**Acute pancreatitis** is an illness of sudden onset, characterised by abdominal pain and raised pancreatic enzymes in blood or urine. Pathogenesis is unclear:

1. Associated gallstones are mainly found in the gallbladder, only occasionally in the common bile duct
2. Reflux of bile up the pancreatic duct associated with occlusion of the ampulla may play a role
3. Autodigestion of the pancreas by proteolytic enzymes (especially trypsin, phospholipase A) may also play a part – note activation of zymogens
   a. Proteolysis
   b. Oedema
   c. Vascular damage
   d. Necrosis

Acute pancreatitis may occur as an isolated event, or it may be recurrent.

1. It may be distinguished from chronic pancreatitis by:
   a. Absence of continuing inflammation
   b. Absence of irreversible structural change
   c. No permanent loss of endocrine or exocrine function
2. Causes of acute pancreatitis
   a. Gallstones
   b. Alcohol intake
   c. Infections – e.g. mumps, Coxsackie B, Mycoplasma
   d. Drugs – e.g. oestrogens, corticosteroids
   e. Iatrogenic – e.g. after surgery, endoscopy
   f. Miscellaneous – e.g. trauma, scorpion bite
   g. Idiopathic

The mildest form of acute pancreatitis is characterised by intestinal oedema with an inflammatory exudate (oedematous pancreatitis). In the severe form there is pancreatic necrosis and haemorrhage (haemorrhagic pancreatitis). In all patients the principle symptom is pain, usually localised to the epigastrium or upper abdomen but may radiate to the back (interscapular). This ranges from mild discomfort to excruciating pain.

In most cases, there is nausea and vomiting. In patients who are severely ill there may be multisystem failure and/or development of complications (e.g. pseudocyst – fluid in lesser sac).

Factors during the first 48hrs that indicate severe pancreatitis and a poor prognosis:

1. Age > 55 years
2. WBC > 15 x 10^9/L
3. Blood urea > 16mmol/L
4. Blood glucose > 10mmol/L
5. Serum albumin < 30g/L
6. Serum aminotransferase > 200U/L
7. Serum Ca^2+ < 2mmol/L
8. Serum LDH > 600U/L
9. PaO_2 < 60mmHg (8.0kPa)

**Chronic pancreatitis** is a continuing inflammatory disease of the pancreas characterised by irreversible morphological change. Pathogenesis:

1. Most cases are associated with raised alcohol consumption
2. The earliest change seems to be deposition of protein plugs in pancreatic ducts
   a. → Dilatation of the ducts, followed by atrophy of acinar cells
3. There is some cellular infiltration, but this is variable
4. Fibrous tissue is deposited near the pancreatic ducts, and protein plugs undergo intraluminal calcification → calculi (unclear if this is due to repeated attacks)
More than 80-85% of cases of chronic pancreatitis are caused by high alcohol consumption. Chronic pancreatitis is not reversible, but the process may be arrested if the patient stops drinking – generally the disease progresses. Other causes include:

1. Cystic fibrosis
2. Haemochromatosis
3. Obstruction of pancreatic or biliary ducts
4. Idiopathic
5. Hypercalcaemia
6. Trauma

Clinical features vary according to severity, but abdominal pain is the principal presentation in all patients. Pain can be as severe as acute pancreatitis with the same distribution, but may often be mild and brief. In other patients chronic pain is interspersed with acute episodes (relapsing pancreatitis). Other symptoms:

1. Weight loss – frequently severe
2. Steatorrhoea – fat in faeces when pancreatic lipase is reduced (50%)
3. Diabetes – more common than weight loss or steatorrhoea

Cystic fibrosis is the commonest cause of pancreatic disease in childhood (around 1:2000 live births). It is inherited as an autosomal recessive condition, with a specific gene deletion identified in 70% of cases. 1 in 25 Caucasians are carriers.

