

## Urinary system 6 Diseases of the renal tubule and interstitium

Professor John Simpson

- lots of different diseases of tubules and interstitium
- very diverse aetiologies, pathogeneses and appearances
- together they account for significant numbers of cases of renal impairment
- but only a few are common

### Two very broad groups of conditions

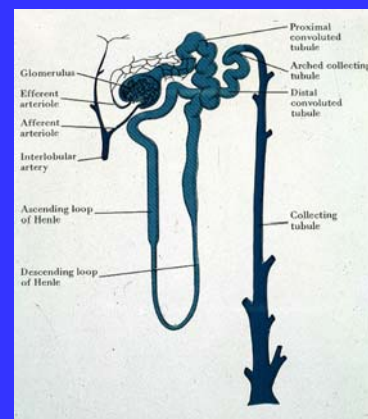
1. Acute tubular necrosis  
(ischaemic or toxic necrosis of tubular cells)
2. Tubulointerstitial nephritis (a.k.a. interstitial nephritis)  
(inflammatory reactions involving the tubules and/or interstitium)

### Acute tubular necrosis (ATN)

- important cause of acute renal failure
- characterized by acute destruction of tubular epithelial cells
- most commonly secondary to ischaemia, but can also be due to direct toxic cell damage
- potentially reversible, since tubular cells can regenerate given time

### ATN due to ischaemia

- due to
  - 1) "shock" (rapid uncompensated fall in systemic BP)  
e.g. in trauma, burns, falciparum malaria, pancreatitis, sepsis, DIC, blood transfusion reactions etc OR
  - 2) reduction in intrarenal blood flow (RPGN, acute interstitial nephritis, urinary obstruction)
- remember, tubular blood flow is from post-glomerular capillary bed - and tubules are metabolically very active, thus susceptible to ischaemia

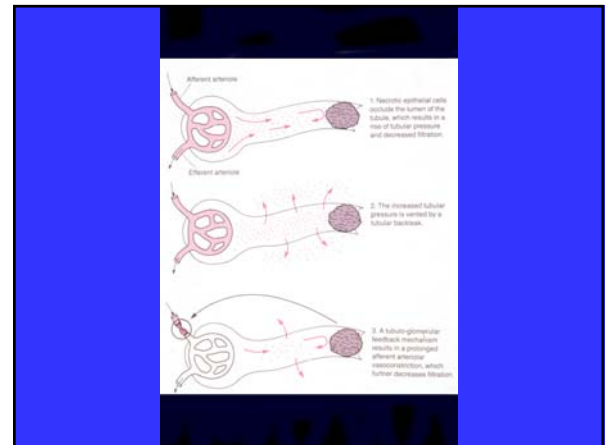
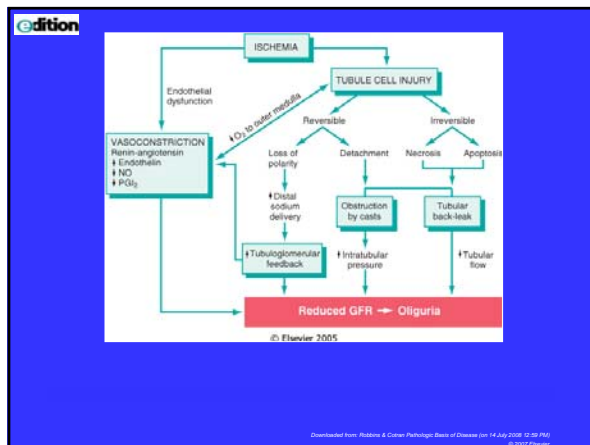


