SURGERY 2020

GROIN HERNIA

Groin hernias are the most common type of hernias.
Risk factors are: obesity, pregnancy, and aging.

ANATOMY:

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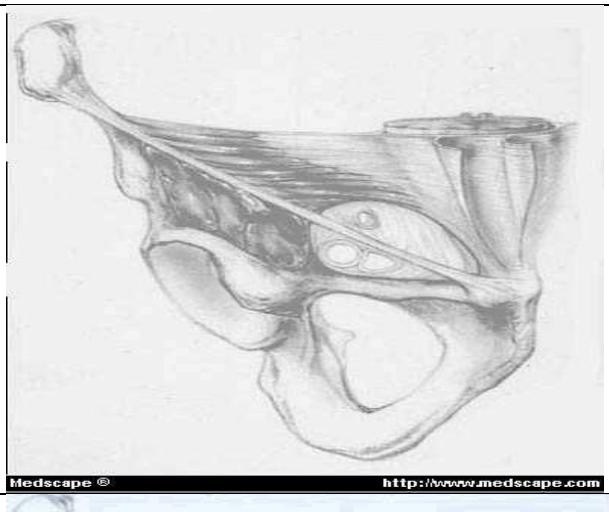
<td> 
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<td>The myopectineal orifice. The passageway for the great vessels to the lower extremity, and for the testicle to reach the scrotum.
The MPO is divided anteriorly by the inguinal ligament, and posteriorly by the iliopubic tract. It is bounded medially by the lateral border of the rectus muscle, superiorly by the arching fibers of the transversus abdominus and the internal oblique muscles, laterally by the iliopsoas muscle and inferiorly by the Cooper ligament.</td>
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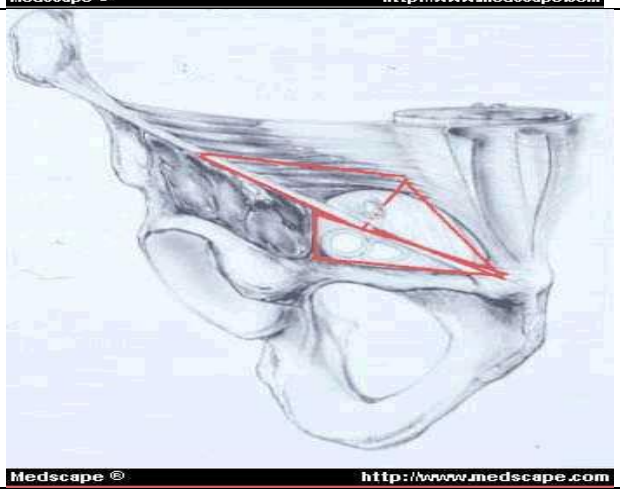
<td> 
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<td>Triple triangles of the groin:
The inguinal ligament anteriorly and the iliopubic tract posteriorly separate the femoral triangle from the medial and lateral triangles. When the femoral triangle is viewed from an anterior approach, it is bounded by the inguinal ligament superiorly, the pectineus fascia posteriorly, and the iliopsoas muscle laterally.</td>
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<tr>
<td colspan="2">The medial triangle (Hesselbach's, Hessert) is bounded by the inguinal ligament, the lateral border of the rectus muscle and the deep epigastric vessels. The lateral triangle is bounded by the deep epigastric vessels medially, and by the inguinal ligament laterally to a variable point approximately halfway between the deep inguinal ring and the anterior iliac spine (the lowest point on the inguinal ligament that the internal oblique and tranversus abdominus muscles are fused). The superior boundary is a line connecting that point on the inguinal ligament to the medial reach of the deep epigastric vessels. Surgery performed for primary hernia in any one of these triangles carries important implications for all 3 triangles</td>
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Classification of Groin Hernias

Gilbert designed a classification for primary and recurrent inguinal hernias done through an anterior approach . It is based on evaluating 3 factors:

- presence or absence of a peritoneal sac

- size of the internal ring
- integrity of the posterior wall of the canal

Types 1, 2 and 3 are indirect hernias; types 4 and 5 are direct.

- **Type 1 hernias** have a peritoneal sac passing through an intact internal ring that will not admit 1 fingerbreadth (ie,<1 cm.); the posterior wall is intact.
- **Type 2 hernias** (the most common indirect hernia) have a peritoneal sac coming through a 1-fingerbreadth internal ring (ie, </=2 cm.); the posterior wall is intact.
- **Type 3 hernias** have a peritoneal sac coming through a 2-fingerbreadth or wider internal ring (ie, >2 cm.). (Type 3 hernias frequently are complete and often have a sliding component. They begin to break down a portion of the posterior wall just medial to the internal ring).
- Type 4 hernias have a full floor posterior wall breakdown or multiple defects in the posterior wall. The internal ring is intact, and there is no peritoneal sac.
- Type 5 hernias are pubic tubercle recurrence or primary diverticular hernias. There is no peritoneal sac and the internal ring remains intact. In cases where double hernias exist, both types are designated (eg, Types 2/4). Descriptors such as *L, Sld., Inc., Strang. Fem.* are used to designate lipoma, sliding component, incarceration, strangulation and femoral components.

In 1993, **Rutkow and Robbins** added a *type 6 to the Gilbert classification to designate double inguinal hernias and a type 7 to designate a femoral hernia.*

Nyhus developed a classification designed for the posterior approach based on the size of the internal ring and the integrity of the posterior wall.

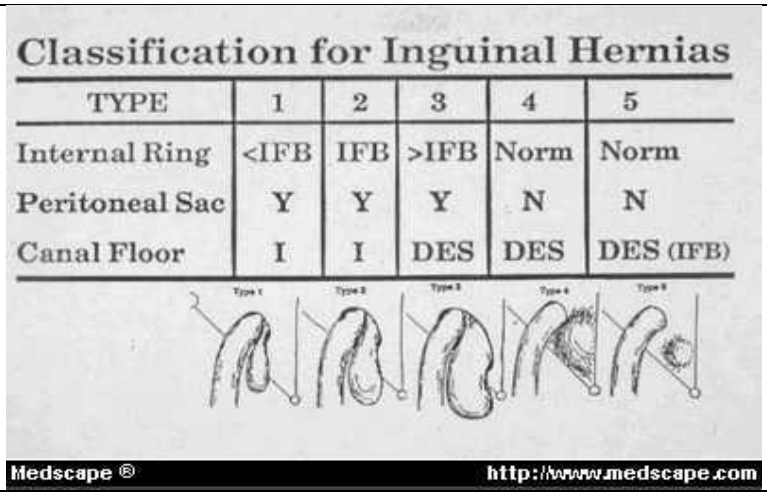


Figure. Gilbert classification. Five types of primary and recurrent inguinal hernias.

Treatment

Most groin hernias are clinically important and should be repaired electively.

Anesthesia

Local anesthesia; Regional anesthesia: Subarachnoid block or spinal anesthesia;

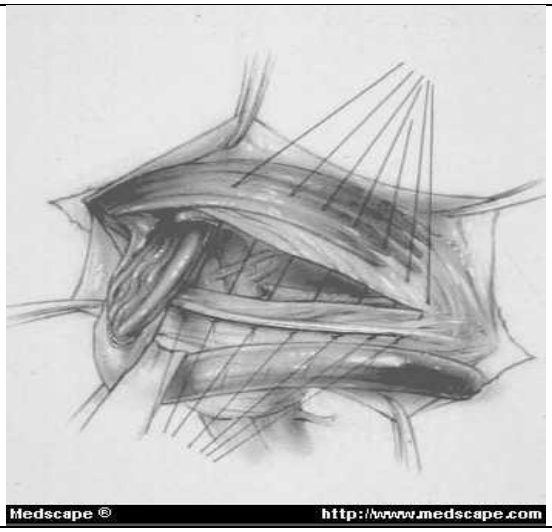
Other options: Such as caudal anesthesia or paravertebral block. **General anesthesia** provides complete relaxation and calms the patient's fears however.

The Evolution of Hernia Repair

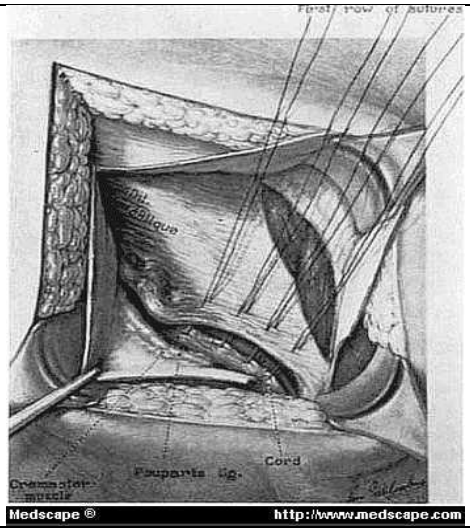
Edoardo Bassini: The Father of Modern Day Hernia Surgery

Bassini's operation epitomized the essential steps for an ideal tissue repair. He opened the external oblique aponeurosis through the external ring, and then resected the cremasteric fascia to expose the spermatic cord. He then divided the canal's posterior wall to expose the preperitoneal space and did a high dissection and ligation of the peritoneal sac in the iliac fossa. Bassini then reconstructed the canal's posterior wall in 3 layers. He approximated the medial tissues, including the internal oblique muscle, transversus abdominus muscle and transversalis fascia to the shelving edge of the inguinal ligament with interrupted sutures. He

then placed the cord against that newly constructed wall and closed the external oblique aponeurosis over it, thereby restoring the step-down effect of the canal and reforming the external inguinal ring.

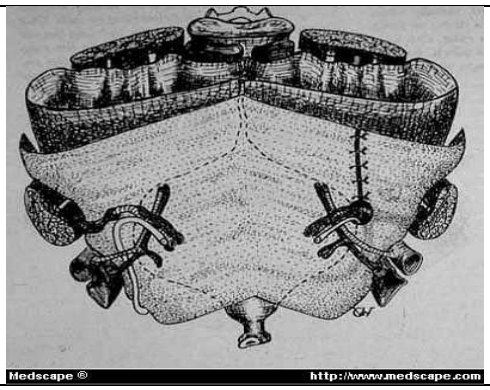


Original Bassini operation. The canal's posterior wall is opened and the deep epigastric vessels are exposed.