1. Resultant protein defect produces an abnormality in a beta-adrenergic-gated chloride channel in the cell membrane
2. This is a basic defect in all exocrine glands and results in thick, viscid secretions with a high Na⁺ content
3. Clinical features:
   a. In the neonate – meconium ileus
   b. In childhood – note that lungs are structurally normal at birth
      i. Haemoptysis
      ii. Limitation of air flow → breathlessness
      iii. Nasal polyps in older children
   iv. Delayed puberty and skeletal maturation
   v. Infertility, particularly in males
   vi. Steatorrhoea (85% of patients)
   vii. Increased gall stone formation
   viii. Cirrhosis (5% older patients)
4. Mean survival ~29 years

Carcinoma of the pancreas:

1. Risk factors
   a. Definite – age >60yrs, male, smoking, chronic pancreatitis, NPCC syndrome
   b. Probably – high cholesterol, high fat diet (high linoleic acid content)
   c. Unlikely – diabetes mellitus, coffee, alcohol, cholecystectomy, gastrectomy
2. Pathophysiology
   a. Ductal adenocarcinoma – 90% of pancreatic carcinoma.
      i. Most are moderately well differentiated mucinous carcinomas that arise from the cuboidal epithelium of the pancreatic ducts
   b. Endocrine tumours – 10% of pancreatic carcinoma
      i. Well-differentiated to poorly-differentiated duct glands embedded in a dense network of fibrous tissue
   c. As the tumour extends into the pancreas and surrounding tissue, it envelopes and fixes vessels, invades fat, lymphatics and perineural tissue
3. **Clinical features**
   a. Pain is present in more than 90% of patients
      i. May be vague and non-specific, and occurs up to 3 months before onset of jaundice
      ii. Tumour most commonly extends into the retroperitoneal space producing visceral pain effects described as persistent, disagreeable, and aching (increased by lying supine and eating, waking patient)
      iii. Sometimes relieved by bending forward, assuming fetal position, crouching forward on arms, legs in crawling position
   b. Jaundice due to obstruction of the common bile duct in 60-70% of carcinomas of the head of the pancreas
      i. Jaundice is not an early feature when carcinoma occurs in the central part or in the uncinate process
      ii. In carcinoma of the body and tail, jaundice is late and may be due to hepatic metastases or obstruction of the bile duct at the porta hepatis by enlarged lymph glands
   c. Glucose intolerance in up to 80% of patients
      i. Due to increased plasma concentrations of islet amyloid polypeptide
   d. Other signs and symptoms:
      i. Pale faeces (60% head)
      ii. Vomiting and weakness (33%)
      iii. Hepatomegaly with jaundice (80% head, 30% body)
      iv. Abdominal mass or ascites (<20%) – due to portal vein occlusion
   e. Five-year survival is < 2%, and there is a high surgical mortality (20%)

Tumours of the colon may be benign (sessile, pedunculated, papillary) or malignant (fungating, ulcerated, annular). Carcinoma of the colon and rectum is the commonest malignancy of the GI tract (98% are adenocarcinomas)

1. **Incidence** varies worldwide (common in US, Europe, NZ)
   a. Rectal cancer more common in men in most parts of the world
   b. Migrants from areas of low incidence to high show a rapid increase in incidence

2. **Aetiology** – inherited and environmental factors are implicated (picture is unclear)
   a. Diet is the environmental factor most studied
      i. Many studies show a correlation between risk and type/amount of fat
      ii. There is a high incidence in countries where 40% of total calories are derived from fat
   b. Risk increases at 50, rises sharply at 60 and doubles with each succeeding decade (peaking at 75yrs)
   c. There is no association with inflammatory bowel disease, except in the case of chronic ulcerative colitis (10-20x increased risk).
   d. Adenomatous polyposis syndromes and hereditary non-polyposis colorectal cancer account for ~7% of colon cancer

3. **Pathology** – the vast majority of malignant tumours are adenocarcinomas, showing varying degrees of glandular differentiation and produce variable amounts of mucin
   a. Gross morphology
      i. Two main types:
         1. Polypoid – more common on the right
         2. Annular – more common on the left
      ii. Adenocarcinomas of the rectum are frequently sessile or polypoid
   b. Location:
      i. 75% of colorectal cancers occur in the descending colon, rectosigmoid and rectum
      ii. 15% are found in the caecum and ascending colon
      iii. 10% are found in the transverse colon
   c. Spread occurs by direct extension through the bowel wall → pericolonic fact and mesentery → invasion of surrounding organs, lymphatics → regional glands, portal vein → liver
      i. Rectal cancer may invade perirectal fat, vagina, prostate, bladder, ureters, and bony pelvis. It metastasises to lungs and liver.