## ATN due to toxins

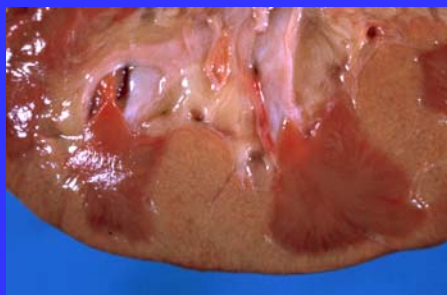
- heavy metals – Pb, Au, As, Cr etc
- organic solvents – CCl<sub>4</sub>, chloroform
- drugs – antibiotics (espec gentamicin), anti-viral agents, NSAIDs, mercurial diuretics
- iodinated contrast agents used for X rays
- pesticides
- glycols – ethylene glycol

## In both types of ATN

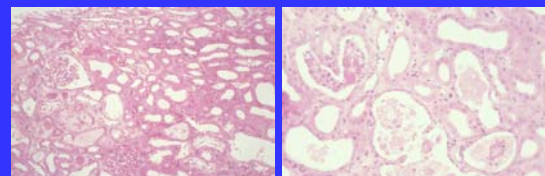
- tubular cell degeneration and death
- tubular casts of dead cells & debris
- (may be accompanied by myoglobinuria in crush injury or Hb/uria in haemolysis)
- interstitial oedema & secondary inflammation
- pale swollen kidneys



## ATN

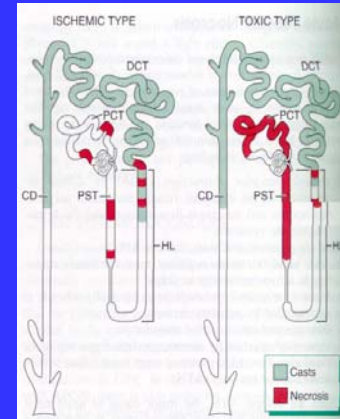


## ATN



## ATN

- distinctly different distributions of tubular damage
  - ischaemic type - any part of nephron
  - toxic type - only proximal tubules
- why?



## ATN causes acute renal failure

Clinically variable, but classically in 3 phases –

1. *initial* (~ 36 hrs) (*often missed*) – slight increase in urine output and rise in serum urea
2. *oliguric* – urine output 400 ml or less/day, so Na<sup>+</sup>, K<sup>+</sup> & water retention, rising urea, metabolic acidosis – danger of pulmonary oedema & cardiac dysrhythmias
3. *diuretic* – urine output above normal, so loss of water, Na<sup>+</sup> & K<sup>+</sup> – danger of dehydration

Complete recovery possible

## Pathophysiology of 3 phases

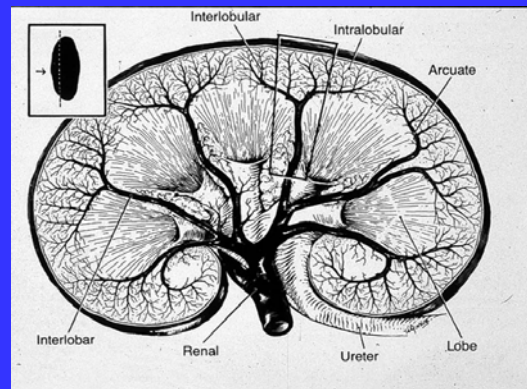
(What normally happens to glomerular filtrate?)

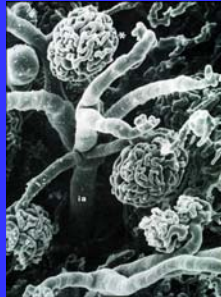
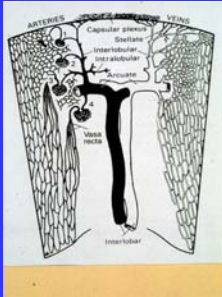
1. *initial* – tubular cells begin to lose concentrating ability
2. *oliguric* – tubular epithelium lost, so reabsorption of most of glomerular filtrate
3. *diuretic* – regenerating epithelium can't yet concentrate, but does prevent much reabsorption

(once concentrating ability restored, complete return to normal)

