Bone Tumours

Introduction

In the first three decades of life, benign tumours are the most frequent. In the elderly, a bone tumour is likely to be malignant, either primary or a metastasis.

<table>
<thead>
<tr>
<th>Histological classification</th>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haematopoietic</td>
<td>Haemangioma</td>
<td>Myeloma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Malignant lymphoma</td>
</tr>
<tr>
<td>Chondrogenic</td>
<td>Osteochondroma</td>
<td>Chondroblastoma</td>
</tr>
<tr>
<td></td>
<td>Chondroma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chondromyxoid fibroma</td>
<td>Chondrosarcoma</td>
</tr>
<tr>
<td>Osteogenic</td>
<td>Osteoma</td>
<td>Osteosarcoma</td>
</tr>
<tr>
<td></td>
<td>Osteoid osteoma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Osteoblastoma</td>
<td></td>
</tr>
<tr>
<td>Fibrogenic</td>
<td>Fibrous cortical defect</td>
<td>Fibrosarcoma</td>
</tr>
<tr>
<td></td>
<td>Non-ossifying fibroma</td>
<td></td>
</tr>
<tr>
<td>Neuroectodermal</td>
<td></td>
<td>Ewing’s sarcoma</td>
</tr>
<tr>
<td>Notochordal</td>
<td></td>
<td>Chordoma</td>
</tr>
<tr>
<td>Odontogenic</td>
<td></td>
<td>Ameloblastoma</td>
</tr>
</tbody>
</table>
Group description: These are tumours that affect the blood, bone marrow, lymph nodes and the lymphatic system. Myeloproliferation and lymphoproliferation (lymphoma and leukaemia) are closely linked to the status of the immune system.

**Haematopoietic**

**Benign**

**Haemangioma**

**Definition:** it is a benign bone lesion characterized by vascular spaces lined with endothelial cells. **Sites:** 50% are found in the vertebral bodies, especially thoracic and 20% in the skull. The remainder are found in the femur, tibia and humerus.

**Peak age:** in the 50's

**Gender:** M : F = 2 : 1

**Other demographic:** nil

**Clinical presentation:** usually asymptomatic and a chance finding. In the spine the may encroach on the epidural space and compress the spinal cord. In the skull may have a compressible soft lump. In high flow cases, patient may get shunt related symptoms.

**Molecular pathogenesis:** nil

**Xray appearance:** depends on location. Often poorly defined as it is a localized area of many dilated vessels. Some are on the surface of the bone, some in the cortex and some extend into the medullary cavity.
When found in the long bones it is in the metaphysis or diaphysis and the bone may have a pathological fracture. One sees multiple small irregular lytic areas surrounded by variable areas of sclerosis in a speculated pattern called 'Irish lace'.

Images below, (a) CT of femur courtesy of Dr Vougiouklis Nikos, Radiopaedia.org, rID 19417 – arrow indicates the expanded bone, with multiple ridges within it. And (b) of tibia/fibula – MRI, courtesy of bonetumour.org 2008, the upper white arrow indicates there is haemangioma inside the medulla of the tibia and the lower white arrow shows the tumour having breached the cortex and involving some soft tissue. Many large vessels traverse the muscles.

The image of the skull shows involvement of the occipital region with the haemangioma. Courtesy of Dr Ahmed Mahrous Saied, Radiopaedia.org, rID 34142.
Haemangioma in the vertebral bodies can result in collapse of the vertebra (a) - MRI image courtesy of bonetumour.org 2008 and also the tumour can spread backwards to involve the epidural space with compression of the spinal cord (b). – MRI image courtesy of Dr Ashutosh Gandhi. Radiopaedia.org, rID 19743.
Microscopic appearance: there is a disorganized collection of veins or vascular spaces.

Types:

- Capillary – have capillary size vessels lined by endothelial cells.
- Cavernous – especially found in the skull – has large dilated vessels with flattened endothelium.
- Arterio-venous – has remnants of foetal capillary beds
- Venous – contain small thick walled venous vessels.

Non-vascular components of the haemangioma include fat, smooth muscle, fibrous tissue, bone, haemosiderin and thrombus. The capillary – see image below courtesy of Wikipedia and cavernous types are the most common in bone.
**Biochemistry:** Nil

**Diagnosis:** radiograph, CT and MRI

**Treatment:** Nil if lesion asymptomatic. If there are minor symptoms, it may be possible to use compression techniques to avoid surgery.

Painful intrasosseous lesions without cord compression may have balloon kyphoplasty, vertebroplasty, and transarterial embolization.

In the spine, it may compress the spinal cord without causing instability or deformity, so there conservative surgical removal may be done. The more aggressive lesion, is treated with embolization followed by complete lesional spondylectomy.

In the skull, the haemangioma is resected including a margin of normal bone.

Long bones if painful, can have the lesion treated with sclerotherapy, excision or embolization. If the lesion is large, it is excised and the area packed with a bone graft.

Complication of surgery is that serious bleeding can occur during the operation if the haemangioma is large or deeply placed.

**Prognosis:** the lesion can recur if excision had to be suboptimal.
Malignant Myeloma

Definition: it is a plasma cell neoplasm characterized by multifocal involvement of the skeleton when it has the name of Multiple Myeloma but solitary types do occur in 5% of cases.

Solitary Myeloma (Plasmacytoma)

Definition: this is when the same neoplasm as in the multiple type, causes a single lesion of bone or soft tissue.

Sites: Bones: Vertebral column (commonest site), ribs, skull, pelvis, femur, clavicle, scapula

Extra-osseous: osseous lesions can be found in the lungs, oronasopharynx, nasal sinuses. Eventually the solitary type will progress to Multiple Myeloma.

Peak age: 65 – 70 yrs

Gender: More frequent in men

Other demographic: Nil

Clinical presentation: Bone pain and may have a pathological fracture. If in the spine, patient may have spinal cord compression with weakness in the limbs

Molecular pathogenesis: Ig genes in myeloma cells always show evidence of somatic hypermutation. The cell of origin is thought to be a post-germinal centre β cell that directs to the bone marrow and has differentiated into a plasma cell. Proliferation and survival of myeloma cells is dependent on several cytokines especially IL-6.

Macro appearance: Myeloma lesions commence in the medullary cavity, erode cancellous bone and progressively destroy the bony cortex.
**X-ray appearance:** Plasmacytoma (solitary myeloma). The x-ray below shows a rib is destroyed (arrow) and a soft tissue mass extends into the thoracic cavity (image courtesy of Bruneo di Muzio. Radiopaedia.org, rID 12537.).
In the MRI below, there is curvilinear low signal intensity areas within the lesion on T1, so it looks like brain sulci. It is so characteristic that if present can avoid biopsy (image courtesy of P.Gupta. Radiopaedia.org, rID 17832).
Microscopic appearance of Plasmacytoma:

The microscopy below shows abundant malignant plasma cells with the occasional 'Mott cell', a plasma cell with intracytoplasmic Russell bodies (an eosinophilic uniformly staining membrane bound body which contains immunoglobulin) (Image courtesy of Wikipedia).

Mott Cell - Plasma cells that contain abundant globular inclusions or vacuoles (Russell bodies) composed of immunoglobulin are called Mott cells (1) morular cells or grape cells. Russell bodies can stain blue-violet or pink but may also be dissolved during fixation and staining. In that case, the plasma cell is more or less filled with colorless vacuoles. (2) A plasmacytoid
lymphocyte or activated and transforming B cell (image courtesy of Dr LG Poels. Health Education Assets Library 2007).