4. **Clinical features** – presentation is related to size and location of tumour
a. Major symptoms – rectal bleeding, pain, change in bowel habit
b. Right-sided tumours are often asymptomatic and bleeding may be occult
   i. Tumours of the caecum and ascending colon rarely obstruct early
c. Left-sided tumours commonly present as changes in bowel habit, reduction in stool calibre, progressive constipation, haematochezia
d. Variations with tumour type:
   i. Adenocarcinoma may present with localised perforation, and signs of liver metastases may be the earliest clinical sign
   ii. Rectal or anal cancers may present with rectal bleeding, perineal pain and a change in bowel habit
5. **Metastatic colon cancer** may be clinically apparent before or after resection of the primary tumour
   a. Massive liver enlargement may lead to pain (distension of the capsule)
   b. Abdominal spread may cause obstruction of the large bowel and ascites
   c. Pelvic spread may cause bladder dysfunction, sacral/sciatic nerve pain, vaginal discharge/bleeding

**Tutorial #3 – Pituitary and Thyroid Glands**

**Hypopituitarism** is defined as a reduction or absence of one or more of the anterior pituitary hormones. It can be categorised as:

1. **Genetic** – e.g. gene deletion of growth hormone
2. **Congenital embryopathic** – e.g. anencephaly
3. **Acquired** – e.g. tumours, trauma
   a. Adenomas are the most common cause, though trauma is also important

**Pituitary adenomas** are classified according to size and the hormones they produce. In general, the concentrations of hormones produced by the tumours parallels their size, although there are exceptions.

1. Microadenomas – less than 10mm diameter
2. Macroadenomas – more than 10mm diameter
3. Macroadenomas with extrasellar extension

<table>
<thead>
<tr>
<th>Type of adenoma</th>
<th>Disorder</th>
<th>Hormone</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somatotroph</td>
<td>Acromegaly</td>
<td>GH</td>
<td>10-15%</td>
</tr>
<tr>
<td>Lactotroph (prolactinoma)</td>
<td>Hypogonadism, galactorrhoea</td>
<td>Prolactin</td>
<td>25-40%</td>
</tr>
<tr>
<td>Corticotroph</td>
<td>Cushing’s disease</td>
<td>ACTH</td>
<td>10-15%</td>
</tr>
<tr>
<td>Gonadotroph</td>
<td>Mass effects, hypopituitarism</td>
<td>FSH and LH</td>
<td>10-15%</td>
</tr>
<tr>
<td>Thyrotroph</td>
<td>Hyperthyroidism</td>
<td>TSH</td>
<td>&lt;3%</td>
</tr>
<tr>
<td>Non-functioning/null cell</td>
<td>Mass effects, hypopituitarism</td>
<td>None</td>
<td>10-25%</td>
</tr>
</tbody>
</table>

Many of the clinical signs and symptoms are related to hypersecretion of hormones, but the effects of the mass of the enlarging tumour can also lead to specific signs and symptoms, especially in the case of non-functioning tumours or in those that involve gonadotropins.

1. Headaches are common – the site varies, but may be retro-orbital or referred to the top of the head
2. Loss of visual fields may occur – the most common abnormality is bilateral / bitemporal hemianopia

**Craniopharyngiomas** are not strictly pituitary tumours as they originate from Rathke’s pouch and are situated between the pituitary and the floor of the third ventricle. Two forms are known:

1. **Adamantinomatous craniopharyngioma** – represents around 5% of intracranial neoplasms in childhood with a peak incidence in the first decade
   a. The vast majority are suprasellar, and ~50% have an intrasellar component
   b. Histologically the tissue consists of cysts alternating with stratified squamous epithelium. There is often calcification, and cysts contain cholesterol-rich oil.
   c. Many have an irregular interface with the brain, as well as occasional firm attachment to blood vessels at the base of the brain
   d. Clinical features in children include:
      1. Visual disturbances
2. Anterior pituitary dysfunction
3. Growth retardation
4. Delayed puberty
5. Diabetes insipidus
6. Frequently raised intracranial pressure
   e. After gross total removal, 10-20% recur – however malignant transformation is rare.

