypertension or arteritis with severe renal failure, it is by no means rare for the urinary sediment to be so abundant as to look like sediment from a case of glomerulonephritis.

Very typical urinary findings occur in some primary or secondary glomerulonephritis cases with diffuse and active glomerular lesions (generally they are cases with extracapillary, membranoproliferative or diffuse proliferative lesions). They are characterized by the abundance of the hematuria with abnormal red cells, and the presence of mononuclear cells and sometimes leukocytes. In these cases polymorphic casts of medium and large diameter are an important indication of the severity of the disease process.

In advanced cases of chronic renal failure, there is less sediment, and even the observation of a few large casts should arouse suspicion [1].

Finally, when sclerohyalinosis predominates and there is considerable polyuria with the urine tending to be alkaline, there may be no casts and the picture as a whole may be non-specific. Under these conditions there are often only traces of proteinuria, and mistakes in diagnosis may easily be made. In these cases, expecially in presence of severe arterial hypertension, it is not unusual to find a microhematuria with apparently undamaged cells.

393 Medium-diameter polymorphic casts. Hematuria. Nucleated cells not identifiable at this magnification (membranoproliferative glomerulonephritis with renal failure) (160x).

394 Findings similar to the above. The casts here are mainly waxy. Such findings are a definite indication of glomerulonephritis with serious anatomical impairment (100x).
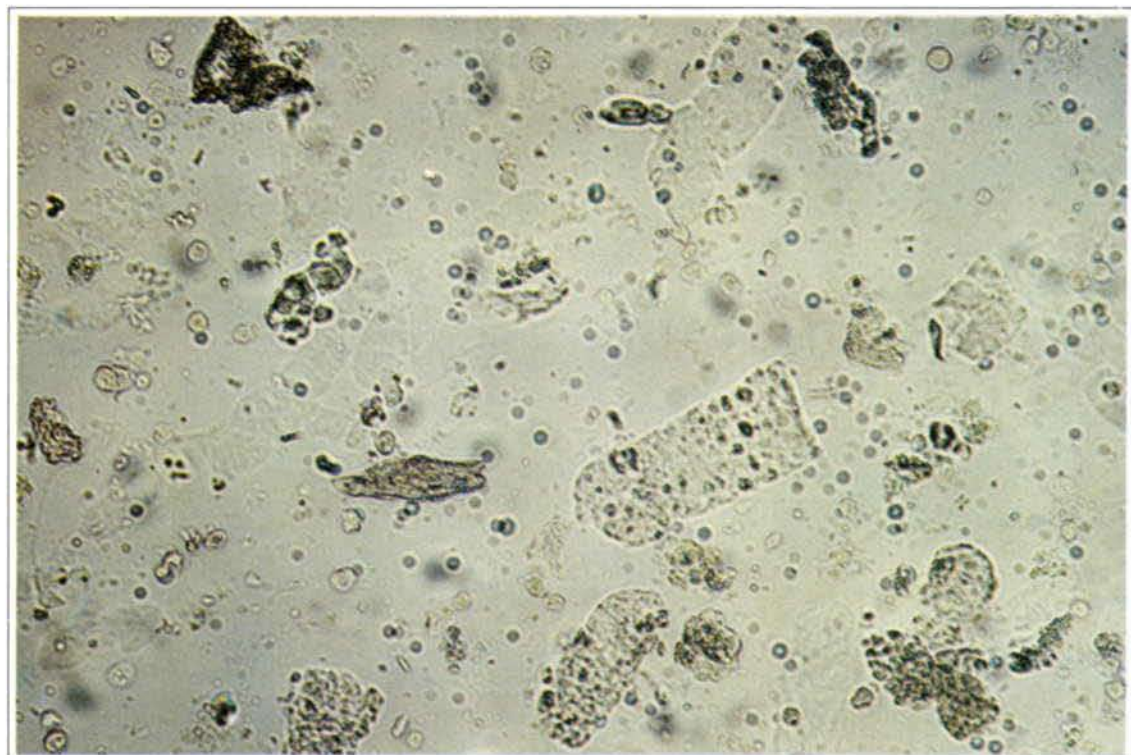
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5.0 TECHNIQUES FOR THE EXAMINATION OF URINARY SEDIMENT

When examining urinary sediment, it is useful to observe certain rules which will improve the technical procedure and interpretation.
First of all, a few points about collection of the urine to be examined are:

— Since urine produced during the night is generally acid and highly concentrated, thus enhancing the possibility of detecting some abnormalities, it is usual for the examination to be made on the first sample voided in the morning. There is, however, no reason for not examining urine voided in the course of the day, provided the patient has not taken a large amount of fluids; in that case the subsequent polyuria is likely to modify the findings.