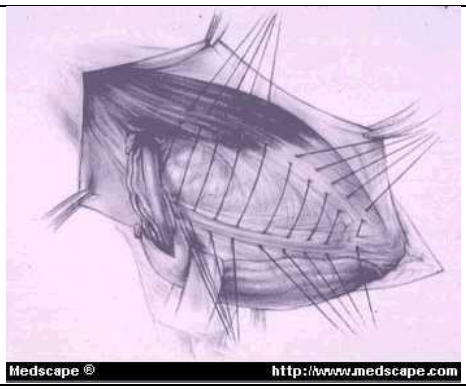


Relaxing incision. Required for most tissue repairs to reduce tension on suture line.

There have been numerous modifications of Bassini's original technique eg. Introduction of *relaxing incisions by surgeons such as Wolfer, Halsted, **Tanner**, and McVay.*
Annandale described a posterior approach to groin hernia repair in 1876.
Stoppa used the posterior approach to implant an impermeable barrier around the entire peritoneal bag, demonstrating that permanent repair of groin hernias does not require closure of the abdominal wall defect per se. Without having stated it, their repair used a tension-free technique In Stoppa's approach, the mesh is held in place by intra-abdominal pressure, an application of Pascal's principle.



Stoppa procedure. The entire peritoneal bag is wrapped with a mesh graft. Expanding intra-abdominal pressure hold the graft in place without suture fixation



Modified Bassini. The posterior wall is not opened. Sutures placed between the transversus arch and the inguinal ligament creates tension on the tissues approximated.

Contemporary Classical Repairs
Among the most notable contemporary classic hernia repairs are the Bassini, Halsted, Shouldice and, McVay (Cooper Ligament) repairs.
Modified Bassini. Bassini's original repair yielded outstanding results for a pure tissue technique, but, as noted above, problems occurred when surgeons failed to open the posterior wall. This operation became

known as the "modified" or "North American" Bassini. By not opening the posterior wall, the wall tissue was damaged in its most medial portion by sutures placed under tension, and recurrences resulted, primarily in the pubic tubercle area.

Shouldice repair: It applies the principle of an imbricated posterior wall closure with continuous monofilament suture. **At the Shouldice hospital, *continuous stainless-steel wire* is used for all layers of the repair.** The Shouldice repair remains an excellent option, however, and has produced the best and most enduring results of any other pure tissue repair.

Tension-Free Hernia Repair

The most important advance in hernia surgery has been the development of tension-free repairs. ***Usher*** opened the posterior wall and sutured a swatch of *Marlex* mesh to the undersurface of the medial margin of the defect (which he described as the transversalis fascia and the conjoined tendon) and to the shelving edge of the inguinal ligament.

The most common prosthetic open repairs done today are the Kugel patch repair, the **Lichtenstein onlay patch repair**, the *PerFix* plug and patch repair, and the *PROLENE Hernia System* bilayer patch repair.

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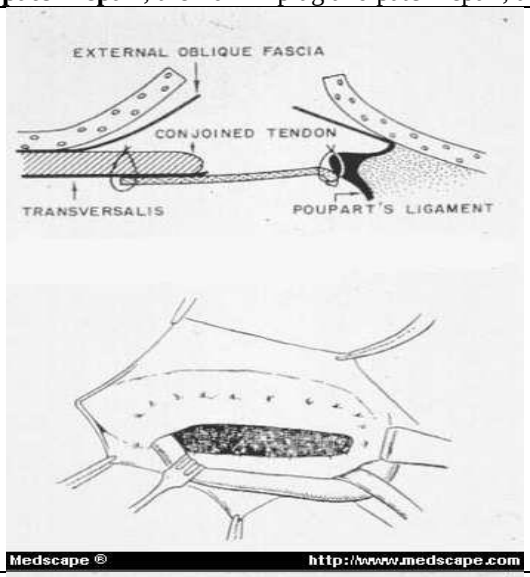
<td> 
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<td>Usher's repair. The mesh is sutured from the transversalis fascia and conjoined tendon medially across the defect to the shelving edge of the inguinal ligament establishing a "tension-eliminating" repair.</td>
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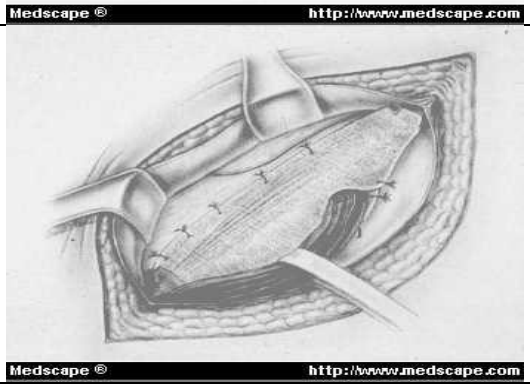
<td> 
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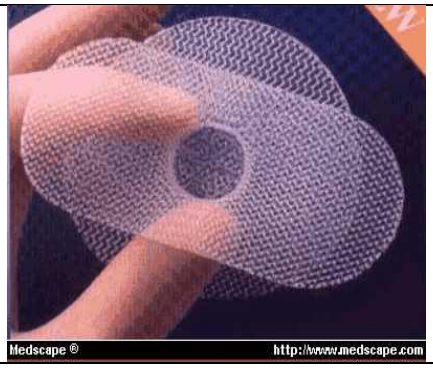
<td> 
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<td>Lichtenstein onlay patch. Mesh is sutured from the transversus arch to the shelving edge of the inguinal ligament creating a "tension-free" repair</td>
<td>*PROLENE Hernia System* (PHS) bilayer patch repair. Three-in-one device with round disc for properitoneal repair, plug effect of connector, and oblong shaped onlay component.</td>
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The Stoppa-Rives giant prosthetic repair of the visceral sac is also an important tension-free technique done through an open posterior approach.

Complications Associated With Hernia Surgery

Infection: Before the use of prosthetics, hernia repair was considered a clean, low-risk operation that did not require prophylactic antibiotics. Because the use of prosthetics later was erroneously associated with increased infection risk

Seroma: A seroma is a collection of serum in a surgical wound. The size of the collection relates to the amount of dissection done between tissue planes and the amount of dead space remaining in the wound.

The wound appears raised but is not inflamed or tender. The mass is fluctuant and the fluid ballotable. Ultrasonography confirms the clinical diagnosis. Treatment consists primarily of observation and expectation. Aspiration is rarely necessary, and in most cases the seroma will completely reabsorb in 2 to 3 weeks. Early aspiration is futile, as the fluid will reaccumulate within a day or 2.

Hematoma: Opening the wound, evacuating the hematoma, and allowing it to close by secondary intention best treats bleeding into the wound.

Postoperative Neuralgia: Symptoms are pain or a burning sensation in the inguinal region, which may radiate to the genitalia and the upper thigh. It is aggravated by activity and relieved by hip flexion. *Tinel's sign helps in identifying a trigger point causing the problem. If localized anesthetic blocks confirm the diagnosis of a specific postoperative neuralgia.* **Treatment is resection of the nerve trunk carried as far proximal as possible.**

Pediatric Inguinal Hernias

Inguinal hernias in the pediatric age group are **almost always indirect**, the *result of persistent patency of the processus vaginalis.* The processus vaginalis is still open in most newborns. *It normally becomes fibrosed during infancy, and by age 2 most are completely obliterated. The persistent processus in itself does not indicate the presence of a hernia.* **Bowel or other intra-abdominal contents must come into the processus for it to clinically become a hernia.** The processus may close inconsistently, leading to a funicular hernia, a scrotal hernia, or, a hydrocele.

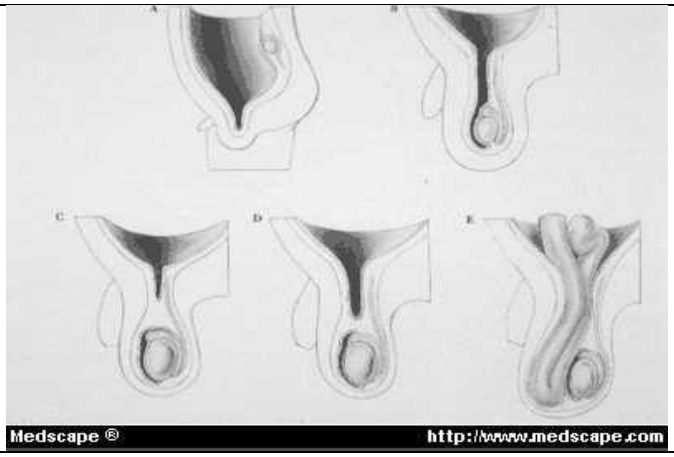

Figure: Various degrees of closure of the processus vaginalis.

The persistence of the processus vaginalis seems to be more common on the right side.

Once the diagnosis of an inguinal hernia is made in a child it should be repaired, **there is a higher incidence of incarceration or strangulation in these young children.**

Repair of Pediatric Hernias

Repair of most pediatric hernias requires *ligation of the true neck of the sac through the internal ring. The sac should be examined to rule out the presence of a sliding component. This is especially important in female patients, as it may contain a Fallopian tube or ovary that could inadvertently be ligated*.

In general, prosthetics should not be used in small children. However, hernias in full-grown teenagers can be safely repaired with mesh.

Laparoscopic Hernia Repair

Intraperitoneal onlay mesh technique (IPOM):

The IPOM technique focused on the placement of an intra-abdominal piece of a prosthetic biomaterial fixed with some type of stapling device); the repair did not involve the dissection of the peritoneum. The advantages of this repair were the lack of significant dissection of the preperitoneal space and the rapid placement of the prosthesis. The recurrence rate, however, was somewhat higher that that of the more widely adopted repairs developed later.

Trans abdominal preperitoneal (TAPP) repair method: In this approach, the preperitoneal tissue is removed from the fascial layer by directly entering the intra-abdominal cavity. This is similar to the IPOM approach, except that TAPP involves more dissection of the preperitoneal space. With TAPP, the prosthesis is placed into the preperitoneal space following dissection, fixed with a stapling device or a spiral tacking device, and covered.

totally extraperitoneal approach (TEP): The TEP approach generally employs a preperitoneal dissection balloon that is introduced via a subumbilical incision. The balloon is inflated, creating the preperitoneal space for the hernia repair. Two or 3 additional working ports are then placed to complete the necessary surgical dissection in which to adequately expose the inguinal floor and the myopectineal orifice. Once the hernia defects are visualized, a polypropylene biomaterial is then inserted and secured to the transversalis fascia and/or Cooper's ligament with tacks or staples. **The material is of a size that completely covers the myopectineal orifice.**

Other terminology and types of hernias.

Maydel's hernia (Hernia in W): Strangulated loop of W lies within the abdomen and local symptoms of strangulation are not marked.