## Renal cortical necrosis

- *more severe effect of shock on the kidneys than ATN produces*
- *also caused by rapid uncompensated fall in systemic BP (“shock”)*
- *but, in this situation, hypotension so severe that renal blood flow diverted into medullary vasa recta away from cortex*
- so whole cortex becomes infarcted
- *irreversible*





## (Tubulo)interstitial nephritis

- heterogeneous group of conditions
- similar morphology and clinical features, but wide variety of causes
- other than acute infective cases, T cell reaction probably involved in most
- some agents (e.g. certain drugs) can cause ATN in some patients, interstitial nephritis in others (and even GN in still others!): not clear why
- interstitial nephritis can be clinically overshadowed by other systemic manifestations of primary cause/condition

## Causes of interstitial nephritis 1

- immunological reactions, notably
  - hypersensitivity reactions
  - transplant rejection
- infection
  - especially pyelonephritis
- direct toxic damage
  - drugs, particularly analgesics
  - heavy metals
- metabolic diseases, e.g. gout

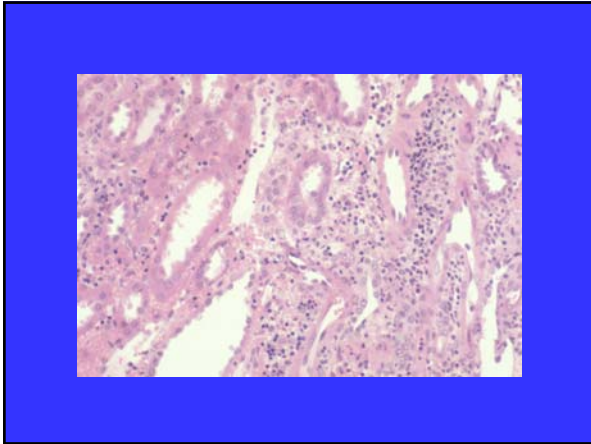
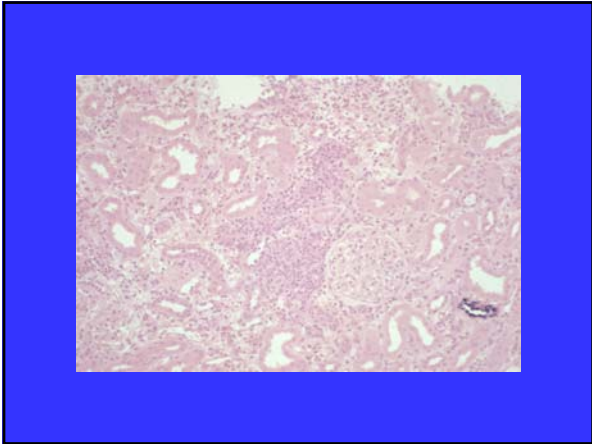
## Causes of interstitial nephritis 2

- physical factors
  - urinary tract obstruction
  - radiation nephritis
- neoplasia, particularly myeloma kidney
- vascular diseases, including
  - hypertension (also causes glomerular damage)
  - papillary necrosis
- *etc etc*
- *in many cases, precise cause never identified*

- will only cover a few of these many causes
- but all the important ones!

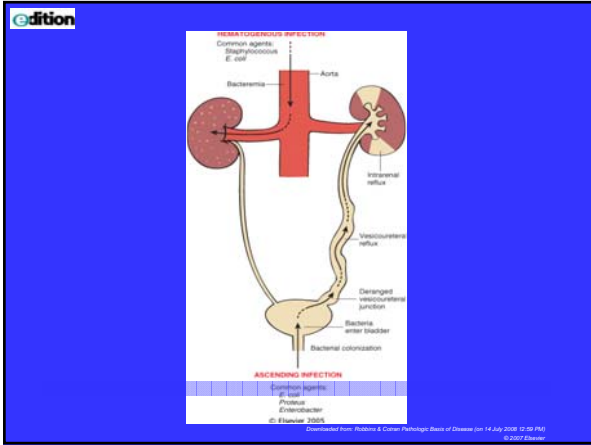
## Interstitial nephritis of hypersensitivity type