— Unlike proteinuria, which may increase considerably in an orthostatic position, the urinary sediment is not usually affected by postural changes, either in healthy people or in patients with nephropathies. A few glomerular diseases, in the active stages, are exceptions to this, and the slightest activity on the part of the patient can then have an adverse effect on the sediment.

— During violent exercise the normal urinary sediment of a healthy person may become very clearly positive. The appearance of hematuria, after physical exertion or certain kinds of activity (travelling in jolting cars, etc.) is typical of urolithiasis, but it may also be present in a number of other urologic disorders and also, though rarely, in healthy people (e.g. the «grossly bloody urine of runners» [22,23].
Sometimes in Berger's glomerulonephritis and much more rarely in other glomerular diseases, a definite increase in hematuria may be caused by intense physical exertion. Hence, unless variations of this kind are being studied specifically, no examination of the urine should be made in any of these unusual circumstances.

— A decided deterioration in the urinary findings is also frequent in many glomerular diseases during intercurrent infections. In such cases an isolated finding of microhematuria may develop into the typical picture of glomerulonephritis, with red cell casts. For this reason, in doubtful cases of microhematuria, it may be useful to look specifically for this kind of variation, as an aid to correct diagnosis.

— Thorough cleansing of the outer genitals and the use of clean containers is essential for the proper collection of samples to be examined. In the male, the foreskin should be retracted and meatus cleansed; it is better to discard the first few ml of urine (except with leukocyturia of uncertain origin, when examination of the first ml of urine voided in the morning may be necessary to identify urethritis). In the female it is important to cleanse the vulva and the meatus thoroughly, to discard the first portion of urine voided and to collect a midstream sample, taking care not to touch the labia. It is better for the patient to make this collection at home. If the sediment examined is taken from a 24-hour collection of urine voided without these precautions, and kept at room temperature, most of its diagnostic value will be lost.

— When inflammation of the urethra has to be distinguished from that of the bladder or the middle or upper urinary tract or the prostate, it is advisable to examine the first and successive voidings separately. For the study of renal disorders, mid-stream urine should be taken for examination. The last 10-25 ml of urine can be richer in cells from the prostate and the neck of the bladder.

— Examination of the sediment should be made, when possible, immediately after voiding, and in any case not more that one or two hours later, because if urine is stored cold there may be considerable precipitation of salts which will make results difficult to interpret, whereas if it is kept in a warm environment there may be a rapid increase in bacteria, which may lead to misinterpretation.

Moreover, some of the red cells, leukocytes and casts are destroyed by being left in the urine. If bacteriuria or crystalluria is specifically suspected, urine should be examined immediately after voiding.

— Examination is generally made after centrifuging for 5 minutes at 1000-1500 r.p.m. In some cases, for example, if hemoglobin or shock casts are likely to be found, their fragility makes it advisable to examine a drop of urine removed with a pipette from the bottom of the collecting flask, after spontaneous sedimentation. When seeking elements which may have been voided in small quantities (e.g. red cell casts in the case of an apparently isolated finding of microhematuria) it is useful to concentrate the samples by a number of centrifugations.

— After centrifugation, the supernatant urine is discarded, leaving 0.3-0.5 ml in the bottom of the test tube. The size of drop placed on the slide must be such that it will not spread beyond the edges of the coverslip.

— Urine should be examined first at 100-160 x; during this first scanning the casts can best be identified by reducing the amount of light in the field, and searching for them particularly round the edges of the slide. Examination at 250-400 x is then necessary for correct identification and to study the individual elements. For a semi-quantitative assessment at least 20 fields should be examined, as large quantities of mucus, which entrap casts and cells, may distort the results. In clinical practice, diuresis is not normally taken into account; yet semi-quantitative assessments are only roughly comparable when the volumes of urine are equal.