Sliding hernia (Hernia en gissade): The posterior wall of sac is also formed by cecum (right), Sigmoid colon (left) or by a portion of bladder (either side).

Spigelian hernia: Occurs commonly at the level of arcute line.

Lumber hernia: Exits through inferior lumber triangle of Petit (formed by iliac crest; external oblique and latissmus dorsi), or rarely through superior lumber triangle (formed by sacrospinalis; lower border of 12^{th} rib and posterior border of internal oblique).

Obturator hernia: it occurs through the obturator canal. Swelling is covered by pectinius but becomes more apparent on flexion abduction and external rotation of the limb.

Gleuteal hernia: passes through greater sciatic foramina either above or below the piriformis.

Schiatic hernia: passes through the lesser schiatic foramen.

Incisional hernia occurs in a previous scar and it is the most common hernia in a female.

Velpeau hernia: A hernia in the groin in front of the femoral blood vessels. Named for the 19th-century Paris surgeon Alfred Armand Louis Marie Velpeau (1795-1867).

Holt·house's hernia: An inguinal hernia with extension of the loop of the intestine along the inguinal ligament.

Femoral Hernia

Epidemiology

- Accounts for 5% (5-10%)of Groin Hernias (96% are inguinal)
- More common in elderly women (F: M = 3:1).

Anatomy:

- Femoral canal - 1.25 cm long from the femoral ring above to the saphenous opening below.

Pathophysiology

- Associated with increased intra-abdominal pressure
- Hernia sac bulges into femoral canal, which is continuation of femoral sheath
- Femoral canal lies immediately medial to femoral vein

Mechanism:

- Hernia is narrow in the canal
- No resistance at the saphenous opening - expands upwards towards abdomen, because the deep fascia of the abdomen is attached lower to the saphenous opening to the fascia lata.
- May form inverted retort shape - may traverse above Ing. lig.

- Predisposes to strangulation d.t. tortuous course, narrow canal, fixed rigid ring.

Symptoms and Signs

- Groin Pain and tenderness often absent, **strangulation occurs often without pain**
- Hernia sac neck location palpable lateral and inferior to pubic tubercle
- Large femoral hernias may bulge over inguinal ligament

Differential Diagnosis

- Inguinal Hernia, Inguinal Lymphadenopathy, Varix of Saphenous Vein (Thrill on palpation; Fills on standing and empties while supine).
- Infectious Bubo (Chancroid, Syphilis, Lymphogranuloma venereum)

Varieties :

Laugier's Femoral hernia - Occurs through a defect in the lacunar ligament (of Gimbernat). A small hernia in a very medial position. Almost always presents as strangulated.

Narath's femoral hernia - Seen in Congenital dislocation of hip. Occurs due to lat displacement of the psoas.

Cloquet's femoral hernia - Occurs behind the pectineus muscle. The hernia is behind the femoral vessels.

Pre-vascular femoral hernia - Occurs in front of the inguinal ligament and the femoral vessels. Has a wide neck and less tendency to strangulate.

Treatment : No role for conservative management e.g. truss

Operations : the hernia is reduced, & repair done by stitching the conjoint tendon to the Cooper's ligament.

1) Low Approach (LOCKWOOD)

Groin crease incision/ high risk of injury to abnormal obturator Artery/ not used in strangulation as intestine not well approached.

2) High Approach (McEVEDY)

Vertical incision over femoral canal extended over the ing. lig. up to the abdomen/ Good control over abnormal obturator Artery/ Useful in strangulated hernias/ higher risk of incisional hernia.

3) Inguinal Approach (LOTHEISSEN)

Incision over inguinal canal/ Good control over abnormal A.

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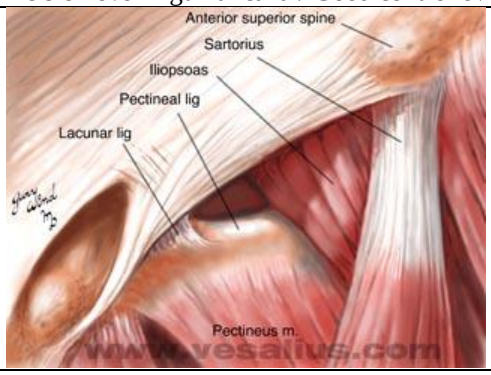
<td> 
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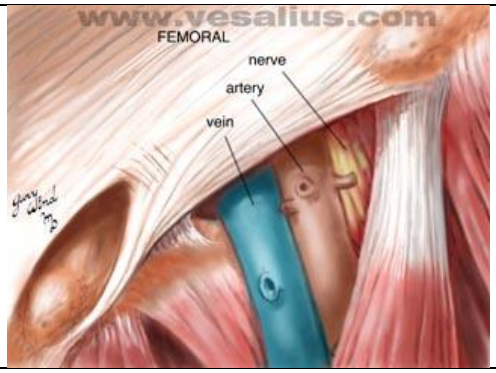
<td> 
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<tr>
<td>The space between the inguinal ligament and the superior ramus of the pubis is filled laterally by the iliopsoas muscle. The pectineal (Cooper's) ligament is thickened periosteum over the pectineal ridge of the superior pubic ramus. The lowest fibers of the external oblique aponeurosis (inguinal ligament) reflect back onto the pectineal ligament forming the lacunar (Gimbernat's) ligament. The pectineus muscle originates from the superior ramus of the pubis</td>
<td>The femoral artery and vein occupy the space between the iliopsoas muscle and lacunar ligament. The femoral nerve emerges through the fibers of the iliopsoas muscle lateral to the vessels. Note the small space between the vein and the lacunar ligament.</td>
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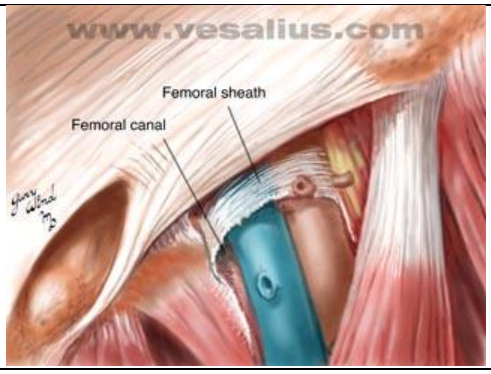
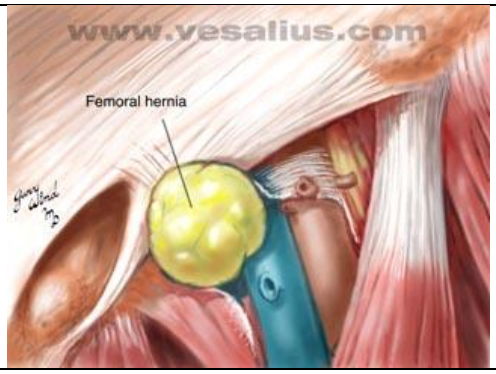
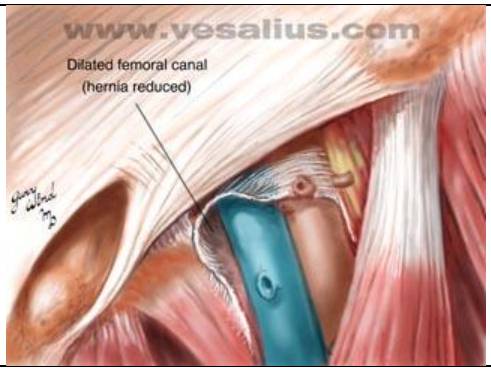
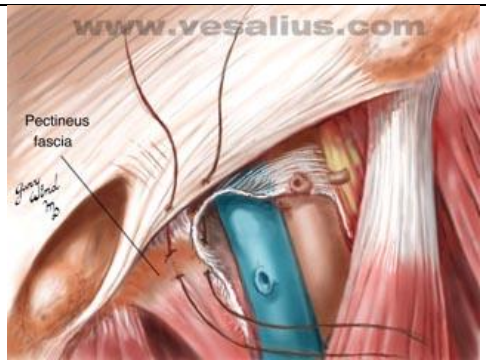
below the pectineal ligament.	
	
A continuation of the transversalis fascia of the abdomen surrounds the femoral vessels forming the femoral sheath. The small space medial to the vein within the femoral sheath is the femoral canal through which lymphatics pass from the leg into the abdomen. The femoral nerve is outside the femoral sheath.	A femoral hernia passes through the femoral canal and reflects up toward the inguinal ligament. It is often difficult to differentiate a femoral from an inguinal hernia. If the majority of the bulge is below the inguinal ligament (a straight line between anterior superior spine and pubic tubercle) it is likely to be femoral.
	
The hernia is freed from surrounding tissue and reduced. The femoral ring can be widened by incising the lacunar ligament medially or the inguinal ligament anteriorly. It is important to isolate only the fascial layer before cutting because of the presence of an aberrant obturator artery immediately above in up to 25% of individuals.	The dilated femoral ring can be narrowed by suturing inguinal ligament to pectineus fascia. In the alternative repair of a femoral hernia from above, the transition stitch of the McVay repair accomplishes the same thing. Some surgeons are now inserting a mesh plug into the canal as well.

UMBILICAL HERNIA

DEFINITION:

A condition caused by a small defect in the periumbilical musculature of the anterior abdominal wall resulting in protrusion of the umbilicus.