**Biochemistry:** testing blood and urine will be negative in most cases of plasmacytoma.

**Diagnosis:** made by biopsy of the site identified by clinical symptoms and imaging.

**Treatment:** the mass is excised and this is followed by chemotherapy and/or radiotherapy. 5% have a local recurrence but 70% disseminate to the phase of Multiple Myeloma. When this happens, the prognosis is bad.

**Multiple Myeloma**

**Definition:** A plasma cell neoplasm characterized by multifocal involvement of the skeleton.

**Peak age:** 65 to 70 yrs

**Gender:** More frequent in males

**Other demographic:** Nil
**Clinical presentation:** May be multiple sites of bone pain, lethargy and evidence of bone fracture.

**Molecular pathogenesis**  Factors produced by the tumour cells inhibit osteoblast function. This causes increased bone resorption which results in hypercalcaemia and eventually pathological fractures.

**Affected sites:** same as for plasmacytoma

- Vertebral column – commonest site, followed by
- Ribs
- Skull
- Can spread to the lymph nodes and skin late in the disease

**Macro appearance:** Myeloma lesions commence in the medullary cavity, erode cancellous bone and progressively destroy the bony cortex.

**X-ray appearance:** Skull – multiple circular areas of bone destruction.
Femur – multiple foci of destruction, weakening the bone which may fracture.

Microscopic appearance: Same as for solitary myeloma (plasmacytoma) – see above.

Diagnosis: blood film, full blood picture, bone marrow biopsy and urine testing. Radiology of the skeleton.

Biochemistry: Testing the blood will show an increase in the Immunoglobulins and in the urine there are light chains (Bence-Jones protein).

Serum electrophoresis is used to screen for a monoclonal immunoglobulin (M protein). Excretion of the protein is toxic to the renal tubules, so kidney failure is the second commonest cause of death from myeloma., infection being the commonest.

Treatment: Chemotherapy and also autologous bone marrow stem cell transplant.

Prognosis: is not good, life expectancy once it has become multiple myeloma is of the order of 2 – 4 years. Whilst the condition remains in a solitary location as plasmacytome, life expectancy could be as much as 10 years. The limiting factor is the toxic effect of the M protein on the kidney structures, as well as succumbing to infection, especially during any period of chemotherapy. Regular monitoring of the serum calcium is undertaken, to give an early warning sign of active myeloma after chemotherapy.

Haemopoietic - Malignant Lymphoma

Overview: Malignant Lymphoma is a group of neoplasms composed of lymphoid or histiocytic cells of different subtypes. Previously called reticulum cell sarcoma, Non-Hodgkin’s lymphoma, lymphosarcoma, osteolymphoma. Primary bone lymphoma is now known as large cell or histiocytic lymphoma.
**Definition:** Primary lymphoma of bone is divided into two groups:

(a) Solitary is when lymphoma is in one bone, with or without regional lymph node involvement and without distant spread for 6 months after diagnosis.

(b) Multifocal type is less common and is when tumour is confined to two or more bones without lymph node or visceral distant spread for 6 months after diagnosis. Primary lymphoma of bone = 5% of bone tumours

**Sites:** the bony pelvis and femur are the most common sites. Less common are humerus, ribs and spine

**Peak Age:** 50 – 60 years. Rare in children under the age of 10 years.

**Gender:** M : F = 1.5 : 1

**Other demographic: nil**

**Clinical Presentation:** localized pain and swelling, pathological fracture, cord compression, fever and weight loss.

**Molecular pathogenesis:** nil

**Macro appearance**  Diffuse large B cell lymphoma is the most common subtype but there may be mixed small and large of B cell lineage. The T-cell primary lymphoma of bone is very rare, except in Japan.
**Xray appearance:** can look normal or show lytic areas which are the most common but also can be sclerotic or a mixed picture. The lytic feature shows permeative bone destruction. MRI – associated soft tissue mass is common. The changes in the bone marrow show as T1 – low signal and T2 – high signal. CT scan can be useful to detect cortical erosion, sequestra and be used to guide biopsy procedure.

**Differential diagnosis:** infection, eosinophilic granuloma, Ewing’s sarcoma, skeletal metastases.

The image of spinal lymphoma in the 5th lumbar vertebra (L5) is shown below. The left black arrow indicates the body of L5 to be of low signal on this T1 image, due to the presence of the lymphoma. The black arrow from the right of the image shows the involvement includes the posterior elements of L5. The white arrow indicates the presence of some associated soft tissue component (image courtesy of F.Gaillard. Radiopaedia.org, rID: 12623).
In the image of a pelvis below, the arrow points to the reduced bone density within the head of the left femur, with almost no cortical destruction of the bone (image courtesy of Dr Matt Skalski. Radiopaedia.org, rID 37078).

The X-ray below shows very moth-eaten bone so this is a permeative lytic lesion and in the metadiaphysis – black arrow. There is evidence of cortical destruction and also some periosteal reaction – white arrow – and associated soft tissue mass.
The mass is due to permeation of tumour cells through small vascular channels in the cortical bone without a frank break in the cortex. The same mechanism occurs in Ewing’s sarcoma and PNET (primitive neuroectodermal tumour) (image courtesy of Dr J C Wittig Tumour.org 2014).

**Microscopic appearance:** Histologically the tumour consists of aggregates of malignant lymphoid cells replacing marrow spaces and osseous trabeculae. The cells contain pleomorphic, irregular or even cleaved nuclei. Also, what distinguishes lymphoma from Ewing sarcoma, is that lymphoma cells stain positively with the immunoreaction for CD45, CD20 and CD3, which are B-cell and T-cell markers. However there is no reliable method to distinguish histologic or immunocytologic features to separate primary bone lymphoma from secondary bone involvement. The image below shows numerous small round blue cells of different sizes and shapes. No matrix. There are also scattered large B cells mixed with any reactive inflammatory infiltrates (image courtesy of Dr J C Wittig).
Biochemistry: Nil

Diagnosis: biopsy

Treatment: Treatment is said to be controversial, with no consensus with regard to radiotherapy, despite lymphoma being radio-sensitive. Some patients require chemotherapy and additional adjuvant radiotherapy.

Prognosis: 5 year survival is 80%

Chondrogenic Group

Group description: This is the second largest group of bone tumours - 22%. A tumour in this group is a tumour of hyaline cartilage and may contain variable amounts of calcification and ossification within its substance.
Benign Chondrogenic Group

Osteochondroma (exostosis)

**Definition:** Most common benign tumour – 33% of all chondrogenic tumours and 85% are solitary.

**Sites:** Osteochondroma arise from the metaphysis near the growth plate of long tubular bones, especially around the knee. It is a benign *hyaline cartilage capped tumour attached to the underlying skeleton by a bony stalk*. This distinguishes it from the ecchondroma.

When Osteochondroma develop from the flat bones of the pelvis, scapula and ribs these will be sessile and attached with a short stalk. It is rare that osteochondroma will affect the short tubular bones of the hands and feet. Osteochondroma tend to stop growing at the time of growth plate closure.

**Peak age:** 10 – 35 years. Develop during skeletal growth 13 – 15 years and this ceases at puberty.

**Gender:** M : F = 2 : 1

**Other demographic:** Nil

**Clinical presentation:** May go undiagnosed and silent in many cases but if the tumour causes pressure on the adjacent muscles, nerves or blood vessels, and on adjacent bone resulting in fracture, symptoms become a problem.