— Examination of unstained sediment by ordinary light microscopy gives good visualization of most of the cells and casts in the sediment. Phase-contrast can improve the picture, thus rendering identification of certain cells [6,19,20] and casts [9] easier.

Examination in polarized light is required for the study of lipids, whether free or in casts or cells to demonstrate the «Maltese crosses».

— The identification and study of nucleated cells can be facilitated by staining. Although at times very useful, none of the supravital stains is always reliable. We have found that the best results can be obtained with Papanicolaou stain, but, unfortunately, this is too time-consuming to be used for routine examination.

— To evaluate crystalluria [11] the urine must be collected, preferably in the morning, directly into a thermos flask at 37°C, and analyzed without delay.

The pH is determined and a sample of about 20 ml is centrifuged in a thermostatic centrifuge at 37°C for 10 minutes at 3000 r.p.m.; 20 microlitres of sediment are removed from the bottom of the test tube with a pipette and examined under the microscope with the stage heated to 37°C. The number of crystals can be counted with a reticule. Using an objective provided with a micrometer scale, the crystals are divided into small (diameter <5 μ), medium (diameter 5-12 μ) and large (diameter over 12 μ). The aggregates can also be divided according to their dimensions, into small (up to 50 μ), medium (between 50 and 200 μ) and large (over 200 μ).

Papanicolaou stain

Preparation and fixation.
A drop of Mayer's glycerinated albumin, diluted with water, is added to the sediment. The latter has to be first washed with physiological saline if the routine examination has revealed considerable quantities of salts.
After collection with a pipette the sediment is placed on a slide and spread out gently with a coverslip, so as not to break the casts. After waiting for a few minutes, until the smear is partly dry, the slide is immersed in alcohol-ether (1/1) to fix it (minimum fixation time 30 minutes). It may be left in the solution for up to ten days with no adverse effects on subsequent staining.

Staining: the standard Papanicolaou technique, using shorter times for the Harris hematoxylin.

1. Ethyl alcohol 95%, 70%, 50%: 1 minute each

2. Distilled water: 3 minutes

3. Harris hematoxylin: 10-15 seconds

4. Tap water: 5 minutes

5. Ethyl alcohol 50%, 70%, 95%: 1 minute each

6. Orange G6: 1-2 minutes

7. Ethyl alcohol 95% - immerse once

8. Ethyl alcohol 95% - immerse once

9. EA 36: 1-2 minutes

10. Ethyl alcohol 95% - immerse once

11. Ethyl alcohol 95% - immerse once

12. Absolute ethyl alcohol: 2 minutes

13. Absolute ethyl alcohol: 2 minutes

14. Absolute ethyl alcohol-xylene (1/1): 3 minutes

15. Xylene: 2 minutes

16. Xylene: 2 minutes

17. Mount rapidly

Sternheimer-Malbin stain

Solution I
— Crystal violet	3	g
— Ethyl alcohol 95%	20	ml
— Ammonium oxalate	0.8	g
— Distilled water to	80	ml

Solution II
— Safranin 0	0.25	g
— Ethyl alcohol 95%	10	ml
— Distilled water to	100	ml

Solutions I and II can be kept at room temperature.
Immediately before use, three parts Solution I and ninety-seven parts Solution II are mixed and filtered.
One or two drops of the stain are added to approximately 1 ml of precentrifuged, concentrated urine sediment.
The Kova stain is a commercially available stabilized preparation of this stain.

Prussian Blue stain

Stains and shows up the ferric iron of hemosiderin, which takes on a dark blue shade. It is particularly useful for identifying hemosiderin in casts and macrophages.
Resuspend the sediment in 5 ml of a freshly made solution of one part 2% potassium ferrocyanide and one part 2% hydrochloric acid. Wait 5 minutes, centrifuge again and pour off the supernatant.

Sudan III stain

Shows up fat. Extracellular and intracellular fats are stained red. It is used especially for revealing fatty casts and oval fat bodies.
Technique: a saturated solution of Sudan III in alcohol is used. Place a drop of Sudan III on a drop of sediment, heat over a flame for a few seconds and then examine.