EPIDEMIOLOGY:

- age of onset: at birth or during the first year of life
- risk factors: blacks > whites/ low birth weight/ hypothyroidism/ chromosomal anomalies (i.e., Trisomy 13)/ Mucopolysaccharidoses (i.e., Hurler Syndrome)/ Beckwith-Wiedemann Syndrome

PATHOGENESIS:

- in normal embryogenesis, the intestines exit the abdominal cavity, return, rotate, then become fixed to the posterior abdominal wall
- an umbilical hernia results from the failure of this process and due to an imperfect closure or weakness of the umbilical ring, a small portion of the intestine remains in the umbilical coelom producing a small sac protruding up through the base of the umbilical cord
- this sac (hernia) may contain omentum or portions of the small intestine

CLINICAL FEATURES:

1. Protuberant Umbilicus: usually varies from 1-5 cm in diameter/ easily reduced when the infant is relaxed/ is soft, non-tender, and covered by normal skin

2. Complications: incarceration (irreducible umbilical hernia)/ strangulation of the intestine within the hernia/ perforation of the hernia

MANAGEMENT:

1. Supportive

- ***observe as most hernias close spontaneously before 5 years of age***
- most hernias that appear before 6 months of age disappear by 1 year of age

2. Surgery: indications for surgery:

- complications (incarceration, strangulation, perforation)
- if the hernia persists to 3-4 years of age
- a large hernia (defects larger than 2 cm in diameter are less likely to close spontaneously)
- the hernia becomes progressively larger after 1-2 years of age or cosmetic reasons

Congenital diaphragmatic hernia

- Occurs in 1 in 2500-4000 live births
- Results from failure of closure of the pleuro-peritoneal canals
- The herniation occurs in the 8-10th week of gestation.
- 95% occur through the posterior foreman of Bochdalek (occur on the left)
- Less than 5% occur through the anterior foreman of Morgagni
- The midgut herniates into the chest impairing lung development
- Abnormalities of the pulmonary vasculature results in pulmonary hypertension
- Usually associated with gastrointestinal malrotation

Anatomy

- The diaphragm is composed of muscle and fascia that separates the chest from the abdominal cavity
- It is composed of three muscles parts about the rim that lead to a central tendinous portion
- The muscle parts are:
    - The sternal portion that attaches to the breastbone area
    - The costal (rib) portion that attaches along the ribs
    - The lumbar portion that attaches along the back
- The tissue formed by the fusion of the various parts of the diaphragm is called the pleuroperitoneal membrane
- The are three openings in the diaphragm that allow passage of:
    - The inferior vena cava
    - The esophagus
    - The aorta
- The diaphragm is covered on both sides by a membranous layer of fascia. The transversalis fascia covers the abdominal side, and the endothoracic fascia covers the thoracic side.
- The phrenic nerves control the muscles of the diaphragm

Diaphragmatic hernia

hiatus hernia

Bochdalek hernia

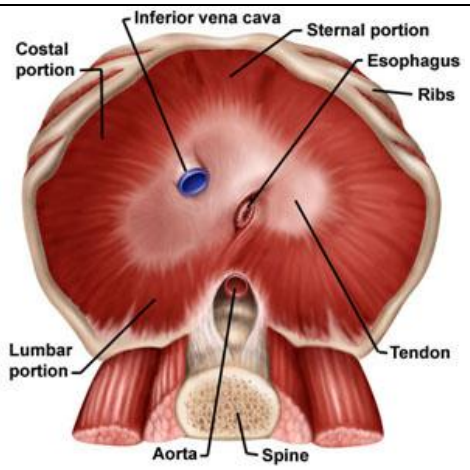
- posterior: pleuroperitoneal membrane
- more common on LEFT

Morgagni hernia

- anterior: retrosternal muscle clefts
- most often on RIGHT, most seen on LEFT

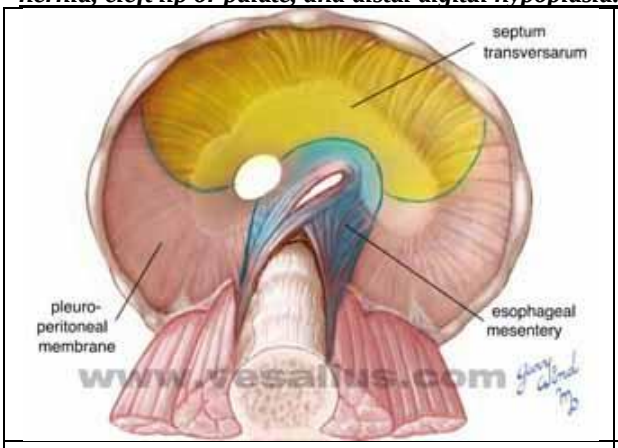
Morgagni hernia is more common in girls than boys; Bochdalek hernia is slightly more common in boys than girls.
Babies with the Bochdalek type of diaphragmatic hernia are more likely to have another birth defect.

- Almost 20% have congenital heart defect.
- Between 5 to16 % have a chromosomal abnormality.

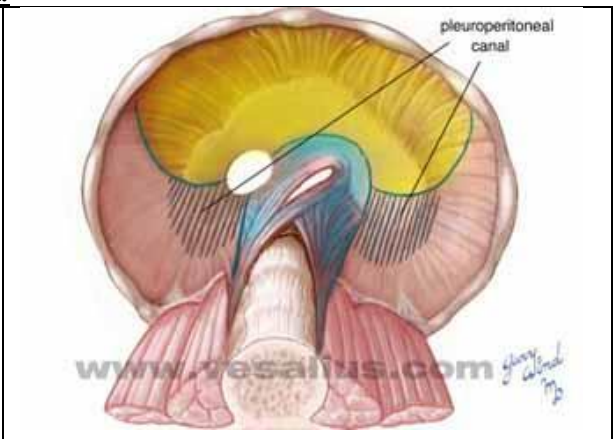


Anatomy of the diaphragm

Fryns syndrome is an autosomal recessive disorder with variable features, including diaphragmatic hernia, cleft lip or palate, and distal digital hypoplasia.



The regions of the mature diaphragm derived from embryonic structures are depicted.



The cross-hatched areas represent the sites of the embryonic pleuroperitoneal canals prior to fusion of the diaphragmatic elements.

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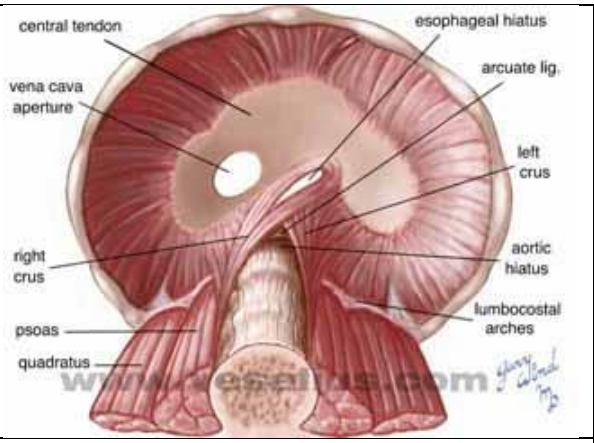
<td> 
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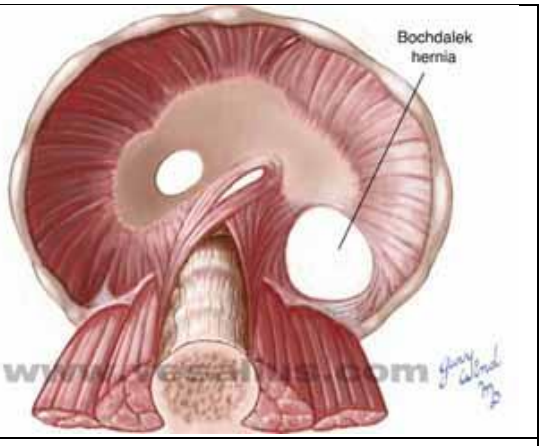
<td> 
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<td>The adult diaphragm consists of a muscular skirt and a three-lobed central tendon. The right lobe of the diaphragm contains the opening for the inferior vena cava.</td>
<td>Failure of closure of the pleuroperitoneal canal, usually on the left results in a Bochdalek type diaphragmatic hernia.</td>
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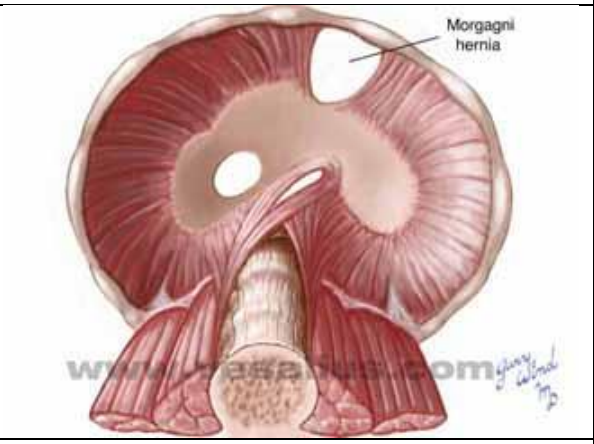
<td> 
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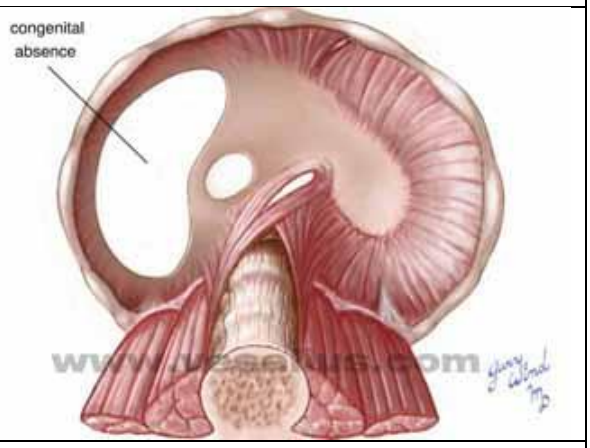
<td> 
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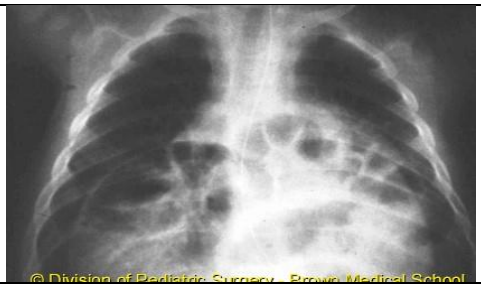
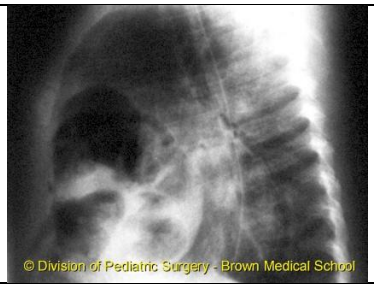
<tr>
<td>Widening of the vascular channel between the sternal and costal muscle slips results in a Morgagne type hernia, usually on the right side.</td>
<td>A wide failure of fusion of the diaphragmatic membrane components results in the absence of a portion of the diaphragm.</td>
</tr>
</table>

Clinical features

- Often presents with cyanosis and respiratory distress soon after birth
- Prognosis is related to the time of onset and degree of respiratory impairment
- The abdomen to flat and Air entry is reduced on the affected side
- Heart sounds are often displaced
- Chest x-ray will confirm the presence of gastrointestinal loops in the chest
- Occasionally presents with respiratory distress of intestinal obstruction later in life

	
Morgagni hernia	Morgagni hernia lateral view

Management

- Respiratory support with intubation and ventilation is usually required/ A Ryle's tube should be passed/ Gas exchange and acid-base status should be assessed/ Acidosis may need correction with bicarbonate infusion/ Surgery should be considered early after resuscitation/ Hernial content are usually reduced via and abdominal approach/ Hernial sac is excised and diaphragm repaired with nonabsorbable suture or a Gortex patch/ A Ladd's procedure may be required for malrotation/ Early respiratory failure is associated with a poor prognosis

Incisional Hernia

It occurs through a weak surgical or traumatic wound. It is a type of Ventral Hernia. Usually, the incisional hernia presents as a bulge near a previous wound. The condition is often asymptomatic but occasionally, presents with pain or strangulation.