2. Papillary craniopharyngioma – occurs almost exclusively in adults and often involves the third ventricle
   a. It lacks calcification and “engine-oil” cystic fluid
   b. Interface with the brain is often smooth, and allows gross removal more readily. Less than 10% recur.

A thyroid nodule is a single, palpable abnormality in the thyroid gland (note that they must be at least 1cm in diameter to be palpable). Thyroid nodules are common (~5% of population), while thyroid cancer is less frequent and only ~4% of patients with nodules have thyroid cancer. Diagnosis is best made on fine-needle biopsy.

A thyroid adenoma is a solitary, encapsulated nodule composed of follicular cells arranged in a pattern that differs from that of the adjacent gland. Follicular adenomas can be classified as micro or macrofollicular.

Thyroid cancer – low doses of radiation (<1500rads) in children increases risk of cancer by ~30-fold. Note that higher doses of radiation (>5000 rad) delivered by $^{131}$I for some forms of thyroid disease (thyrotoxicosis) do not lead to increased incidence. Other risk factors are genetic and include familial forms of papillary cancer.

1. Papillary cancer accounts for ~70% of all thyroid cancers and are the least aggressive
2. Follicular cancer accounts for ~15%
3. Other primary tumours include medullary cancer, anaplastic cancer and lymphoma
4. Secondary tumours may be metastases from malignant melanoma, cancers of the breast, lung and kidney

• Tutorial #4 – Adrenal, CNS Degeneration

The catecholamines (adrenaline, noradrenaline and dopamine) function as neurotransmitters and circulating hormones. In the adrenal medulla, chromaffin cells (derived from neuroectoderm) store adrenaline and noradrenaline in catecholamine secretory granules.

Phaeochromocytoma is a neoplasm of chromaffin cells, which typically causes symptoms and signs of episodic release of catecholamines including paroxysmal hypertension. It is an unusual cause of hypertension – at most 0.1-0.2% of patients with high blood pressure.

1. Found typically in young to middle-aged adults, most commonly in the 4th or 5th decade – it is found in about 10% of children, usually male
2. Histological examination shows groups of cells in clusters or ‘nests’ that stains for chromogranin A.
3. Tumour features:
   a. About 90% solitary, unilateral, encapsulated adrenal medullary tumour
   b. About 10% bilateral, more commonly seen in several members of a family
   c. Tumours are vascular – may have internal haemorrhage or cystic formation
   d. Average size is ~40g, ranging from 1g to several kilograms
4. Paragangliomas are extra-adrenal tumours (~10%)
   a. ~90% are intra-abdominal, mostly arising from chromaffin cells near the bifurcation of the aorta in the organ of Zuckerkanld and near the kidney
   b. Other sites include paravertebral sympathetic ganglia, urinary bladder, other autonomic ganglia (e.g. coeliac)
5. Clinical manifestations:
   a. History – classic triad is headaches, palpitations and perspiration occurring in paroxysms. Minutes to hours, gradually increasing in frequency and duration
      i. History of extraordinary of labile hypertension
      ii. Family history of phaeochromocytoma
   b. Physical findings – labile, refractory, orthostatic hypertension
**Degenerative diseases of the nervous system** are diseases in which nerve cells from selective populations die in a progressive and relentless manner. Pathology is usually but not invariably symmetrical.