Murexide Test

Indicates the presence of uric acid salts. Heat the precipitate to be identified in a porcelain crucible with a few drops of nitric acid and dry off.
The test is positive if the residue turns orange and then deep violet when moistened with alkali.

The colour plates

The colour plates are of slides, collected over a period of years, that were made with sediments stained as described above, studied and photographed with a Zeiss Standard RA microscope, equipped with simplified phase contrast optics, Ph planochromatic objectives and a non-automatic microphotographic device.

BIBLIOGRAPHY

1. **Addis T.**: Renal failure casts. J.A.M.A., 84:1013, 1925.
2. **Addis T.**: A clinical classification of Bright's diseases. J.A.M.A. 85:163, 1925.
3. **Addis T.**: The number of formed elements in the urinary sediment of normal individuals. J. Clin. Invest. 2:409, 1926.
4. **Appel G. B., Neu H. C.**: The nephrotoxicity of antimicrobial agents. N. Engl. J. Med. 296:663, 1977.
5. **Berman L. B., Schreiner G. E., Feys J.**: Observations on the glitter-cell phenomenon. New England J. Med. 255:989, 1956.
6. **Birch D. F., Fairley K. F.**: Haematuria: glomerular or non-glomerular? Lancet 2:845, 1979.
7. **Boyd P. J. R.**: Haematuria. Br. Med. J. 2:445, 1977.
8. **Bradley M., Schumann G. B., Ward P. C. J.**: Examination of urine, in Henry J. B., ed.: Todd-Sanford-Davidson's: Clinical Diagnosis and Management by Laboratory Methods. 16th ed. W. B. Saunders Co. Philadelphia, 1979.
9. **Brody L., Webster M. D., Kark R. M.**: Identification of elements of urinary sediment with phase-contrast microscopy. J.A.M.A. 206:1777, 1969.
10. **Brody L. H., Salladay J. R., Armbruster K.**: Urinalysis and the urinary sediment. Med. Clin. North Am. 55:243, 1971.
11. **Caudarella R.**: Personal comunication.
12. **Cifuentes Delatte L.**: Cristalluria in: Stones, Clinical management of urolithiasis, Williams & Wilkins, Baltimore, London 1983.
13. **Cifuentes Delatte L.**: Il Laboratorio dell'urologo, Piccin Editore, Padova, 1980.
14. **Coe F. L.** in: **Brenner B. M.** and **Rector F. C. Jr**: The Kidney, W.B. Saunders Co. - Philadelphia: 1135, 1981.
15. **Cohn M.**: Ueber Fixation und Conservirung von Harn sediment. Ztschn für Klin. Med. 30:26, 1899.
16. **Di Voogy H. J., Rather P., Beyer-Boon M. E.**: Urinary cytology. Springer-Verlag, Berlin Heidelberg, New York, 1977.
17. **Dogliotti G. C., Lenti A., Vercellone A.**: La pielonefrite cronica. Relazione al 64° Congresso Soc. Ital. Med. Int. Padova, 1963.
18. **Fairley K. F., Birch D. F.**: Hematuria: A simple method for identifying glomerular bleeding. Kidney Int. 21:105, 1982.