Pathophysiology

- Develops in scar of prior laparotomy or drain site
- Risks for post-operative hernia development
    - Vertical scar more commonly affected than horizontal/ Wound infection/ Wound dehiscence/ Malnutrition/ Obesity/ Tobacco abuse/ Presence of drains in wounds/ DM, jaundice, renal failure, immunosuppression/ Malignant disease.

Incisions commonly affected :

- Lower midline
- Subcostal
- Lateral muscle splitting incisions

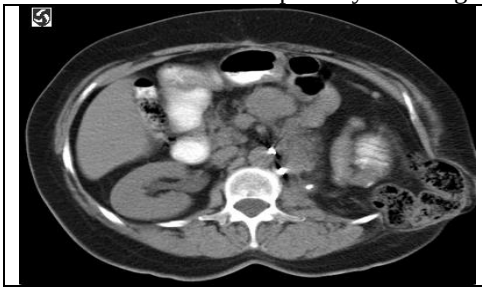
C/F: Like any other hernia. May get obstructed and strangulated.

Treatment

Smaller incisional hernias (< 3 cm.) can be repaired with primary tissue approximation. Repair of larger defects generally requires the use of **prosthetic materials, which allows for a tension free repair.** Laparoscopic techniques may also be used.

Operative -

- Layer to layer repair - where defect is small to moderate without much tissue loss.
- **Keel repair** (MAINGOT'S) - Scar is excised. The peritoneum and the layers are invaginated into the cavity and successive sutures taken.
- Mesh - Used especially with large defects and tissue loss.

	*CT of the abdomen*

SALIVARY GLAND

A. **Parotid Gland**

1. Located on side of face, anterior to mastoid tip and external auditory canal, inferior to zygomatic arch, and superior to the lower border of the angle of the mandible. Anteriorly, it overlaps the masseter muscle.
2. Stenson's duct enters oral cavity through buccal mucosa opposite upper 2nd molar.
3. Parasympathetic secretory afferents to the parotid leave the inferior salivary nucleus with the glossopharyngeal nerve and travel via Jacobson's plexus in the middle ear to synapse in the otic ganglion. Post-synaptic fibers are distributed to the parotid by the auriculotemporal nerve.
4. Facial nerve passes through this gland.

B. **Submandibular Gland**

1. Beneath floor of the mouth, inferior to mylohyoid muscles and superior to digastric muscle.
2. Marginal mandibular branch of the facial nerve travels in the fascia on the lateral surface of this gland.
3. Parasympathetic secretory afferents to the submandibular gland arise from the superior salivatory nucleus, and leave the brainstem in the facial nerve. They exit the facial nerve at the geniculate ganglion and travel via the chorda tympani to the lingual nerve. Fibers synapse in the submandibular ganglion, and post-synaptic fibers then enter the gland.
4. The lingual and hypoglossal nerves lie deep to this gland.
5. Wharton's duct enters the floor of the mouth near the lingual frenula.

C. **Sublingual Glands** - located below the mucous membrane of the floor of the mouth, adjacent to mandible and mylohyoid muscle. Ten to twelve small caliber ducts drain the gland, some emptying into the submandibular duct, and others draining directly into the floor of the mouth.

D. **Minor Salivary Glands** - small collections of salivary gland tissues are scattered throughout the oral mucosa, and can also be seen in the pharynx, supraglottis, nose and sinuses.

Parotid Gland:

- Parotid gland appears on the 4th week of gestational life from the epithelium of the oro-pharynx.
- Agenesis of the parotid glands is rare; may be associated with other facial abnormalities.
- Cyst arising from the first branchial cleft may be located within the parotid gland
- Largest of the salivary glands and it overlaps the masseter muscle.
- VIIth Nr. passes through and divides the gland into a superficial and deep lobe
- The deep surface of the gland lies alongside the back of the throat, near the tonsils
- Stenson's duct enters oral cavity through buccal mucosa opposite upper 2nd molar.
- Parasympathetic secretory afferents to the parotid leave the inferior salivary nucleus with the glossopharyngeal nerve and travel via Jacobson's plexus in the middle ear to synapse in the otic ganglion. Post-synaptic fibers are distributed to the parotid by the auriculotemporal nerve.

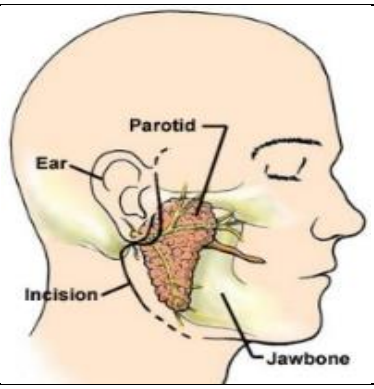


Figure 1 - The superficial lobe of the parotid gland lies outside the mandible (jawbone) while the deep lobe wraps around the back angle of the mandible. The most common incision is represented by the continuous line and possible extensions are indicated by the dotted lines.

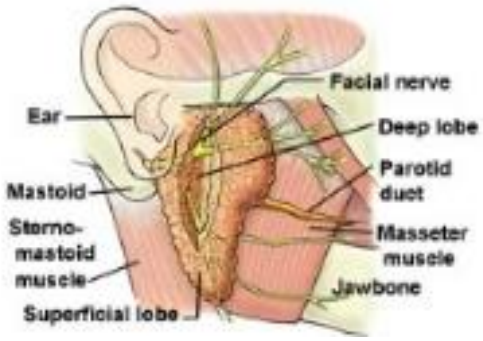


Figure 2 - The parotid lies on the masseter muscle. It lies in front of the sternomastoid muscle. The facial nerve divides the parotid gland into superficial and deep lobes.

Submandibular Gland

- Beneath floor of the mouth, inferior to mylohyoid muscles and superior to digastric muscle.
- Marginal mandibular branch of the facial nerve travels in the fascia on the lateral surface of this gland.
- Parasympathetic secretory afferents to the submandibular gland arise from the superior salivatory nucleus, and leave the brainstem in the facial nerve. They exit the facial nerve at the geniculate ganglion and travel via the chorda tympani to the lingual nerve. Fibers synapse in the submandibular ganglion, and post-synaptic fibers then enter the gland.
- The lingual and hypoglossal nerves lie deep to this gland.
- Wharton's duct enters the floor of the mouth near the lingual frenula.

Sublingual Glands - located below the mucous membrane of the floor of the mouth, adjacent to mandible and mylohyoid muscle. Ten to twelve small caliber ducts drain the gland, some emptying into the submandibular duct and others draining directly into the floor of the mouth.
Minor Salivary Glands - small collections of salivary gland tissues are scattered throughout the oral mucosa, and can also be seen in the pharynx, supraglottis, nose and sinuses. Minor glands are muco-serous only Ebner gland (posterior lingual gland) like parotid, is pure serous.

TRAUMA:

A: Laceration: Parenchymal damage only – usually heals by itself.
Injury to Stenson's duct – should be repaired over a small catheter.
Injury to facial nerve – should be repaired within 72 hours.

- *Injury to Stenson's duct may cause chronic salivary fistula.*
- *Acute obstruction or ligation of parotid duct causes complete atrophy of the gland*.

B: Any foreign body should be removed.

SIALOADINITIS:

- In viral infection Mumps is the most common infection. Its treatment is symptomatic.
- Low grade bacterial infection of salivary gland is usually self limiting.
- Stenson's duct obstruction by Stone/stricture also causes intermittent painful swelling → Sialogram should be done → obstruction should be relieved by →

1. Transorally (if the stone is near the duct end).
2. By external incision (If the stone is deep).

3. Parotidectomy (If multiple stone / stricture is present).

ACUTE SUPPURATIVE PAROTITIS:

- Characterized by presence of pus and seen in debilitated/ dehydrated/ or in patients with poor oral hygiene.
- Commonest causing organism is Staph. aureus.
- Initial treatment is proper hydration/ antibiotics/ improving oral hygiene.
- If abscess develops then it is drained by giving a J shaped incision (see 1st diagram).
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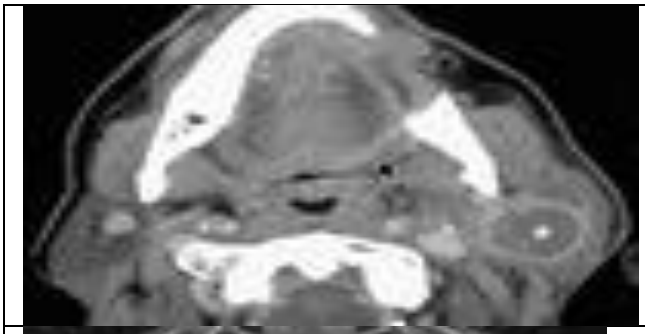
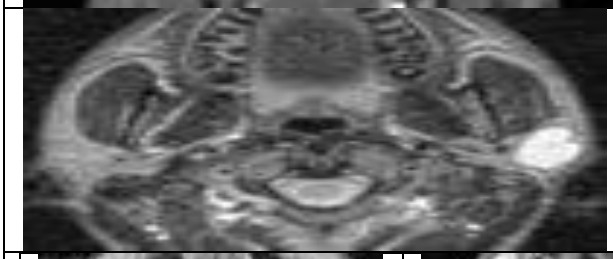
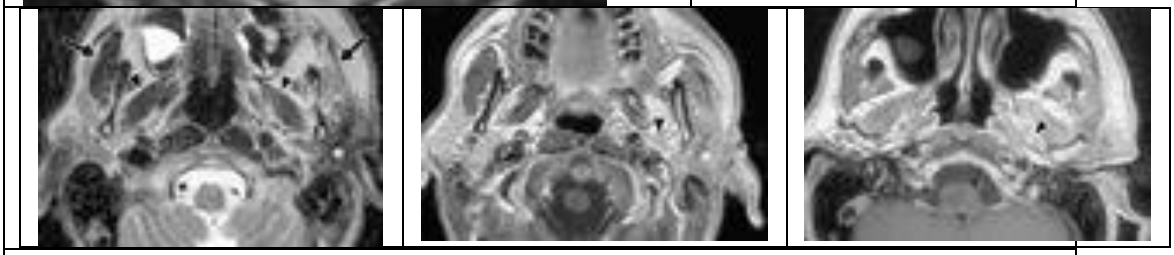


Parotid gland, Fig. 1
Axial contrast-enhanced CT images of parotid glands. Increased attenuation of left parotid gland due to sialadenitis, with intraglandular abcedation (asterisk). Note associated cellulitis of parapharyngeal space (arrowhead).