- drugs probably act as haptens
  - include antibiotics, antiviral agents, NSAIDS
  - also self-administered “traditional or complementary” medicines
  - often suspected rather than proven
  - presumably also non-“drug” causes
- probably type IV (T cell) hypersensitivity reaction causing interstitial inflammation (often with eosinophils) and oedema
- usually acute reduction in renal function with fever and sometimes eosinophilia – if severe, can cause ATN
- may be white cell (“granular”) casts in urine
- reversible if cause removed



## Pyelonephritis

- common
- bacterial infection of kidney, spread either -
  1. haematogenous spread due to septicaemia, miliary TB or
  2. (more commonly) ascending infection in association with urinary tract infection
- most ascending infections due to endogenous gram negative bacilli from patient's own faecal flora
  - e.g. E. coli, Proteus, Klebsiella and Enterobacter
- acute and chronic forms



## Acute pyelonephritis - presentation

- malaise & fever
- often loin/back pain and tenderness
- frequency and dysuria
- significant bacteriuria – also may be pyuria (pus cells in urine)
  - – and white cell (“granular”) casts, if present, are pathognomonic

## Acute pyelonephritis

- more common in women
  - short urethra
  - trauma during intercourse and childbirth
  - pregnancy
- also more common with
  - diabetes
  - urinary obstruction or reflux
  - immunosuppression/deficiency
  - instrumentation of urinary tract
  - pre-existing renal damage/structural abnormality

## Acute pyelonephritis

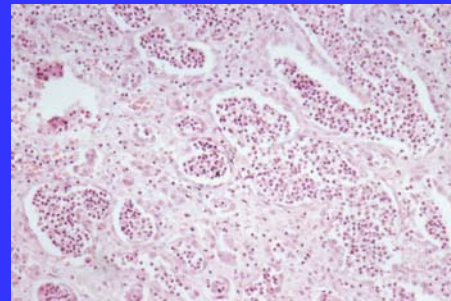
- patchy suppurative inflammation
  - abscesses – if severe, large wedge shaped areas of suppuration
- distributed randomly if infection haematogenous, but towards two poles if associated with obstruction/ascending infection
- PMNs in tubules (may aggregate as “granular casts”) as well as interstitial nephritis



edition

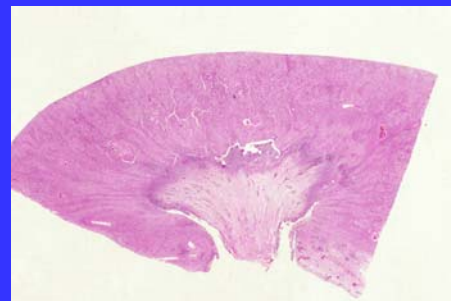


Downloaded from *Robbins & Cotran Pathologic Basis of Disease* on 14 July 2015 12:25 PM  
© 2015 Elsevier



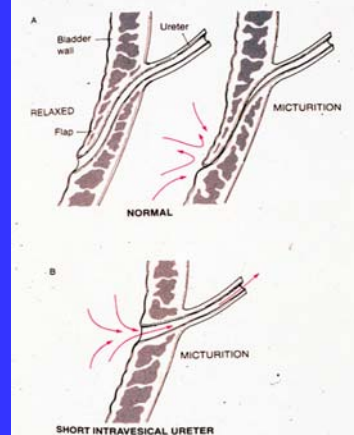
## Complications of acute pyelonephritis

- pyonephrosis (if total obstruction)
  - pus fills pelvicalyceal system +/-ureter
  - (N.B. *pyelo v pyo*)
- perinephric abscess
  - due to extension through renal capsule
- papillary necrosis, especially in diabetics
  - distal parts of pyramids undergo coagulative necrosis (? ischaemic)