19. **Fairley K. F., Birch D. F.**: Urinary erythrocyte morphology in microscopic hematuria. The American Society of Nephrology. Abstracts, 1982.
20. **Fasset R. G., Horgan B. A., Mathew T. H.**: Detection of Glomerular Bleeding by Phase-contrast Microscopy. Lancet 1:1432, 1982.
21. **Fasset R. G., Owen J. E., Fairley J., Birch D. F., Fairley K. F.**: Exercise and urinary red cell morphology. Second Asian Pacific Congress of Nephrology Programme and Abstracts, Melbourne, 1983.
22. **Fred H. L., Natelson E. A.**: Grossly bloody urine of runners. South Med. J., 70:1394, 1977.
23. **Fred H. L.**: More on grossly bloody urine of runners. Arch. Intern. Med. 138:1610, 1978.
24. **Galpin J. E., Shinaberger J. H., Stanley T.M., Blumenkrantz M. J., Bayer A.S., Friedman G. S., Montgomerie J. Z., Guze L. B., Coburn J. W., Glassock R. J.**: Acute interstitial nephritis due to methicillin. Am. J. Med. 65:756, 1978.
25. **Graff L.**: A Handbook of Routine Urinalysis. J. B. Lippincott Co., Philadelphia, Toronto, 1983.
26. **Greenhill A., Gruskin A. B.**: Laboratory evaluation of renal function. Pediatr. Clin. North Am. 23:661, 1976.
27. **Heintz R., Althof S.**: Das Harnsediment. Georg Thieme Verlag, Stuttgart, 1976.
28. **Hellerstein S.**: Urinary Tract Infections in Children. Year Book Medical Publishers, Inc. Chicago-London, 1982.
29. **Hoffman W. S.**: The biochemistry of clinical medicine. 4th ed. Chicago: Year Book Medical Publishers, Inc., 1970.
30. **Imhof P. R., Hushak J., Schumann G., et al:**: Excretion of urinary casts after the administration of diuretics. Brit. Med. J. 2:199, 1972.
31. **Kesson A. M., Talbott J. M., Gyory A. Z.**: Microscopic examination of urine. Lancet 2:809, 1978.
32. **Kleinknecht D., Kanfer A., Morel-Maroger L., Mery J. P.**: Immunologically mediated drug-induced acute renal failure. Contributions to Nephrology 10:42, 1978.
33. **Kleinknecht D., Vanhille Ph., Morel-Maroger L., Kanfer A., Lemaitre V., Méry J. Ph., Leaderich J., Callard P.**: Les néphrites interstitielles aïgues immuno-allergique d'origine medicamenteuse: aspects actuels. Actualités nephrologiques de l'Hôpital Necker, 1982, Paris, Flammarion.