Parotid gland, Fig. 2
Axial T2-weighted spin-echo image of parotid glands. Lobulated soft tissue mass with high signal intensity, in the superficial part of the left gland. Pleomorphic adenoma.



Parotid gland, Fig. 3: Axial T2-weighted (a) and gadolinium-enhanced T1-weighted spin-echo images (b 1 cm caudal to c) of a patient with a history of left facial nerve paralysis for several months. Ill-defined soft tissue mass in the left parotid gland (asterisk); by perineural tumour spread along the auriculotemporal nerve (arrowhead, b-c), the neoplasm reaches the main stem of the mandibular nerve, causing denervation muscle atrophy of the masticator muscles (compare masseter muscles (arrows) and lateral pterygoid muscles (arrowheads, a).

SALIVARY GLAND TUMORS

- Tumors of the salivary glands are grouped into epithelial, nonepithelial, and metastatic categories. Benign epithelial tumors include pleomorphic adenoma (80%), Warthin tumor, monomorphic adenoma, intraductal papilloma, oncocytoma etc.
- Benign nonepithelial tumors (mesenchymal origin) include lipoma, hemangioma, lymphangioma (cystic hygroma), and neural sheath tumors.
- Pleomorphic adenomas make up 70% of parotid gland tumors and 50% of submandibular gland tumors.
- Of minor SGTs, 50% are malignant.

- *Mucoepidermoid cancer is the most common parotid malignancy.*
- Overall, *adenoid cystic carcinoma is the most common malignant tumor of all minor salivary glands* and, specifically, the submandibular gland

BENIGN EPITHELIAL TUMORS

1. Pleomorphic adenoma

- Commonly located at the tail of the parotid.
- Lesions arising from the deep lobe develop primarily within the parapharyngeal space and present late with symptoms related to pharyngeal compression
- It consists of epithelial and connective tissue. It is round, smooth, and freely mobile.
- The term pleomorphic adenoma describes its multiples histological components, including myxoid, mucoid, chondroid, and other element.
- Malignant mixed tumour has a tendency for perineural and perivascular invasion and significant cellular atypia
- It has a thin, delicate capsule with occasional *projections into the surrounding parotid tissue*, so obtaining clean margins is mandatory to minimize recurrence.
- If the parotid is the gland involved, *superficial parotidectomy* with standard facial nerve dissection and preservation is the procedure of choice.

2. Warthin tumor (ie, papillary cystadenoma lymphomatosum, cystic papillary adenoma, adenolymphoma)

- It is the second most common benign tumour of the parotid gland.
- In gross appearance, it is a smooth, soft parotid mass.
- It is well encapsulated and contains multiple cysts.
- Histologically, it has a heavy lymphoid stroma and aciniform epithelial cells lining the cystic areas with papillary projections.
- Malignant transformation has not been observed. The recurrence rate is 5%.
- The Warthin tumor tends to be bilateral (10% of cases)

3. Lymphoepithelial hyperplasia (Mikulicz disease)

- Manifest as a diffuse enlargement of the parotid gland, or it may manifest as a discrete mass.
- Histologically, the lesion is composed of a diffused, well-organized lymphoid tissue and lymphocytic interstitial infiltrate.
- More frequent in females, with peak incidence in the fourth and fifth decades.
- Growth of this tumor is slowly progressive, and it gives rise to pain around the ear or the retromandibular area.

4. Intraductal papilloma

Intraductal papilloma is a small, smooth lesion that is found in the submucosal layer. Microscopically, it consists of a cystically dilated duct partially lined with a cuboidal epithelium with complex anatomizing papillary fronds filling the cystic area.

5. Oxyphil adenoma (oncocytoma)

Oncocytomas of the salivary glands are very uncommon.

Such neoplasms occur in women, after fifth decade (female-to-male ratio of 2:1), and the superficial lobe of the parotid is commonly involved.

BENIGN NONEPITHELIAL TUMORS

Hemangiomas

Two forms, capillary and cavernous, develop in the major salivary glands. The capillary type is the most prevalent tumor in the first year of life. Capillary hemangiomas are rapidly growing, lack a capsule and are formed by purple, spongy, lobular masses that infiltrate salivary gland tissue. Observation is recommended in children.

Cavernous hemangiomas, which present in an older age group, rarely show spontaneous regression. Recurrent ulceration or bleeding may require conservative surgical resection.

Lymphangioma (cystic hygroma)

They manifest as painless masses that may involve parotid, submandibular, or both. Diagnosis is made based on clinical findings. Surgical excision with preservation of the vital structures is the treatment of choice.

Lipoma

These tumors manifest as soft, mobile, painful masses and peak in the fifth and sixth decades, with a male-to-female ratio of 10:1. They are slow-growing tumors with an average diameter of 3 cm. Treatment is surgical excision.

Metastatic disease of the parotid gland

Melanoma (46%), squamous cell carcinoma (37%), and a variety of tumors (17%) are included in this category.

MALIGNANT TUMOURS:

Mucoepidermoid carcinoma, Adenoid cystic carcinoma, Adenocarcinoma, Malignant mixed tumour, Acinic cell carcinoma, epidermoid carcinoma.

Acinic cell carcinoma:

It is a rare, low grade malignancy commonly seen in parotid. Infrequently invade the facial nerve and are late to metastasize (to lung).

Mucoepidermoid carcinoma:

Most common Major salivary gland tumour

It can be of low grade or high grade type. High grade version is locally aggressive and prone for invasion of nerves and vessels and to early metastasis (to regional nodes).

Treatment of high grade type is generous primary excision with regional node dissection followed by radiotherapy.

Adenocarcinoma:

It is more common in minor salivary glands than parotid. It again has a low grade and high grade type and high grade has a very poor prognosis.

Adenoid cystic carcinoma:

It makes up one fourth of malignant salivary gland tumours. Lung is most common metastatic site but it is known for its prolonged natural history (eg. Pt. may live for 10-15 years even after lung metastasis). When visceral or bone metastasis occurs prognosis is poor. Adenoid cystic carcinoma invades nerve tissue. Treatment is wide surgical excision with radiation therapy.

Clinical:

- SGTs manifest as a painless mass on the face (parotid), the angle of the jaw (parotid tail, submandibular), neck (submandibular), or a swelling at the floor of mouth (sublingual).
- New onset of pain, rapid growth of the mass, facial nerve weakness, paresthesias, and hoarseness of the voice are indicators of possible underlying malignancy.
- Trismus usually represents invasion to the masseter or pterygoid muscles. Skin involvement and fixation to the mastoid tip are also signs of malignancy.

Etiology: An associated long-standing history of smoking and a strong family history may be risk factors. SGTs are indolent, painless, and well-circumscribed tumors.

TREATMENT:

Medical therapy: Inflammatory, infectious masses (eg, reactive, fungal), and lymphoma should be treated medically.

Salivary gland excision is also sometimes done for symptomatic, recurrent chronic gland infection, refractory to conservative treatments.

Surgical therapy:

Standard in the management of SGTs is surgical therapy.

Treatment of the benign neoplasm is complete surgical excision of the affected gland -Superficial parotidectomy with nerve preservation. Tumor spillage of a pleomorphic adenoma is undesirable because it can lead to tumor recurrence and should be avoided.

Excision of the tumor with clear margins is the aim for malignant tumours. No adjuvant chemotherapy is required.

GENERAL SURGERY

TETANUS

- It was first documented by Hippocrates, and records dating back to the 5th century. Etiology of the disease was discovered in 1884 by Carle and Rattone.
- Tetanus is an illness characterized by an acute onset of ***hypertonia, painful muscular contractions (usually of the muscles of the jaw and neck), and generalized muscle spasms without other apparent medical causes.***
  - *Clostridium tetani*, an obligate anaerobic gram-positive bacillus, causes tetanus.
  - This bacterium is nonencapsulated and forms spores, which are resistant to heat, desiccation, and disinfectants. The spores are ubiquitous and are found in soil, house dust, animal intestines, and human feces.
  - Spores that gain entry can persist in normal tissue for months to years. Under anaerobic conditions, these spores geminate and elaborate tetanospasmin and tetanolysin. Tetanospasmin that is released by the maturing bacilli is distributed via the lymphatic and vascular circulations **to the end plates of all nerves.**
  - Tetanospasmin then enters the nervous system peripherally at the myoneural junction and is transported centripetally into neurons of the CNS.
  - These neurons become incapable of neurotransmitter release.
  - The neurons, which release gamma-aminobutyric acid (GABA) and glycine, the major inhibitory neurotransmitters, are particularly sensitive to tetanospasmin, leading to failure of inhibition of motor reflex responses to sensory stimulation.
  - This results in generalized contractions of the agonist and antagonist musculature characteristic of a tetanic spasm.
  - *The shortest peripheral nerves are the first to deliver the toxin to the CNS, which leads to the early symptoms of facial distortion and back and neck stiffness.*
  - Once the toxin becomes fixed to neurons, it cannot be neutralized with antitoxin. Recovery requires sprouting of new nerve terminals and new synapses.

History:

- The median incubation period is 7 days, and, for most cases incubation ranges from 4-14 days. Patients with clinical manifestations occurring within 1 week of an injury have more severe clinical courses.
- Patients with generalized tetanus present with trismus in 75% of cases.
  - Other presenting complaints include stiffness, neck rigidity, dysphagia, restlessness, and reflex spasms.
  - Subsequently, muscle rigidity becomes the major manifestation.
  - Muscle rigidity spreads from the jaw and facial muscles over the next 24-48 hours to the extensor muscles of the limbs.
  - Reflex spasms can be triggered by minimal external stimuli such as noise, light, or touch. The spasms last seconds to minutes; become more intense; increase in frequency with disease progression; and can cause apnea, fractures, dislocations, and rhabdomyolysis.
  - Laryngeal spasms can occur at any time and can result in asphyxia.
- Sustained contraction of facial musculature produces a risus sardonicus.