**Molecular pathogenesis:** Nil

**Macro appearance:** lesions commence near the growth plate of long tubular bones.
X-ray appearance:

The images below are a lateral view of the knee on the left and a MRI on the right. The arrow points to the osteochondroma. Note the tiny bony outgrowth from the cartilaginous growth plate,
with the calcified mass of cartilage perched above it as a cap. Courtesy of M. Carmont, S. Davies, D. Gey van Pittius, R. Rees 2008.

Microscopic appearance:

- cartilaginous cap is seen to have the same pattern as normal growth plate but it will be less organized
- underlying trabeculae form by endochondral ossification of cap and contain central cores of calcified cartilage
- many uniform but expanded cartilage cells with small round or elongated nuclei which may be positioned in rows (see arrow in image)
- polymorphism and hyperchromasia of cartilage cells is an expected finding in young children
- note that the cartilaginous cap may be up to 1 cm in width in adolescence and that a cap greater than 3 cm is consistent with low grade chondrosarcoma
Treatment:

- no treatment is required if the diagnosis is not in doubt and if the patient is relatively asymptomatic
- surgical resection is indicated for persistent irritation (from bursitis) or for neurovascular compromise
- surgical resection is also indicated for continued osteochondroma growth after skeletal maturity (in which case malignancy is suspected)
- definitive treatment includes marginal excision of an active exostosis, including the cartilaginous cap & overlying perichondrium
- deep bony base has minimal activity and may be removed piecemeal
- the cartilaginous cap should not be traumatized during its removal

Prognosis: Prognosis for a solitary exostosis is excellent (< 5% recurrence following marginal excision). In the case of hereditary multiple osteochondroma, there is always the possibility of malignant transformation of one of the lesions.

Chondroma

Definition: Chondroma are tumours of hyaline cartilage and arise in the medullary cavity of bone marrow where they are called enchondromas. If these tumours grow out from the surface of the bone, they are called periosteal or juxtacortical chondromas or ecchondromas.
**Enchondromas**

**Definition and classification:** Enchondroma is the most common of the intraosseous cartilage tumours. It is a benign tumour arising in the metaphysis of a bone, and can also have a subperiosteal chondroma variety. Rare to involve an epiphysis.

- **Solitary** - metaphyseal lesions of tubular bones
- **Multiple** – Enchondromatosis – Ollier Disease. This can progress to chondrosarcoma
- **Multiple plus haemangiomas** – Maffuci Syndrome. These patients may also develop ovarian carcinoma and brain gliomas.

**Sites:** the short tubular bones of the hands (35%) and feet if the solitary type. Can also involve the femur, tibia and humerus.

**Peak age:** 20’s to 40’s, although can be seen at any age between 5 years and 80 years.

**Gender:** M : F = 1 : 1

**Other demographic:** Nil

**Clinical presentation:** Often there are no symptoms. Pain can occur at the site of the tumour or if it is a large one, or if the weakened bone has fractured. If located in a finger, the digit can be seen to be enlarged.

**Molecular pathogenesis:** Etiology is unknown. Cytogenetic studies find a broad range of genetic alterations, but most frequent chromosomal changes involve 6 and 12.

**Macro appearance:** Found in the meta-diaphysis or diaphysis. It is a white-grey mass and opalescent while any yellow or red foci are areas of calcification or ossification. Cartilaginous matrix may be as rings or arcs so referred to as a ‘popcorn’ appearance. The tumour is central in 80% and eccentric in 20%. The gross specimen shows multiple enchondroma – see arrows on just 3 of those in the tibia.
X-ray appearance: In the image of a hand, the arrow points to the early fracture of the cortex of the base of the proximal phalanx of the middle finger. The fracture is due to the expanding lesion within the marrow cavity. Image courtesy of Dr Frank Gaillard. Radiopaedia.org r.ID6681
Differential diagnosis of enchondroma:
1. Bone infarct: The enchondroma has endosteal scalloping. Also a bone infarct has a well defined sclerotic border and enchondroma does not.
2. Chondrosarcoma: The tumour has periostitis and enchondroma does not.

**Microscopic appearance:** enchondroma are hypocellular, nonvascular tumours with abundant hyaline cartilage matrix. The nuclei are small and round – see arrow in image below. Courtesy Wikipedia

![Microscopic appearance of enchondroma](image)

**Biochemistry:** Nil

**Treatment:** this tumour is best left alone. If it is unsightly or has fractured the bone, it can be removed by curettage and the defect with a bone graft.

**Prognosis:** After treatment, 10% may grow back. Only 1% progress to malignancy.

**Ecchondromas – Juxta-cortical periosteal chondroma**

**Definition:** is a cartilaginous tumour which arises as an overgrowth out from normally situated cartilage as a mass protruding from the articular surface of a bone, in contrast to enchondroma.

**Sites:** long bones but sometimes flat bones like the pelvis

**Peak age:** as for enchondroma

**Gender:** as for enchondroma
Other demographic: Nil

**Clinical presentation:** The protruberance can be painful. It is similar to osteochondroma.

**Molecular pathogenesis:** nil

**Affected sites:** long bones and pelvis

**Macro appearance:** The echondroma grow slowly but a high percentage are either malignant from the outset or become malignant. Myxomatous degeneration occurs in all cartilaginous tumours.

**X-ray appearance:** There is a lytic mass in the distal femur confined to the cortex and this sits within a cup formed by buttresses of reactive bone – see arrows. This patient had pain and swelling for a few months. Image courtesy of Dr Mark R. Wick. Pathology Outlines.com 2013.
Microscopic appearance: As for enchondroma except for the relationship to the periosteum.

Biochemistry: Nil

Treatment: Wide excision to remove the cartilaginous component beneath the periosteum.

Prognosis: There is malignant potential, hence the need for the wide excision.

Chondromyxoid fibroma

Definition: Rarest of cartilage tumours - 1% of tumours. Can be mistaken for a sarcoma.

Sites: Metaphysis of long tubular bones, small bones of the feet, skull base (clivus) but in any bone.

Peak age: Teens and 20’s.

Gender: equal in both sexes.

Other demographic: nil

Clinical presentation: Dull aching pain.
Molecular pathogenesis: anomalies are found at 6q25.

Macro appearance: Solid, glistening tan-gray intra-osseous tumour. It is a combination of chondroid, myxoid and fibrous tissue organized in pseudo-lobulated architecture. The tumour in the image below is in a slightly eccentric position and involves the metadiaphysis. See arrow on a lobule.

X-ray appearance: Eccentric lobulated geographic lucency well delineated from adjacent bone by a rim of sclerosis. Can expand the overlying cortex.
**Microscopic appearance:** There is a combination of chondroid, myxoid and fibrous tissue organised in pseudo-lobulated architecture. It is a neoplasm of incompletely differentiated cartilage like chondroblastoma. There may be an occasional osteoclast-like giant multinucleated cell. Mitotic figures are rare or absent. Secondary cystic change in the form of aneurysmal bone cyst is not rare.

In the low power image below, note the vague lobularity caused by alternating highly cellular and less cellular areas. Note increased cellularity at the periphery of the lobules – see arrow.

In the high power image below, note the mildly pleomorphic, angular and stellate cells set in bluish-pink chondromyxoid stroma. Note the stroma lacks true hyaline cartilage matrix that is seen in enchondromas and chondrosarcomas and there is a lack of mitotic activity.
Biochemistry: nil

Treatment: Curettage.

Prognosis: 25% recur. Do not undergo malignant transformation or metastasis.

Malignant Chondrogenic Tumours

Chondroblastoma

Definition: Accounts for less than 1% of primary bone tumours.