1. The rate of progression is variable, and is accompanied by:
   a. Gliosis of astrocytes
   b. Minimal microglial reaction
   c. Very little other cellular response
2. A characteristic feature is the systemic nature of neuronal loss – this corresponds to neuroanatomically discrete and some cases functionally interdependent groups
3. However, this is independent of regional location and blood supply → selective dismantling of parts of the nervous system concerned with particular functions.
4. Onset is variable – some begin in infancy or childhood, several in late middle or old age, some are familial, others are sporadic
5. **Pathology:**
   a. In some, structural changes are found in those neurones that survive in affected populations
   b. In others, the neurones just disappear sometimes after undergoing atrophy
   c. Frequently the distal ends of long neurones are affected first, before the cell body shows pathology. This is often called ‘dying back’ of neurones.
6. Causes are largely unknown/unclear

**Prion diseases** are unique – they may be hereditary, spontaneous, or acquired by contamination with the agent. They are sometimes referred to as ‘slow infection’ but this term is now avoided except in certain conditions (progressive rubella panencephalitis, subacute sclerosing panencephalitis and progressive multifocal leukoencephalopathy).

**Creutzfeldt-Jakob Disease (CJD)** was first shown by Gajdusek, Gibbs, Alpers in 1966 to be transmissible to chimpanzees. It is a subacute spongiform encephalopathy and is the prototypical prion disease. Others include Kuru, Gerstmann-Straussler-Scheinker syndrome, familial fatal insomnia, bovine spongiform encephalopathy, variant CJD, and scrapie.

1. The gross appearance of the brain is variable and is not diagnostic.
   a. In some, no recognisable abnormalities may be seen
   b. Others show varying degrees of atrophy of the cerebral cortex with widening of the sulci and compensatory hydrocephalus
   c. The brain may weight as little as 850g (normal 1200-1500g)
2. Histologically, the hallmarks are:
   a. Spongiform degeneration of neurones and their processes
   b. Loss of neurones
   c. Intense reactive gliosis, amyloid plaques
   d. Vacuoles tend to be round to oval, about 5-25μm in diameter
      i. In other cases there is status spongiosis’ with larger vacuoles surrounded by a dense meshwork of reactive astrocytic processes
3. **Clinical features** are protean and CJD is frequently misdiagnosed in early stages
   a. Rapid, progressive, mental deterioration with, dementia, myoclonus, broad range of motor disturbances, EEG – periodic short-wave activity
   b. If the quartet of clinical signs and symptoms was present in life, the diagnosis at death is virtually certain if there is spongiform degeneration of grey matter
   c. PrP amyloid plaques in the cerebellum is also confirmation – in some centres a diagnosis can be made on fresh frozen sections with new methods
4. **Incidence:**
   a. Worldwide, around 1 in 10⁶ – males and females affected equally, peak incidence ~60yrs with a range of 40-90yrs
   b. Clinical course is generally rapid, 4-12 months from start of signs and symptoms – but 2-5 years is not uncommon
   c. There have been reports of CJD in health workers (incidence is still 1 in 10⁶)
5. **Transmission** – CSF is a potential source of infection, and the infectious agent is high in brain and spinal cord tissue
530.307 – Pathophysiology Notes

a. Possible sources include contaminated neurosurgical instruments, transplantation of infected CNS tissue (corneal, dura mater).
b. VCJD associated with hGH and gonadotrophins from cadaveric pituitaries had early onset (20-40yrs) and most presented with cerebellar abnormalities
c. So far every person who has contracted vCJD shares a common genetic factor present in about 1/3 of the population

Tutorial #5 – Radiation, Tuberculosis

Ionising radiation is measured in units called Becquerels (Bq) – one Bq is one disintegration per second. This year marks the 15th anniversary of the world’s worst nuclear disaster at Chernobyl. Huge levels of radioactive isotopes were released (~\(10^{19}\) Bq), and one prediction was a small increase in thyroid cancer with a 10-year latent period, contradicting theories of a large increase after 4-5 years.

1. There have been about 2000 cases of thyroid cancer in those exposed as children or adolescences, though there have been few deaths in this group
2. However, despite the dominance of radioactive iodine in the initial fallout, it must not be assumed that there will only be thyroid problems.
3. There are anecdotal claims of increases in immune-related diseases, birth defects and a number of cancers though adequate studies are lacking
4. We do not know the long-term effects of living in an environment contaminated with \(^{137}\)Caesium and there could be late radio-iodine effects (e.g. in breast)

New research has begun into the gastrointestinal tract in the pathogenesis in vCJD – in particular the part played by M cells.