Physical:

- Autonomic dysfunction manifests as extremes in blood pressure, dysrhythmias, and cardiac arrest.
- Neonatal tetanus presents with an inability to suck 3-10 days after birth. Presenting symptoms include irritability, excessive crying, grimaces, intense rigidity, and opisthotonus.
- Tetanic seizures may occur and portend a poor prognosis.
  - Seizures frequently occur in the muscle groups causing opisthotonos, flexion and abduction of the arms, clenching of the fists on the thorax, and extension of the lower extremities.

- Cephalic tetanus usually is secondary to chronic otitis media or head trauma.
    - Cephalic tetanus is characterized by variable cranial nerve (CN) palsies; CN VII most frequently is involved.
- Ophthalmoplegic tetanus is a variant that develops after penetrating eye injuries and results in CN III palsies and ptosis.
- The diagnosis is clinically based on the presence of trismus, dysphagia, generalized muscular rigidity, and/or spasm.

Lab Studies:

- No laboratory tests specific for the diagnosis of tetanus exist.
- Laboratory studies may demonstrate a moderate peripheral leukocytosis.

Other Tests:

- An assay for antitoxin levels is not readily available. However, a level of 0.01 IU/mL or greater in serum generally is considered protective, making the diagnosis of tetanus less likely.
- Cerebral spinal fluid (CSF) studies usually are within normal limits.

TREATMENT

Emergency Department Care: Treatment of tetanus is directed toward the treatment of muscle spasm, prevention of respiratory and metabolic complications, neutralization of circulating toxin to prevent the continued spread, and elimination of the source.

- Admit patients to the ICU. Due to risk of reflex spasms, maintain a dark and quiet environment for the patient. Avoid unnecessary procedures and manipulations.
    - Consider prophylactic intubation in all patients with moderate-to-severe clinical manifestations.
    - Perform tracheostomy in patients requiring intubation for > 10 days.
- Surgical therapy includes debridement of wounds to remove organisms and to create an aerobic environment.
    - The current recommendation is to excise at least 2 cm of normal viable-appearing tissue around the wound margins. Incise and drain abscesses.
- The maintenance of nutrition is extremely important and should be carried out in seriously ill patients via nasoduodenal tubes, gastrostomy tube feedings, or parenteral hyperalimentation.

MEDICATION

Drugs used to treat muscle spasm, rigidity, and tetanic seizures include sedative-hypnotic agents, general anesthetics, centrally acting muscle relaxants, and neuromuscular blocking agents. Antibiotics are used to prevent multiplication of *C tetani,* thus halting production and release of toxins.

Medical Care: Passive immunization with human tetanus immune globulin (TIG) shortens the course and may lessen its severity. A dose of 500 U appears effective.

- Supportive therapy include ventilatory support and pharmacologic agents that treat reflex muscle spasms, rigidity, and tetanic seizures.
- Benzodiazepines have emerged as the mainstay of symptomatic therapy for tetanus. To prevent spasms that last longer than 5-10 seconds, administer diazepam intravenously, typically 10-40 mg every 1-8 hours. Vecuronium (by continuous infusion) or pancuronium (by intermittent injection) are adequate alternatives.
- Penicillin G, which has been used widely for years, has been the drug of choice. Metronidazole (eg, 0.5 g q6h) has comparable or better antimicrobial activity.
- Other drugs used are sedative hypnotics, narcotics, inhalational anesthetics, neuromuscular blocking agents, and centrally acting muscle relaxants (eg, intrathecal baclofen).

Complications:

- Prior to 1954, asphyxia from tetanic spasms was the usual cause of death. However, with the advent of neuromuscular blockers, mechanical ventilation, and pharmacologic control of spasms, sudden cardiac death has become the leading cause of death.

- Sudden cardiac death has been attributed to excessive catecholamine productions, direct action of tetanospasmin, or tetanolysin on the myocardium.
- Further complications include the following:
    - Long bone fractures
    - Glenohumeral joint and temporomandibular joint dislocations
    - Hypoxic injury, aspiration pneumonia, and pulmonary emboli
    - Adverse effects of autonomic instability, including hypertension and cardiac dysrhythmias
    - Paralytic ileus, pressure sores, and urinary retention
    - Malnutrition and stress ulcers
    - Coma, nerve palsies, neuropathies, psychological aftereffects, and flexion contractures

Prognosis:

- The prognosis is dependent on incubation period, time from spore inoculation to first symptom, and time from first symptom to first tetanic spasm.
- In general, shorter intervals indicate more severe tetanus and a poorer prognosis.
- Patients usually survive tetanus and return to their predisease state of health.
- Recovery is slow and usually occurs over 2-4 months.
- Some patients remain hypotonic.
- Clinical tetanus does not produce a state of immunity; therefore, patients who survive the disease require active immunization with tetanus toxoid to prevent a recurrence.

Gas Gangrene

- Gas gangrene is caused by exotoxin-producing clostridial species (large, gram-positive, spore-forming bacilli).
- These anaerobic organisms normally are found in soil and the gastrointestinal tract. *Clostridium perfringens* causes 80-95% of cases of gas gangrene.
- Spontaneous gas gangrene is caused by hematogenous spread (in immunocompromised or with diabetes). *Clostridium septicum* is the most common causative organism of spontaneous gas gangrene.
- Exotoxin, not bacterial proliferation, is responsible for rapid spread of infection.
- Exotoxin causes muscle destruction and creates an anaerobic environment conducive to further bacilli growth.
- Products of tissue breakdown (eg, creatine phosphokinase, myoglobin, potassium) cause secondary toxicity.
- Mortality from traumatic gas gangrene is greater than 25%.
- Mortality from nontraumatic gas gangrene caused by *C septicum* ranges from 67-100%.

Pathophysiology: An anaerobic, gram-positive, spore-forming bacillus of the genus *Clostridium* causes gas gangrene.

- *C perfringens* is the most common cause of gas gangrene.
- Other common clostridial pathogens causing gas gangrene are *Clostridium bifermentans, Clostridium septicum, Clostridium sporogenes, Clostridium novyi, Clostridium fallax, Clostridium histolyticum,* and *Clostridium tertium.*
- These organisms are true saprophytes and are ubiquitous in soil and dust.
- Clostridia are obligate anaerobes, but some species are relatively aerotolerant. Bacterial multiplication and the production of soluble proteins called exotoxins require a low oxygen tension.
- *C perfringens* produces at least 20 exotoxins.
- Disrupted or necrotic tissue provides the necessary enzymes and a low oxidation/ reduction potential, allowing germination of spores.
- The typical incubation period for gas gangrene frequently is short (ie, <24 h), but extreme incubation periods of 1 hour to 6 weeks have been reported.

- Systemically, exotoxins may cause severe hemolysis. Hemoglobin levels may drop to very low levels and, when occurring with hypotension, may cause acute tubular necrosis and renal failure.
- Unconcentrated filtrate from *C perfringens*, purified alpha-toxin, and purified phi-toxins cause hypotension, bradycardia, and decreased cardiac output when injected into laboratory animals.

History:

- Incubation period usually is fewer than 3 days, with rapid onset of symptoms. Infection can advance as much as 1in/h.
- Pain commonly is out of proportion to physical findings.
- Progression to toxemia and shock can be rapid.

Physical:

- Local swelling and a serosanguineous exudate appear soon after the onset of pain.
    - The skin characteristically turns to a bronze color, then progresses to a blue-black color with skin blebs and hemorrhagic bullae.
    - Within hours, the entire region may become markedly edematous.
    - The wound may be nonodorous or may have a sweet mousy odor.
    - Crepitus follows gas production; at times, due to brawny edema, crepitus may not be detected with palpation.
    - Pain and tenderness to palpation disproportionate to wound appearance are common findings.
- Tachycardia disproportionate to body temperature is common.
- Late signs include hypotension, renal failure, and a paradoxical heightening of mental acuity.
- In summary, the typical signs and symptoms are severe pain and tenderness, local swelling to massive edema, skin discoloration with hemorrhagic blebs and bullae, nonodorous or sweet odor, crepitus, fever, relative tachycardia, and altered mental status.

Lab Studies:

- Gram stain of bullae fluid or muscle tissue: Pleomorphic, gram-positive bacilli with a paucity of leukocytes are considered diagnostic.
- Complete blood count: hemolysis and anemia secondary to release of toxins.
- Liver function tests: Hyperbilirubinemia and liver dysfunction.
- Electrolytes: Hyperkalemia can result from cell breakdown.
- Renal panel: Kidney dysfunction.
- Arterial blood gas: Gas gangrene can cause metabolic acidosis.
- Coagulation panel: Coagulopathy and thrombocytopenia can result.
- Myoglobin: Myoglobinemia and myoglobinuria dur to cellular breakdown.

Imaging Studies:

- Plain radiographs may reveal soft tissue gas within the fascial planes.
- Computed tomography demonstrates the extent of tissue involvement.

TREATMENT

Prehospital Care: Oxygenation/ Intravenous (IV) fluids/ Rapid stabilization of patient, because the disease may progress rapidly

Emergency Department Care: Resuscitation, supplemental oxygen, and aggressive volume expansion may be indicated.

- Use vasoconstrictors only if absolutely necessary; they can decrease perfusion to already ischemic tissue.
- Administer antibiotics.
- Tetanus toxoid and immune globulin may be administered if indicated.
- Surgical debridement is the definitive treatment.

Surgical Care:

- Fasciotomy for compartment syndrome may be necessary immediately.
- Daily debridement as needed to remove all necrotic tissue.
- Amputation of the extremity may be necessary and life-saving.
- Abdominal involvement requires excision of the body wall musculature.
- Uterine gas gangrene following septic abortion usually necessitates hysterectomy.
- ***Aggressive surgical debridement and intensive medical therapy are the mainstays of treatment of gas gangrene;*** however, HBO therapy has become an important adjunct therapy, especially in patients with truncal involvement.

MEDICATION

- Antibiotics may not penetrate the ischemic muscle but are important adjuncts to surgery.

***Antibiotics*:** Although penicillin G is effective against clostridial species, mixed infections are common, thus treatment include aminoglycosides, penicillinase-resistant penicillins, or vancomycin. If a patient is allergic to penicillin, alternative choices are clindamycin, third-generation cephalosporin, metronidazole, & chloramphenicol.

***Medicinal gas*:** Oxygen is used at a pressure greater than 1 atm in an attempt to minimize tissue necrosis caused by clostridial species.