Sites: Most occur at the knee. Less common the pelvis and ribs in older patients. There is a predilection for epiphyses and apophyses (iliac crest).

Peak age: Commonest age is 20 years.

Gender: M : F = 2: 1

Other demographic: Nil

Clinical presentation: Painful site and 30% have effusions which restrict joint mobility. Have no response to Non-steroidal anti-inflammatory drugs. A swelling or a mass appears. If it occurs in the spine, the patient will experience back pain.

Molecular pathogenesis: Nil

Macro appearance: The tumour is well-circumscribed white-blue-grey and firm. Grow to 3 – 6 cm with variable calcification and necrosis. Cystic areas occur in 20%. Do not have entirely benign features because local invasion of the diaphysis and soft tissues can occur. Also lung metastases can occur after surgery.
The specimen shown below is the proximal tibial epiphysis. There is a well-demarcated partially cystic – see white star - lesion. It shows focal extension through the growth plate into the metaphysis – black arrow. The articular cartilage is partially disrupted – white block arrow.

![Image of the specimen](image)


**X-ray appearance:** The xray of the knee shows a well-defined lucent lesion with a smooth margin and a sclerotic rim (see arrow) which is arising eccentrically in the epiphysis. This tumour is usually 3 – 4 cms diameter at the time of diagnosis. CT and MRI will show fluid levels.
Microscopic appearance: Chondroblastoma is made up of uniform, polygonal cells that are closely packed. These primitive cells are derived from the epiphyseal cartilage plate and have abundant cytoplasm. There are oval shaped nuclei with a prominent groove – see arrow in the image below. Very little mitotic activity. Giant cells are often present.

Image courtesy of Drs B.Di Muzio and Saqba Farooquet. Radiopaedia.org rID 11302.
Differential diagnosis: enchondroma, aneurysmal bone cyst and central chondrosarcoma.

Biochemistry: nil

Treatment: Excision or curettage with a bone graft.

Prognosis: This tumour commonly recurs, often with atypia. May develop pulmonary metastases following repeated curettage, as the tumour cells can get pushed into the systemic circulation. Patients survive after removal of localized metastases but not if there are multiple metastases. It rarely invades locally.

Chondrosarcoma

Definition: a group of tumours which produce neoplastic cartilage and is the second most common malignant matrix-producing tumour of bone.

Sites: long bones – 45%, pelvis 25%, ribs, spine but rarely involves the distal extremities.

Peak age: usually 40’s or older. Teens or 20’s for clear cell and mesenchymal variants.

Gender: M : F = 2: 1

Other demographic: nil

Clinical presentation: patient presents with painful, progressively enlarging masses, pathological fracture. Hyperglycaemia may occur as a paraneoplastic syndrome.

Molecular pathogenesis: nil

Histologically 4 types: conventional central (90%), clear cell, dedifferentiated and mesenchymal types.

Macro appearance: There are Central and Peripheral types:

Conventional central type: 15% of these arise from a pre-existing enchondroma or osteochondroma and are peripheral in location. 10% of conventional low-grade chondrosarcomas have a second high-grade component with morphology of a poorly differentiated sarcoma – this is the dedifferentiated chondrosarcoma type.

Clear cell type: this can look like osteosarcoma and originates in the epiphyses of long tubular bones.
Mesenchymal chondrosarcoma type - this can mimic Ewing’s sarcoma.

The image below shows a central type and has the medullary cavity filled with cartilaginous tumour replacing the bone marrow – see arrow. Scallopimg of the endosteal surface is shown at the 's' labeled arrow. Specimen – courtesy of A HM Taminiau et al. Europ Surg Orthop and Traumatology 01/2014 : 4079-4104.

X-ray appearance: There is a lytic lesion with endosteal scalloping. Calcified matrix appears as foci of flocculent densities. The tumour can cause thickening of the cortex if slow growing, or destroy the cortex if aggressive. The higher grades have a moth eaten appearance to the bone. The arrow in the image below indicates endosteal scalloping of the lateral aspect of the bone and the block arrow is pointing to the calcified matrix in the tumour. Image courtesy of Dr F Gaillard. Radiopaedia.org, rID : 6171.
The image below shows a Chondrosarcoma arising from the bony pelvis and displaying extensive flocculent densities – block arrow. Image courtesy of Dr Iqbal Naseem. Radiopaedia.org, rID 19698.

Microscopic appearance: In the specimen below this one can see abundant hyaline matrix with moderate cellularity and cells with double nuclei – see arrow on the left image. The right image shows bone entrapment by the tumour. Courtesy of A H M Taminiau et al. Europ Surg Orthop and Traumatology 01/2014: 4079-4104.
Biochemistry: this tumour can be associated with hyperglycaemia, as a paraneoplastic syndrome.

Treatment: Conventional chondrosarcoma - has wide excision Mesenchymal and de-differentiated - have additionally chemotherapy

Prognosis: grade 1 – do not metastasize and 90% have a 5 year survival. Grade 3 – 70% of these metastasize to the lungs and skeleton, so only 30% have a 5 year survival. Location affects prognosis: patients with tumours in the long bones have a better prognosis than those with tumours in the axial skeleton.

Osteogenic Tumours

Benign Osteogenic Tumours

Osteoma

Definition: A slow growing osteoblastic lesion.

Sites: Commonly seen in the outer table of the calvarium and in the frontal (80%) and ethmoid (15%) sinuses and in the humerus. Occasionally seen in long (femur) and short tubular (metacarpals) bones and at those sites it is known as a parosteal osteoma.

Peak Age: 4th and 5th decade commonest but can occur between 10 years and 80 years.

Gender: M : F = 2.6 :1

Other demographic: Nil
**Clinical presentation:** Is usually asymptomatic but cosmetic deformity may cause the patient to seek help. Also may obstruct normal drainage of a paranasal sinus.

**Molecular pathogenesis:** Nil

**Macro appearance:** Its importance lies in its similar xray presentation to the aggressive parosteal osteosarcoma and its common association with cutaneous and subcutaneous masses and intestinal polyps in Gardner Syndrome. The latter has intestinal adenomatous polyps, particularly in the colon which may undergo a malignant transformation to carcinoma. The syndrome is a familial, autosomal-dominant disorder.

Osteoma has a sessile, polypoid shape with an average size of 3 cm. It has a smooth bosselated surface. The cut surface shows dense compact bone (ivory osteoma), trabecular bone (mature osteoma) or may have both patterns. The image below, courtesy of Dr David Lucas, Pathology Outlines May 2013 shows a specimen dissected out.

![Image of osteoma](image_url)

Another image, courtesy of Dr. Mark R. Wick, also PathologyOutlines May 2013, shows an osteoma still within the skull.
**Xray appearance:** Dense, ivory-like sclerotic mass attached to the cortex with sharply demarcated borders. Image courtesy of Dr Farzad Pirzad Radiopaedia.org, rID 14544, shows a massive osteoma in the frontal sinuses. The arrows indicate the perimeter of the tumour.
**Micro appearance:** composed mainly of bone, with a mature lamellar architecture consisting of concentric rings as in compact bone or more common to see parallel plates as in cancellous bone.

Image courtesy of Dr David Lucas. Pathology Outlines.com

**Diagnosis:** xray, sometimes CT and MRI to determine extent.

**Biochemistry:** nil
**Treatment:** if asymptomatic, surgeon may prefer to leave it alone but if it is obstructing drainage of a sinus and causing formation of a mucocoele, excision is undertaken and this may be by the endoscopic method. If it is attached to a short tubular bone such as the phalanx of a finger, it may need to be removed.