1. M cells link digestive and immune systems, providing an entry point for ingested bacteria and viruses to lymphoid tissue below the intestinal lining
2. M cells appear to sample pathogens so that the body can mount an effective immune response
3. M cell defence is not foolproof, and prions may sneak past, like some other bacteria and viruses
   a. *Salmonella typhimurium* destroys M cells and adjacent follicle-associated epithelium that overlies Peyer’s patches
   b. Polio viruses (virulent and disabled) replicate in Peyer’s patches, crossing M cells to the lymphocytes that ferry them to the nervous system
   c. M cells also pick up HIV in rectal tissue and transfer the virus to lymphocytes

Mycobacteria are rod-shaped organisms with a distinctive staining property called acid-alcohol fastness. *M. tuberculosis* was first discovered by Robert Koch, grows slowly in culture and is stimulated by lipids and fatty acids.

1. A glycerol-whole egg medium is often used in primary isolation of *M. tuberculosis* from pathological material e.g. Lowenstein-Jansen medium
2. There are three clinically important species:
   a. *M. tuberculosis* – most cases of human tuberculosis
   b. *M. bovis* – cattle, rarely human tuberculosis
   c. *M. leprae* - leprosy
3. Disease caused by *M. tuberculosis* is characterised by:
   a. Prolonged latent period between initial infection and overt disease
   b. Prominent pulmonary disease (but other organisms can be involved)
   c. Granulomatous response in tissue with intense inflammation/damage
   d. Tissues attacked are characterised by high regional oxygen tension (e.g. lung, bone)
   e. The ability of the bacterium to invade and spread throughout the body is largely related to its capacity to survive and proliferate within mononuclear phagocytes
4. Transmission of tuberculosis is almost exclusively by aerosols containing contaminated respiratory secretions
   a. Patients with pulmonary tuberculosis with cavities are especially infectious – their sputum contains 1-100million bacilli per mL and they cough frequently
   b. Fortunately, intact skins and respiratory mucous membranes of healthy individuals are quite resistant to infection.
530.307 – Pathophysiology Notes

i. For infection to occur, the bacilli must be delivered to the alveoli where they are not cleared by mucus and cilia of bronchioles/bronchi

ii. To reach the alveoli, the bacilli must be suspended in tiny droplets about 1-5μm in diameter

5. Pathogenesis of tuberculosis
   a. Alveolar macrophage engulfs bacillus, intracellular environment nurtures bacillus, bacilli survive/replicate within phagosome, infected phagocyte releases compounds that attract T lymphocytes, which produce cytokines that activate macrophages, enhancing their antimicrobial ability
   b. In normal healthy adults the body wins in more than 95% of cases. However, in some cases there are several months during which the number of bacilli increased massively and have undergone varying degrees of dissemination.
   c. During this bacteraemia, "seeding" occurs in tissues (apices of lungs, kidneys, bones, and meninges) that are potential foci for later reactivation tuberculosis
      i. Initial site of contact between bacilli and human → Ghon focus
      ii. Secondary tuberculosis – typical granulomas with caseation
      iii. Miliary tuberculosis – consequence of 1° or 2° disease, and is an acute medical emergency

As an infectious disease, it is a leading cause of morbidity and mortality worldwide. In more industrialised countries it is seen less in the general population and more in selected groups.