34. **Kurtzman N. A., Rogers P. W.**: A Handbook of Urinalysis and Urinary Sediment. Charles C. Thomas, Springfield Illinois, 1974.
35. **Lippman R. W.**: Urine and the urinary sediment. Thomas, Springfield Illinois 1957.
36. **McQueen E. G., Sydney M. B.**: Composition of urinary casts. Lancet 1:397, 1966.
37. **Melamed M. R., Wolinska W. H.**: On the significance of intracytoplasmic inclusions in the urinary sediment. Amer. J. Path. 38:711, 1961.
38. **Papanicolaou G. N.**: Atlas of exfoliative cytology. Harvard University Press Cambridge Mass., 1956.
39. **Pellet H., Donne C., Deteix P., Colon S., Zech P.**: Urine sediment in glomerular haematurias. Comparative Study with Kidney biopsy findings. Abstracts. 2ème Réunion conjointe des Soc. Espanola de nefrologia. Soc. Italiana di nefrologia, Soc. de néfrologie, Lyon 1982.
40. **Piccoli G., Varese D., Rotunno M.**: Lo studio del sedimento urinario. Attualità Nefrologiche e Dialitiche. Atti 3° Corso Aggiornamento in Nefrologia e Metodiche Dialitiche dell'Ospedale Maggiore S. Carlo Borromeo, 1977, Pensiero Scientifico Editore, Roma.
41. **Piccoli G., Varese D., Verzetti G.**: Rilievi sulla leucocituria nell'insufficienza renale acuta anurizzante. Atti 64° Congresso Soc. Ital. Med. Int. Padova, 1963.
42. **Pinto B., Rocha E., Ruiz-Marcellan F. J.**: Isolation and characterisation of uricine from uric acid stones. Kidney Int. 10:437, 1976.
43. **Prescott L. F.**: The normal urinary excretion rate of renal tubular cells, leukocytes and blood cells. Clin. Sci. 31:425, 1966.
44. **Quinn J. R., Zimmerman H. J.**: Significance of oval fat bodies in urinary sediment. Am. J. Clin. Path. 24:787, 1954.
45. **Race G. J., White M. G.**: Basic urinalysis. Medical dep. Harper & Row Hagerstown Maryland, 1979.
46. **Rizzoni C., Braggion F.**: Ematurie «glomerulari» o «non glomerulari»: è possibile distinguerle? Riv. Ital. Ped. 7:457, 1981.
47. **Rizzoni G., Braggion F., Zacchello G.**: Differentiation of glomerular hematuria (GH) from non glomerular hematuria (NGH) by phase-contrast microscopy (PCM) in children. The International Journal of Pediatric Nephrology 3:141, 1982.
48. **Roberts A. M.**: Some effects of exercise on the urinary sediment. J. Clin. Invest. 14:31, 1935.
49. **Rose A. G.**: Urinary Stones. Clinical and laboratory aspects, MTP, Lancaster, England 1982.
50. **Ross D. L., Neely A. E.**: Textbook of Urinalysis and Body Fluids. Appleton-Century-Crofts Norwalk, Connecticut, 1983.
51. **Rutecki G. J., Goldsmith C., Schreiner G. E.**: Characterization of protein in urinary casts. New Engl. J. Med. 284:1049, 1971.
52. **Schreiner G. E.**: Some observations on telescoped urinary sediments. Ann. Intern. Med. 42:826, 1955.
53. **Schreiner G. E.**: The identification and clinical significance of casts. Arch. Intern. Med. 99:356, 1957.
54. **Schumann G. B.**: Urine Sediment Examination. The Williams & Wilkins Company, Baltimore, London, 1980.
55. **Schumann G. B., Weiss M. A.**: Atlas of Renal and Urinary Tract Cytology and Its Histopathologic Bases. J. B. Lippincott Co. Philadelphia, 1981.
56. **Senator H.**: Farbenanalytische Untersuchungen der Harnsedimente bei Nephritis. Virchow Archiv. Path. Anat. 131:385, 1893.
57. **Spencer E. S., Pedersen Ib.**: Atlante dei sedimenti urinari. Cortina S.p.A., Milano, 1980.
58. **Sternheimer R., Malbin B.**: Clinical recognition of pyelonephritis with a new stain for urinary sediments. Am. J. Med. 11:312, 1951.
59. **Sternheimer R.**: A Supravital Cytodiagnostic Stain for Urinary Sediments. J.A.M.A. 231:826, 1975.
60. **Sterpellone L.**: L'Esame dell'urina. Tecnica e interpretazione clinica. Soc. Ed. Universo, Roma, 1959.
61. **Thomas V. L., Forland M.**: Antibody-coated bacteria in urinary tract infections. Kidney Int. 21:1, 1982.
62. **Triger D. R., Smith J. W. G.**: Survival of urinary leucocytes. J. Clin. Pathol. 19:443, 1966.
63. **Varese D., Linari F., Piccoli G., Vercellone A.**: Il sedimento urinario nelle tubulo nefrosi tossico ischemiche. Minerva Anestesiologica 31:1, 1965.
64. **Varese D., Piccoli G., Emanuelli G., Vercellone A.**: Gli elementi cellulari nucleati nel sedimento urinario della pielonefrite e della glomerulonefrite. Minerva Nefrol. 10:178, 1963.
65. **Varese D. Piccoli G., Grimaldi E.**: Reperto urinario di cellule a gocce ialine nelle sindromi nefrosiche. Atti 61° Congresso Soc. Ital. Med. Int., Napoli 1960, Luigi Pozzi Ed., Roma.
66. **Vercellone A., Piccoli G.**: Pielonefrite cronica. Trattato Italiano di Medicina Interna: 653. USES Ed. Scientifiche. Firenze.
67. **Vercellone A., Piccoli G., Varese D., Verzetti G.**: Significato diagnostico delle cellule di Sternheimer-Malbin. Minerva Nefrol. 10:184, 1963.
68. **Vercellone A., Varese D., Piccoli G.**: La colorazione del sedimento urinario secondo Papanicolaou nella pratica nefrologica. Minerva Nefrol. 9:217, 1962.
69. **Wilson D. M.**: Urinalysis and other tests of renal function. Minn. Med. 58:9, 1975.
70. **Wright W. T.**: Cell counts in urine. Arch. Intern. Med. 103:76, 1959.
71. **Zimmer J. G., Dewey R., Waterhouse C., Terry R.**: The origin and nature of anisotropic urinary lipids in the nephrotic syndrome. Ann. Intern. Med. 54:205, 1961.

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