**Prognosis:** does not recur once excised.

---

**Osteoid Osteoma and Osteoblastoma**

These have identical histological features but differ in size, sites of origin and symptoms.

**Osteoid Osteoma**

**Definition:** It is a vascular lesion consisting of an area of immature bone, surrounded by osteoblasts and osteoclasts – benign hamartomatous lesion - less than 2 cm in greatest dimension, arising in the cortical bone of young persons. These lesions contain small sclerotic bone forming areas with a small central nidus which produces large amounts of prostaglandin E.

**Sites:** any bone but especially the appendicular skeleton and the posterior elements of the spine. In 50% the femur or tibia is involved.

**Peak age:** 75% of patients are under the age of 25 years.

**Gender:** M : F = 3 : 1

**Other demographic:** nil

**Clinical presentation:** severe nocturnal pain relieved by aspirin.

**Molecular pathogenesis:** nil

**Macro appearance:** Consists of 3 concentric layers: a nidus of vessels, osteoblasts etc. – black arrow a fibrovascular rim and surrounding reactive sclerosis – white arrow. Image courtesy of Dr. F. Gaillard. Radiopaedia.org, rID 28806
**X-ray appearance:** The arrows in the images below point to radiolucent nidus. The star on the MRI indicates reactive cortical sclerosis.

**Microscopic appearance:** The image below, courtesy of Wikipedia, shows anastomosing bony trabeculae with osteoblasts rimming the bony spurs. The long arrows in both images indicate the osteoblasts. The short arrow is on a bony spur. One sees a small red nidus of osteoid and woven bone with interconnecting trabeculae and a background and a rim of highly vascularized, fibrous connective tissue. Sclerotic bone reaction may surround the lesion. The benign osteoblastoma has an identical appearance histologically but differs in size, site of origin and symptoms.
Biochemistry: The osteoblasts in the tumour produces large amounts of prostaglandin E and this is thought to cause the pain.

Treatment: may be just prescription of non-steroidal anti-inflammatory drugs, especially aspirin because the tumour may undergo involution after a few years. It may be surgically excised if the pain is not relieved by medication. The newest treatment is percutaneous radiofrequency ablation done under general anaesthetic by a radiologist. Since 2014, a technique using ultrasound and MRI to destroy the tumour without piercing the skin has been introduced. The MRI guides high-intensity ultrasound waves to destroy this benign bone tumour.

Prognosis: Excellent.

Osteoblastoma

Definition: It is a benign, painful, vascular tumour of bone characterized by formation of osteoid tissue and primitive bone.

Sites: 40% occur in the spine, especially the posterior elements. Also found in the long bones where it involves the diaphysis, a few in the metaphysis and is rare
in the epiphysis. In tumours with secondary aneurysmal bone cyst changes, the bone is expanded.

**Peak age:** 80% occur under the age of 30 years

**Gender:** M : F = 2: 3. i.e. 60% are found in females.

**Other demographic:** Nil

**Clinical presentation:** Dull, aching pain that is not relieved by salicylates. In the spine the tumour may interfere with the spinal cord and nerve roots with neurological deficit and scoliosis. If in a long bone, the swelling due to the mass may be obvious by palpation.

**Molecular pathogenesis:**

**Macro appearance:** The mass grows to more than 2 cm, unlike the osteoid osteoma which cannot exceed 2 cm. It does not provoke a bony reaction, whereas osteoid osteoma provokes an abundant reaction. Arrows define the lesion. Image courtesy Pathology Outlines 2011.

**Xray appearance:** Plain xray can diagnose the tumour but CT scan may add more regarding the margins of the tumour and defining the nidus for surgery. MRI is useful to show any soft tissue extension, although this feature is unusual in osteoblastoma. Arrow on the CT scan indicates the calcified nidus in the posterior arch of the 7th thoracic vertebra. Image courtesy of Dr David Lucas.
**Microscopic appearance:** It is considered identical to an osteoid osteoma and in fact is sometimes called a giant osteoid osteoma. The image courtesy of Dr David Lucas shows an arrow on the row of osteoblasts forming a rim around the bone. The block arrow points to the pink material which is bone.

**Biochemistry:** Nil.

**Treatment:** Curettage or excision en bloc. It is not good to irradiate because this can promote malignant transformation to osteosarcoma. Wide excision is preferable which involves removing the tumour and also a surrounding rim of normal tissue and this is usually results in a complete cure.
**Prognosis:** Very good as a rule. The controversial aggressive variant can be associated with metastases and it is this type that is more likely to occur after surgery. Radiation can later result in growth of an osteosarcoma but as that tumour is difficult to distinguish histologically from osteoblastoma, possibly those cases were osteosarcoma originally.

**Malignant Osteogenic Tumours**

**Osteosarcoma**

**Definition:** It is a malignant mesenchymal tumour in which the cancerous cells produce bone matrix. It is the most common primary malignant tumour of bone, excluding myeloma and lymphoma.

**Sites:** Occurs in the metaphyseal region of long bones of extremities; 50% occur about the knee. Over the age of 25 years, the incidence in flat bones like the pelvis and in the long bones is equal.

**Peak age:** Occurs in all age groups but 75% are in patients less than 20 years of age. There is a second peak in the elderly who have conditions predisposing to osteosarcoma e.g. Paget’s disease, bone infarcts and prior radiation.

**Gender:** M : F = 1.6 : 1

**Other demographic:**

**Clinical presentation:** The tumour presents as painful enlarging masses and the bone can fracture. As pulmonary metastases are present in 20% at the time of presentation, haemoptysis may occur.

Metastases also occur to other bones and the brain.

**Molecular pathogenesis:** Defects are present in the retinoblastoma gene RB and p53 which are important in the development of this tumour. The tumour occurs at the sites of bone growth, perhaps because proliferation makes osteoblastic cells prone to acquire mutations that could lead to transformation.

**Macro appearance:** The tumour can break through the cortex and form large soft tissue masses and also can grow into joints. Vascular invasion is common.
X-ray appearance: Radiographs show mixed lytic and blastic masses with infiltrative margins. The tumour bursts through the cortex, lifting the periosteum with subsequent reactive periosteal bone formation. The triangular shadow between cortex and raised periosteum is called Codman’s triangle.
**Microscopic appearance:** Tumour has very pleomorphic cells often with a spindle shape. In the image there is a large cell with very large nuclei – see arrow. There are islands of reactive new bone.

**Biochemistry:** alkaline phosphatase and lactic dehydrogenase levels may be increased in both localized and metastatic disease. Those with metastatic disease have higher levels of LDH than seen in localized disease. Also those patients with an increased LDH pre-treatment are more likely to relapse.

**Treatment:** May need to have a limb amputation but sometimes limb salvage is done. Need to have chemotherapy after surgery.

**Prognosis:** If localized the 5 year survival is 60 – 80%. If the tumour has already metastasized to the lungs, 5 year survival drops to 40%. If spread has occurred to the lungs and to other organs like the brain, 5 year survival only 15%

**Other factors improving prognosis:**
- A child has a better outcome than an adult
- Female patient
- If the tumour is on an arm or leg rather than the pelvis
- The tumour has been completely resectable
- A normal alkaline phosphatase and lactic dehydrogenase
- The tumour showing an initial good response to chemotherapy

**Fibrogenic Tumours**

Benign Fibrogenic tumours
Fibrous cortical defect and Non-ossifying fibroma

**Definition:** Are composed solely or predominantly of fibrous elements.

**Sites:** Arise eccentrically in the metaphysis of the distal femur and proximal tibia. 50% are bilateral or multiple.

**Peak age:** Found in 50% of children over the age of 2 years. Peak age is 15 years.

**Gender:** M : F = 1.5 : 1

**Other demographic:** nil

**Clinical presentation:** Usually the fibrous cortical defect is asymptomatic and found on xray as an incidental finding. Those fibrocortical defects that progress to non-ossifying fibroma may present with pathologic fracture or require biopsy and curettage to exclude other types of tumour.