1. Recognition of high-risk groups is vital –
   a. WHO estimates that around 1/3 of the world’s population is latently infected with M. tuberculosis from which 8-10 million new active cases emerge annually
   b. About 50% of these are communicable forms of pulmonary disease

2. WHO estimates that 26% of preventable deaths in developing countries are attributable to tuberculosis, and this may be due to drug resistance

3. Most cases of overt tuberculosis occur because of late reactivation of the remains of primary infection in the lungs or extrapulmonary sites. People at high risk include:
   a. Children from infancy to four years, the elderly infirm
   b. Immunocompromised people – those with HIV/AIDS, recipients of organ transplants, other immunosuppressive illnesses, those on chemotherapy
   c. Chronic alcoholism
   d. Diabetes mellitus

Clinical manifestations of tuberculosis:
   1. Respiratory system – lungs/pulmonary tuberculosis is the most common
   2. Gastrointestinal tract – mainly ileo-caecal area, occasionally peritoneum
   3. Genitourinary tract – mainly kidney but can also cause painless craggy swelling of epididymis, salpingitis, tubal abscesses, infertility
   4. Skin – lupus vulgaris
   5. Skeleton – arthritis, osteomyelitis and ‘cold’ abscess formation in adults
   6. CNS – tuberculous meningitis, tuberculomas
   7. Eye – choroiditis, iridocyclitis, phlyctenular keratoconjunctivitis
   8. Pericardium – constrictive pericarditis
   9. Adrenal glands – destruction leading to Addison’s disease
   10. Lymph nodes – common presentation in children and young adults (hilar and paratracheal most commonly affected)

• Tutorial #6 - Kidney

In order to understand renal pathology, we need to understand the structure and function of the kidney – notably the nephron, the functional unit of the kidney. General pathology:

1. Increased cellularity
   a. Hypercellularity may result from an increase in mesangial or endothelial cells, or from accumulation of leukocytes in the lumen of capillaries, beneath endothelial cells or in the mesangium
   b. While this is not strictly correct, lesions in the glomeruli with increased cells in the tufts are often described as proliferative glomerulonephritis

2. Increase in extracellular matrix – implies an increase in mesangial matrix or BM
a. In the case of the mesangial matrix, this may be a uniform, diffuse pattern in all lobules, or give a nodular appearance to the mesangium
b. Increased basement membrane material usually leads to thickening

3. **Sclerosis** refers to increased extracellular matrix and other material leading to obliteration of capillaries and solidification of all or part of the tufts
   a. When the entire glomerulus is involved, this is known as complete sclerosis (formerly known as glomerular hyalinisation)
   b. Segmental glomerulosclerosis implies a completely different pathology – only portions of the capillary tufts are involved and capillaries are obliterated by extracellular matrix or large precipitates of plasma proteins

4. **Crescents** represent accumulation of cells and extracellular material in urinary space
   a. They are the result of severe damage to the capillary wall with disruptions in continuity and spillage of fibrin from inside the damaged capillaries
   b. The cellular content of crescents depends on the type of disease and associated damage to Bowman's capsule
   c. Crescents commonly heal by organisation, and then the capillary tuft is frequently collapsed and distorted

5. **Peripheral migration and interposition of mesangium**
   a. In certain diseases, mesangial cells and matrix extend from the central lobular portion of the tuft into the peripheral capillary wall
   b. Migration between endothelial cell and basement membrane → thickening

6. **Tubules**
   a. Atrophy results in thickening and wrinkling of basement membranes even before diminution in size (hence early indicator of tubular atrophy)
   b. Tubular casts mainly consist of Tamm-Horsfall protein, a mucoprotein produced by cells of the thick ascending limb of the loop of Henle.

7. **Interstitial**
   a. Acute interstitial processes are defined by the presence of oedema
   b. Chronic interstitial processes are characterised by fibrosis, and this is associated with tubular atrophy
   c. Note that the type of cell (e.g. polymorph or lymphocyte) does not determine the acute or chronic nature of the interstitial process

8. **Arteries and arterioles**
   a. With few exceptions, changes in these are not unique to the kidney

**Pyelonephritis** is a common and important cause of renal disease

1. **Acute pyelonephritis** is characterised by pus in the tubules and by abscess formation in the renal substance. Complications include:
   a. **Pyonephritis:**
      i. Due to complete obstruction high in the urinary tract
      ii. Stagnant fluid in the pelvis and calyces suppurates, and eventually the kidney becomes grossly distended with pus
   b. Renal papillary necrosis
   c. Perinephric abscess

2. **Chronic pyelonephritis** is characterised by coarse scarring and contraction of the kidneys