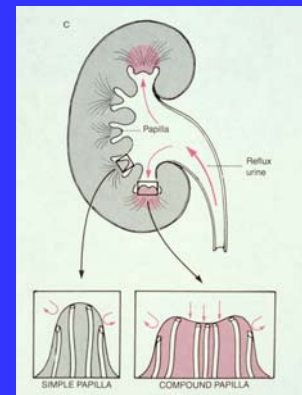
## Chronic pyelonephritis

- important cause of end stage kidney/chronic renal failure
- also another renal cause of secondary hypertension
- notable association with vesicoureteral reflux
  - due to “incompetent vesicoureteral valve”
  - aka “short intravesical ureter”

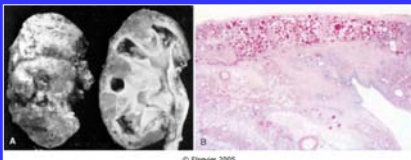


## Pathogenesis of chronic pyelonephritis

- urine refluxes into ureter during micturition
- but reflux into renal parenchyma essential
- structure of papillae at renal poles (“refluxing papillae”) promotes this – so chronic pyelonephritis is common at the poles

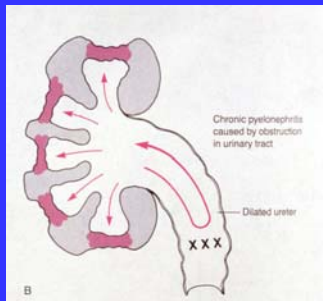


edition



## Healing of chronic pyelonephritis

- occurs by organisation, usually with deformation of pelvicalyceal system
- so, classically, deep irregular renal scars aligned with dilated calyces



## Chronic pyelonephritis

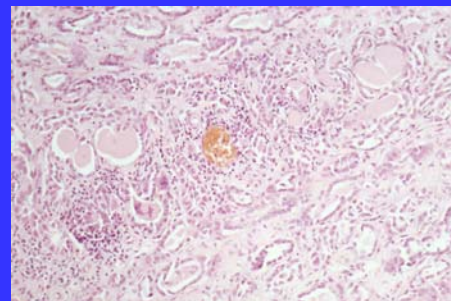
- clinical course varies -
  - often insidious
  - acute recurrent pyelonephritis
    - backloin pain, fever, frequent pyuria/bacteriuria
  - hypertension

## Analgesic nephropathy

- excess & long-term intake (“abuse”) of analgesic mixtures
  - especially aspirin (ischaemic effect) & phenacetin (toxic effect)
  - chronic accumulative damage
- chronic interstitial nephritis, often with renal papillary necrosis as the initial feature
- more common in women
- headache, anaemia, hypertension and GI symptoms are common
- rarely, carcinoma of renal pelvis supervenes

## Myeloma kidney

- the most common example of “cast nephropathy”
  - protein casts block tubules, causing them to rupture producing tubulointerstitial nephritis
  - due to glomerular filtration of Bence-Jones protein (light chains)
- in myeloma, kidneys may also show
  - (primary) amyloidosis
  - pyelonephritis secondary to UTI
  - calcification (“metastatic” type) secondary to bone disease
  - glomerular lesions because of trapped Igs
- *“cast nephropathies” – associated with diseases producing abnormal plasma proteins which tend to block renal tubules*



- and finally, two overviews

## TB and the kidney/UT

- miliary TB – multiple small foci of infection
- abscesses – tuberculomas
- TB pyelonephritis – complete destruction of kidney – (“sterile” pyuria)
- amyloidosis
- GN
- anti-TB drug reactions (most commonly hypersensitivity interstitial nephritis)
- HIVAN

## Vascular diseases and the kidney

- Nephrosclerosis – benign & accelerated
- Renal artery stenosis
- Infarcts
- Cortical necrosis
- Sickle cell disease
- Haemolytic uraemic syndrome – ATN in severe haemolysis