**Molecular pathogenesis:** Believed to be developmental defects, rather than tumours.

**Macro appearance:** Small, about 0.5 cm in diameter. Those that may grow to 6 cm in diameter develop into non-ossifying fibromas, which are usually not detected until adolescence. They consist of gray to yellow-brown cellular lesions containing fibroblasts and macrophages.

**X-ray appearance:** Both fibrous cortical defect and non-ossifying fibroma produce elongated, sharply demarcated radiolucencies that are surrounded by a thin rim of sclerosis. The images, courtesy of Dr Stacey E Smith, Medscape 2013, shows a lobulated, well circumscribed lucency, with a peripheral sclerotic border, eccentrically located within the distal tibia metaphysis on the left which is a non-ossifying fibroma and a small fibrous cortical defect on the right – see single arrow.
**Microscopic appearance:** Cellular lesions contain fibroblasts and macrophages (histiocytes). The fibroblasts are frequently arranged in a pinwheel pattern and the histiocytes are either multinucleated giant cells – see arrow - or clusters of foamy macrophages. Image below courtesy of Robbins and Cotran. Pathologic basis of disease. 8th ed.

**Biochemistry:** Nil
**Treatment:** Frequently do nothing because over time resolves. However, if the non-ossifying fibroma involves more than 50% of the diameter of the bone, curettage and bone graft is offered.

**Prognosis:** May undergo spontaneous resolution in several years, replaced by normal cortical bone.

---

## Malignant Fibrogenic tumours

### Fibrosarcoma

**Definition:** A malignant mesenchymal tumour derived from fibrous connective tissue and characterised by the presence of immature proliferating fibroblasts or undifferentiated anaplastic spindle cells arranged in a pinwheel pattern (herringbone). These are collagen producing sarcomas with a fibroblastic phenotype which usually arise de novo but may develop in pre-existing benign tumours, bone infarcts and previously irradiated tissue. Account for 5% of bone tumours.

**Sites:** Arise in the fibrous tissue of bone in the metaphysis of long bones and invades long or flat bones such as femur, tibia, mandible. It also involves the periosteum and overlying muscle.

**Peak age:** Any age but most common in 30 – 40 year olds

**Gender:** Slight preponderance in males

**Other demographic:** Nil

**Clinical presentation:** Present as an enlarging painful mass. Pathological fracture is frequent.

**Molecular pathogenesis:** Losses have been most commonly detected at 6q, 8p, 9p, 10, 13q, 20p. Gains are seen on 1q, 5q, 8q, 12q, 15q, 16q, 20q and especially in 22q. Also Xp. Ring chromosome has been reported on chromosome 6.

**Macro appearance:** Large haemorrhagic, tan-white masses that destroy the underlying bone and frequently extend into adjacent soft tissue. There is a collagen matrix but it does not produce osteoid or chondroid.

The tumour can be peripheral arising from the periosteum or intramedullary. Also it has 2 types – infantile and adult. The image below, courtesy of David Secord, shows the tumour involving the wrist area in a child, with both bone and soft tissue involvement.
And his second image shows the extensive soft tissue extension from the tibia in a child.

X-ray appearance: It is permeative and lytic and often extends into the adjacent soft tissue. The images below, courtesy of Dr J D Pitcher. OrthopaediaOne 2011, show in (a) the lytic lesion in the distal femur without matrix within the lesion – see arrows. Irregular cortices indicate a chronic process. In (b) the lateral view there is destruction of the posterior cortex of the femur and the arrows point to the perimeter of a large posterior soft tissue mass.
Microscopic appearance: Malignant fibroblasts are arranged in a herringbone pinwheel pattern. The level of differentiation determines the amount of collagen produced and degree of cytologic atypia. In the image, courtesy of Wikimedia Commons, see these features.

Diagnosis: Radiology imaging and biopsy
Biochemistry: Nil
Treatment: Radical surgical excision and adjuvant chemotherapy
Prognosis: 30% survive 5 years for the high grade type
50 – 80% survive 5 years for the low grade type.
Secondary fibrosarcomas, only 10% survive 10 years.
Congenital type – if less than 10 years old at time of diagnosis, metastatic rate at 5 years is 5%. Local recurrence after surgery occurs in 43%.

**Neuroectodermal Group**

**Ewing’s Sarcoma**

**Definition:** It is a malignant, undifferentiated sarcoma of bone in children – second most common malignant tumour of childhood - and young adults and closely related to PNET of soft tissues and the Askin tumour of the chest wall.

**Types:** Classical Ewing’s sarcoma - 87%  
PNET – primitive neuroectodermal tumour – usually found in the brain - 5%  
Askin tumour of the chest wall – 8% -grows very fast and silently and accounts for 15% of all primary chest wall.  
All three have the same type of cell with the same DNA abnormalities and the same proteins, as well as p53 mutations.

**Sites:** Pelvis, long bones especially the femur, tibia and humerus and the bones of the trunk. Extra-osseous.

**Peak age:** 10 – 20 years, rare over the age of 30 years

**Gender:** Slightly more common in males than females

**Other demographic:** Very rare in African-Americans and Asian-Americans

**Clinical presentation:** Severe pain in the tumour and swelling of the limb. Breathlessness in the Askin tumour and those with metastases to the lung – 30% - from the Classical Ewing’s. The tumour spreads to other bones and bone marrow, as well as to the lungs

**Molecular pathogenesis:** 85% of Ewing’s are the result of translocation between chromosomes 11 and 22, which fuses the EWS gen of chromosome 22 to the FL11 gene of chromosome 11. The EWS/FL1 functions as the master regulator. Other translocations are t (21,22) and t (7,22) . The genetic change is after birth so it is not inherited.

**Macro appearance:** Extensive involvement of the medulla and cortex, associated with elevation of the periosteum. In the image below, the upper arrow is the tumour permeating the marrow. The lower arrow is the surrounding soft tissue mass. Image courtesy of Dr Vandana Singh 2012
**X-ray appearance:** Lytic lesion with an onion skin periosteal reaction on femur (left) – see arrows. Image courtesy of Dr Frank Gaillard Radiopaedia.org. The image on the right of a humerus is courtesy of Dr Jeremy Jones Radiopaedia.org, rID27379 – arrow on periosteal reaction.
In the image below, the tumour can be destructive as in the example of a middle and terminal phalanx of the middle finger. Image courtesy of Dr Hani Al Salim Radiopaedia.org, rid 7995.

**Microscopic appearance:** In the image below, there is a diffuse pattern of growth and sheets of monotonous small round cells, cytologic appearance in ES/PNET. There are prominent nuclei and minimal cytoplasm - see arrow in the image below. One may see pseudo-rosettes (circle of cells with necrosis in the centre) – the arrow is on a tumour cell which is part of the circle. Image courtesy of Dr Patrick O’Donnell 2014. Orthobullets.
Differential diagnosis of a small round cell tumour by age:

< 5 years – neuroblastoma or leukaemia
5 – 10 years – eosinophilic granuloma
5 – 30 years – Ewing’s sarcoma
>30 years - lymphoma
>50 years - myeloma

Other Imaging tests:

- CT scan will demonstrate metastases to the lungs, liver, lymph nodes.
- A bone scan will assess metastases to other bones.

The image below shows the same patient as image of gross appearance. Arrow indicates the massive uptake of the isotope in the tumour in the left humerus. Image courtesy of Dr Vandana Singh 2012.
- A PET/CT scan demonstrates abnormal metabolism at sites of metastases.
Images courtesy of Dr Vandana Singh 2012. Upper images CT scans – left -white arrow on tumour mass in the groin and right – black arrow on a metastasis in the right lung. The lower images are from a PET scan showing abnormal metabolism in the mass in the groin – white arrow and several lung metastases in the right image – black arrows.

A cardiac 2D echo is done pre-operatively because one of the chemotherapy drugs, Adriamycin can cause cardiomyopathy.

**Blood tests:** Haematology. Full blood picture as anaemia is common and there is often a raised white cell count

**Biochemistry:**

- Alkaline phosphatase will be elevated
- Liver function tests
- Kidney function tests because one of the chemotherapy drugs Ifosphamide is toxic to the kidney
- Lactic dehydrogenase (LDH) is assessed as it is a good guide to tumour burden and it falls with effective treatment and increases with recurrence of the tumour.

**Treatment:** Almost all patients require multi-drug chemotherapy as well as local disease control with surgery and/or radiation. An aggressive approach is necessary because almost all patients with apparently localized disease at the time of diagnosis actually have asymptomatic metastatic disease.

Treatment starts with chemotherapy for 8 – 12 weeks to shrink the tumour. Drugs may include vincristine, doxorubicin and cyclophosphamide with ifosfamide and etoposide.

After this course of chemotherapy, the remaining tumour is surgically resected, irradiated or both. The surgical resection may involve limb salvage or amputation. Complete excision at the time of biopsy may be performed if malignancy is confirmed at the time it is examined.

Post-operative, the length of maintenance chemotherapy varies depending on the location and stage of the disease at diagnosis. Radical chemotherapy may be short as 6 treatments at 3 week cycles. However, most patients will undergo chemotherapy for 6 – 12 months and radiation therapy for 5 – 8 weeks. Radiotherapy has been used for localized disease, non-resectable tumours such as large spinal tumours and patients with widespread metastatic disease. The tumour has a unique property of being highly sensitive to radiation, “melts like snow” but the drawback is that it recurs dramatically if maintenance chemotherapy has not also been given.

Recently, antisense oligodeoxynucleotides have been proposed as possible treatment by down-regulating the expression of the oncogenic fusion protein associated with the development of Ewing’s sarcoma resulting from the EWS-ETS gene translocation.

**Prognosis:** If the tumour has not spread at the time of diagnosis, 70% 5-year survival. If the tumour is metastatic only 20 – 30% 5-year survival. However, if it has only spread to the lungs, there is more than a 30% survival.

**Other prognostic factors:** size and site of tumour, response to chemotherapy, age and the presence of a genetic marker that indicates a better prognosis.
**Notochordial Group**

**Chordoma**

**Definition:** chordoma is a rare, slow growing neoplasm thought to arise from cellular elements of the notochord. The evidence for this is the locations of the tumour, the similar immunohistochemical staining pattern and the demonstration that notochordal cells are preferentially left behind in the clivus and sacrococcygeal region when the remainder of the notochord regresses during foetal life. It accounts for 3% of all bone tumours and 20% of primary spinal tumours.

**Sites:** clivus in the base of skull (32%), spine 29% of which 60% are in the sacrum and coccyx. Rarely found in the ribs, lower limbs including the feet.

**Peak age:** any age but the median age for skull chordoma is 49 years and for sacral chordoma is 69 years.

**Gender:** M : F = 1.6 : 1

**Other demographic:** incidence is one patient per million per year.

**Clinical presentation:** pain and neurological deficit. Sacral chordomas have symptoms late when they have become quite large.

**Molecular pathogenesis and genetics:** All patients who develop sporadic chordoma have a genetic variant called a SNP in a gene called brachyury which increased the chance of getting chordoma but it is not the actual causative factor. Families with multiple relatives diagnosed with chordoma, have been found to have a duplication of the brachyury gene. However, search is still in progress to find the causative factor. There is also an increased incidence in children who have tuberose sclerosis.

**Macro appearance:**

The tumour is well-demarcated. In the image courtesy of K Farsad, SV Kattapuram, R Sacknofff, J Ono, GP Nielsen. Radiographics 2009, 29(5) September note the features;
Haemorrhage – solid arrows
Gelatinous cystic material – arrowhead
Destruction of sacral segments with posterior extension into the epidural space – dotted arrow.
X-ray appearance: The image below shows an MRI of a brain of a 17 year old, with the chordoma extending from the nasopharynx posteriorly to reach the brainstem. Image courtesy of S.Hassan, JM Abdullah, SJ Wan Din, Z. Idris
J Medical Case Reports 2: 49, 2008.
(a) – sagittal view – arrows show the perimeter of the tumour, with the posterior limit indenting the brainstem.
(b) – axial view – the lower arrow shows clearly the tumour where it is indenting the brainstem.
The MRI of the sacrum, courtesy of Dr Harry Gouvas, Wiki 2008 shows the perimeter of the tumour.

**Microscopic appearance:** There are 3 types – classical, chondroid and dedifferentiated, the last being fast growing and prone to metastasize.

Classical: this is a lobulated tumour composed of groups of cells separated by fibrous septa. The cells have small round nuclei and abundant vacuolated cytoplasm – see image below courtesy of Dr Harry Gouvas. Pathology Outlines 2008. Arrow indicates a cell with a small round nucleus.
Chondroid: has features of both chordoma and chondrosarcoma and looks very much the same under the microscope. The chondrosarcoma is more radiosensitive and has a better prognosis.

**Metastasis:** 20 – 40% occur from chordomas of the spine. Less than 10% of clivus chordoma metastasize. Metastasis usually occurs late, not found at the initial time of diagnosis, when the tumour has become advanced.

**Biochemistry:** Nil

**Treatment:** complete surgical resection followed by radiotherapy if possible. However the tumour is radioresistant, so needs a high dose which restricts its use as it could also damage adjacent brain or spinal cord and nerves. Many patients have multiple operations over the years to remove recurrent tumour. Those patients deemed inoperable or with advanced disease may receive chemotherapy but unfortunately most of the drugs are designed to kill fast growing tumours, not the slow growing chordoma.

**Prognosis:** depends on age, size and location of the tumour, histological subtype, method of treatment and extent of resection. The Mean 10 year survival for the sacral chordoma is 46%, with the chondroid type being more indolent.

---

**Odontogenic Bone Tumours**

**Ameloblastoma** (previously called adamantinoma)

**Definition:**
Sites: 2 types: paranasal and gnathic (jaw) – 80% located in the posterior mandible and 20% in the maxilla near the third molar where it is difficult to excise.

**Peak age:** Paranasal – 60 years : gnathic 39 years

**Gender:** Equal both sexes

**Other demographic:** Nil

**Clinical presentation:**
Paranasal – nasal obstruction  
Gnathic : difficulty with mastication

**Molecular pathogenesis:** Nil

**Macro appearance:**  
Paranasal variety. Maxillary sinus location most common. It can involve exclusively the nasal cavity or sinuses or both. Looks solid on xray.

**Gnathic variety:**

The images below, courtesy of Robbins and Cotran. Atlas of Pathology 2nd ed, show on the left, a coronal section through an excised portion of the mandible revealing a mass lesion – see diamond – that is below a molar tooth. The head CT scan on the right shows the mass lesion – diamond – expanding the left mandibular ramus of a teenage boy.

These are multi-locular, radiolucent, lytic, expansile. These are slow growing, locally aggressive (30% recur). Metastasizes rarely to the lungs or CNS. This deterioration occurs in long standing tumours, with multiple operations and treatment with radiotherapy.
Risk factors for Gnathic: Impacted teeth, dentigerous cysts

X-ray appearance: Image of the right side of the mandible - courtesy of Dr F Gaillard Radiopaedia.org, rID 2577.
Multiloculated lesion – see arrows at perimeter of lesion. There is an expansile soap bubble appearance, with sharp borders and no matrix calcification. If teeth are present, the tumour can erode into adjacent tooth roots. Large tumours can break the cortex and erode into adjacent soft tissues.

Gnathic: recurrent cystic ameloblastoma was completely cystic and lined with oedematous epithelium with palisaded basal cells.

**Diagnosis:** imaging using plain films, CT and MRI

**Biochemistry:** Nil

**Treatment:** Paranasal variety: complete surgical excision. Curettage is discouraged because there is a 50% recurrence from that procedure.

**Gnathic variety:** surgical en bloc excision. Paranasal variety: slow growing but can recur locally.

**Prognosis:** Paranasal variety: slow growing but can recur locally.

---

**Bone Tumours of Unknown Origin**

These account for 10% of bone tumours.

**Osteoclastoma (Giant cell tumour)**

**Definition:** usually benign but can be locally aggressive.

**Sites:** involves the epiphyses and metaphyses. In adolescents, it is confined by the growth plate so are limited to the metaphysis. Commonest site is the knee.

**Peak age:** 20’s – 40’s

**Gender:** similar
Other demographic: Nil

Clinical presentation:
- causes arthritis-like symptoms as arise near joints.
- May present with fractures
- Can be solitary or multiple, especially in the lower limbs
- May be a bulging soft tissue mass

Molecular pathogenesis: Nil

Macro appearance: notes Erosion into subchondral bone plate destroys the overlying cortex which produces the soft tissue mass delineated by a thin shell of reactive bone.

X-ray appearance: In the image below, the radiograph of the knee shows the expanding lesion in the distal femur – arrows on the left image. The right image is the lateral view and the white arrow indicates the very thin shell of bone overlying the tumour.
Microscopic appearance: there is a mixture of mononuclear cells and multinucleated osteoclast-type giant cells. Frequently undergo cystic degeneration, necrosis, haemorrhage, haemosiderin deposition and reactive bone formation.

Biochemistry: Nil

Treatment: Conservative curettage may be done but this is associated with up to 60% recurrence rate and 4% metastasize to the lungs.

Prognosis: Good outcome if completely excised.
Aneurysmal bone cyst

**Definition:** A benign tumour with multiloculated blood-filled cystic spaces that may present as a rapidly growing expansile tumour.

**Sites:** Metaphyses of long bones and posterior elements of vertebral bodies.

**Peak age:** Any age but especially the first two decades.

**Gender:** Nil

**Other demographic:** Nil

**Clinical presentation:** Pain and swelling of a joint. In the spine, it can compress nerves and cause neurologic symptoms.

**Molecular pathogenesis:** Nil

**Macro appearance:** Image below, courtesy of Rubin and Strayer. Rubin’s Pathology 6th ed, shows the periosteum around the cyst ballooned but intact. The cut surface looks like a sponge filled with blood and blood clots. The walls and septa are composed of fibrous tissue with multinucleated giant cells and occasional osteoid trabeculae.

**X-ray appearance:** Eccentric, expansile lesion with sharp margins in the tibia – arrow on radiograph (a). Usually completely lytic and contain a thin shell of reactive bone at the periphery – arrow on (b) CT scan (c) MRI – shows fluid-fluid level – arrow.
Microscopic appearance:

- Large cystic spaces filled with blood and separated by fibrous septa, alternating with solid areas
- Cysts and septa lined by fibroblasts, myofibroblasts and histiocytes but not endothelium
- Clusters of osteoclast-like multinucleated giant cells with loose spindly stroma to cellular stroma, reactive woven bone, degenerated calcifying fibromyxoid tissue
- Variable mitotic figures and hemosiderin
- No malignant osteoid, no atypia
Biochemistry: Nil

Treatment: Curettage or en bloc resection

Prognosis: Recurrence rate is low and spontaneous regression can occur following incomplete removal.

Unicameral cyst

Definition: It is a benign bone tumour that occurs almost exclusively in children and adolescents who are skeletally immature.

Sites: Occurs in any bone but the commonest is the proximal humerus (90%) and proximal femur. Called active when adjacent to the growth plate.

Peak age: 9 years (5 – 15 years)

Gender: M : F = 2 : 1

Other demographic: Nil
**Clinical presentation:** It can be asymptomatic if the bone has not fractured or the bone can bend, without breaking and the limb be deformed.

**Molecular pathogenesis:** Etiology is unknown but there are theories that venous obstruction in the bone results in the formation of a cyst. Cytogenetic analysis of resected cysts shows aberrations of chromosomes 4, 6, 8, 12, 16 and 21, so there may be a place for gene-based therapy.

**Macro appearance:** The cyst is centrally located, with sclerotic margins and no periosteal reaction or soft tissue component. Expansion of the cyst will cause the bone to bulge with thinning of the endostium but not necessarily cause it to fracture. The cyst contains clear yellow fluid and is lined by a fibrous membrane. In the image below, the arrow indicates where the central cystic mass is bulging the bone beside it.

![Image of bone with cyst](image)

**X-ray appearance:** In the image below, the lesion is lytic, centrally located with a sclerotic margin. The short arrow points to the upper level of the cyst, stopping short of the epiphysis. The long arrow indicates a break in the cortex and the fragment is falling down. The image courtesy of Dr Matt Skalski. Radiopaedia.org, rID29278.
The image below of another patient shows the slippage of the dependent bony fragment now that the cyst has caused fracture of the bone. Image courtesy of F.Gaillard. Radiopaedia.org, rID 12551.
The image below shows that the cyst can involve a considerable length of the bone which softens and bends, with cortical fracture. Image courtesy of Dr M.T. Niknejad, Radiopaedia.org, rID 20470.
CT and MRI add very little. If the lesion has bled, one can demonstrate fluid levels within it with these modalities.

**Microscopic appearance:** The image below shows the walls of the cyst encase blood filled spaces and the cyst is composed of thick septa with uniform fibroblasts and scattered multinucleated giant cells. The long arrow indicates a multinucleated giant cell. The arrow head points to a clump of fibroblasts.
Diagnosis: Differential diagnosis

- Fibrous dysplasia
- Eosinophilic granuloma
- Giant cell tumour – patients usually older
- Non-ossifying fibroma (eccentric with a cortical base)
- Haemophilic pseudotumour (intra-osseous)
- Aneurysmal bone cyst – usually eccentric

Biochemistry: Nil

Treatment: If it is a chance finding and is asymptomatic, the lesion may be monitored only. Also if there is no compromise of the involved bone, for example extensive cortical thinning, best left alone. After it has caused a fracture, simple treatment of fracture by immobilization, results in cyst resolution in 25%. Sometimes steroid injection is made into the cystic lesion when the bone has fractured and after that, the fractured bone will still heal normally. However, it can interfere with growth and it can be painful. Surgery with curettage and bone grafting may be needed.

Prognosis: The outcome is very good but follow-up clinical and imaging is prudent, in case a malignancy develops at the same site as the cyst.