- Typical therapy is 100% oxygen at 3 atm of pressure for 90 min with 2-3 dives in first 24 h, followed by 2-3 dives/d for a total of 7-10 dives

***Toxoids* --** Used to induce active immunity.

- **Adult Dose:** Primary immunization: 0.5 mL IM; administer 2 injections 4-8 wk apart; third dose 6-12 mo after second injection
- Booster dose: 0.5 mL q10y
- **Pediatric Dose:** Administer as in adults

***Immunoglobulins* --** Used to induce passive immunity.

- **Adult Dose:** Prophylaxis: 250-500 U IM in opposite extremity to tetanus toxoid lesion Clinical tetanus: 3,000-10,000 U IM
- **Pediatric Dose:** Prophylaxis: 250 U IM in opposite extremity to tetanus toxoid Clinical tetanus: 3,000-10,000 U IM

SHOCK

Hypovolemic Shock

- Hypovolemic shock refers to a medical or surgical condition in which rapid fluid loss results in multiple organ failure due to inadequate perfusion.
- Most often, hypovolemic shock is secondary to rapid blood loss (hemorrhagic).
- Hypovolemic shock can result from significant fluid (other than blood) loss. E.g. refractory gastroenteritis and extensive burns.

Pathophysiology:

The human body responds to acute hemorrhage by activating 4 major physiologic systems: the hematologic, cardiovascular, renal, and neuroendocrine systems.

- The hematologic system responds to an acute severe blood loss by activating the coagulation cascade and contracting the bleeding vessels (by local thromboxane A_2 release). In addition, platelets are activated and form an immature clot on the bleeding source.
- The cardiovascular system initially responds to hypovolemic shock by increasing the heart rate, increasing myocardial contractility, and constricting peripheral blood vessels. This response occurs secondary to an increased release of norepinephrine and decreased baseline vagal.
- The renal system responds to hemorrhagic shock by stimulating an increase in renin secretion from the juxtaglomerular apparatus. Renin converts angiotensinogen to angiotensin I, which subsequently is converted to angiotensin II by the lungs and liver. Angiotensin II has 2 main effects, vasoconstriction of arteriolar smooth muscle, and stimulation of aldosterone secretion by

the adrenal cortex. Aldosterone is responsible for active sodium reabsorption and subsequent water conservation.

- The neuroendocrine system responds to hemorrhagic shock by causing an increase in circulating antidiuretic hormone (ADH).

History:

- Symptoms, like weakness, lightheadedness, and confusion, should be assessed.
- Chest, abdominal, or back pain may indicate a vascular disorder.
- The classic sign of a thoracic aneurysm is a tearing pain radiating to the back. Abdominal aortic aneurysms usually result in abdominal or back pain.
- In patients with GI bleeding, inquire about hematemesis, melena, drinking history, excessive NSAID use, and coagulopathies (iatrogenic or otherwise).
- If a gynecologic cause is being considered, gather information about: last menstrual period, risk factors for ectopic pregnancy, vaginal bleeding, vaginal passage of products of conception, and pain.

Physical: The physical examination should always begin with an assessment of the airway, breathing, and circulation.

Once these have been evaluated and stabilized, the circulatory system should be evaluated for signs and symptoms of shock.

Do not rely on systolic BP as the main indicator of shock. Compensatory mechanisms prevent a significant decrease in systolic BP until the patient has lost 30% of the blood volume.

More attention should be paid to the pulse, respiratory rate, and skin perfusion.

- Class I hemorrhage (loss of 0-15%)
    - In the absence of complications, only minimal tachycardia is seen.
    - Usually, no changes in BP, pulse pressure, or respiratory rate occur.
    - A delay in capillary refill of longer than 3 seconds corresponds to a volume loss of approximately 10%.
- Class II hemorrhage (loss of 15-30%)
    - Clinical symptoms include tachycardia (rate >100 beats per minute), tachypnea, decrease in pulse pressure, cool clammy skin, delayed capillary refill, and slight anxiety.
    - The decrease in pulse pressure is a result of increased catecholamine levels, which causes an increase in peripheral vascular resistance and a subsequent increase in the diastolic BP.
- Class III hemorrhage (loss of 30-40%)
    - By this point, patients usually have marked tachypnea and tachycardia, decreased systolic BP, oliguria, and significant changes in mental status, such as confusion or agitation.
    - In patients without other injuries or fluid losses, 30-40% is the smallest amount of blood loss that consistently causes a decrease in systolic BP.
    - Most of these patients require blood transfusions, but the decision to administer blood should be based on the initial response to fluids.
- Class IV hemorrhage (loss of >40%)
    - Symptoms include the following: marked tachycardia, decreased systolic BP, narrowed pulse pressure (or immeasurable diastolic pressure), markedly decreased (or no) urinary output, depressed mental status (or loss of consciousness), and cold and pale skin.
    - This amount of hemorrhage is immediately life threatening.

Lab Studies:

- Initial laboratory studies should include analysis of the CBC, electrolyte levels (eg, Na, K, Cl, HCO_3, BUN, creatinine, glucose levels), prothrombin time, activated partial thromboplastin time, ABGs, and urinalysis (in patients with trauma). Blood should be typed and cross-matched.

TREATMENT

Prehospital Care:

- Most prehospital interventions involve immobilizing the patient (if trauma is involved), securing an adequate airway, ensuring ventilation, and maximizing circulation. Appropriate treatment usually can be initiated without delaying transport. Some procedures, such as starting intravenous (IV) lines or splinting of extremities, can be performed while a patient is being extricated.

Emergency Department Care: Three goals exist in the emergency department treatment of the patient with hypovolemic shock as follows:

(1) Maximize oxygen delivery - completed by ensuring adequacy of ventilation, increasing oxygen saturation of the blood, and restoring blood flow,

(2) Control further blood loss, and

(3) Fluid resuscitation; Should be rapid and appropriate.

Whether crystalloids or colloids are best for resuscitation continues to be a matter for discussion and research. Many fluids have been studied for use in resuscitation; these include isotonic sodium chloride solution, lactated Ringer solution, hypertonic saline, albumin, purified protein fraction, fresh frozen plasma, hetastarch, pentastarch, and dextran 70.

- current recommendations still advocate the use of normal saline or lactated Ringer solution.

Another area of interest regarding resuscitation is whether the goal should be to restore normal circulating volume and BP prior to definitive control of bleeding.

- Current recommendations are for aggressive fluid resuscitation with lactated Ringer solution or normal saline in all patients with signs and symptoms of shock, regardless of underlying cause.

A common error in the management of hypovolemic shock is failure to recognize it early.

This error leads to delay in diagnosing the cause and in resuscitating the patient.

- This error often is caused by a reliance on BP or initial hematocrit level, rather than signs of decreased peripheral perfusion, to make the diagnosis.
- Injuries in patients with trauma can be missed. This error can be avoided by a full physical examination, continuously and closely monitoring the patient's status.
- Elderly individuals have less tolerance for hypovolemia.
- In patients who require extensive volume resuscitation, care should be taken to prevent hypothermia, because this can contribute to arrhythmia or coagulopathy.
- Patients taking beta-blockers or calcium-channel blockers and those with pacemakers may not have a tachycardic response to hypovolemia.
- Coagulopathies can occur in patients receiving large amounts of volume resuscitation.

Cardiogenic Shock

- Cardiogenic shock is a physiologic state in which inadequate tissue perfusion results from cardiac dysfunction, most commonly following acute myocardial infarction (MI).
- The clinical definition of cardiogenic shock is decreased cardiac output and evidence of tissue hypoxia in the presence of adequate intravascular volume. Hemodynamic criteria for cardiogenic shock are sustained hypotension (systolic blood pressure <90 mm Hg for at least 30 min) and a reduced cardiac index (<2.2 L/min/m^2) in the presence of elevated pulmonary capillary occlusion pressure (>15 mm Hg).
- The diagnosis of cardiogenic shock can sometimes be made at the bedside by observing hypotension and clinical signs of poor tissue perfusion, which include oliguria, cyanosis, cool extremities, and altered mentation. These signs usually persist after attempts have been made to correct hypovolemia, arrhythmia, hypoxia, and acidosis.

Pathophysiology:

Myocardial pathology

- Patients who develop cardiogenic shock from acute MI consistently have evidence of progressive myocardial necrosis with infarct extension. Decreased coronary perfusion pressure and increased myocardial oxygen demand play a role in the vicious cycle that leads to cardiogenic shock.

Cellular pathology

- Tissue hypoperfusion, with consequent cellular hypoxia, causes anaerobic glycolysis, the accumulation of lactic acid, and intracellular acidosis. Also, myocyte membrane transport pumps fail, which decreases transmembrane potential and causes intracellular accumulation of sodium and calcium, resulting in myocyte swelling. If ischemia is severe and prolonged, myocardial cellular injury becomes irreversible and leads to myonecrosis, which includes mitochondrial swelling, the accumulation of denatured proteins and chromatin, and lysosomal breakdown.

Reversible myocardial dysfunction

- This potentially reversible dysfunction is often described as myocardial stunning or hibernating myocardium.
- By definition, myocardial dysfunction from stunning eventually resolves completely. The mechanism of myocardial stunning involves a combination of oxidative stress, abnormalities of calcium homeostasis, and circulating myocardial depressant substances.

Cardiovascular mechanics of cardiogenic shock

- The main mechanical defect in cardiogenic shock is that the left ventricular end-systolic pressure-volume curve shifts to the right because of a marked reduction in contractility. As a result, at a similar or even lower systolic pressure, the ventricle is able to eject less blood volume per beat. The attempt to enhance cardiac output by this mechanism comes at the cost of having a higher left ventricular diastolic filling pressure, which ultimately increases myocardial oxygen demand and causes pulmonary edema.

Systemic effects

- Systemic perfusion is compromised by decreased cardiac output, with tissue hypoperfusion intensifying anaerobic metabolism and instigating the formation of lactic acid, which further deteriorates the systolic performance of the

Shock state

- Shock state, irrespective of the etiology, is described as a syndrome initiated by acute systemic hypoperfusion that leads to tissue hypoxia and vital organ dysfunction. All forms of shock are characterized by inadequate perfusion to meet the metabolic demands of the tissues. A maldistribution of blood flow to end organs begets cellular hypoxia and end organ damage, the well-described multisystem organ dysfunction syndrome. The organs of vital importance are the brain, heart, and kidneys.

History:

- Patients demonstrate clinical evidence of hypoperfusion (low cardiac output), which is manifested by sinus tachycardia, low urine output, and cool extremities. Systemic hypotension, defined as systolic blood pressure below 90 mm Hg or a decrease in mean blood pressure by 30 mm Hg, ultimately develops and further propagates tissue hypoperfusion.
- Patients also may report associated autonomic symptoms, including nausea, vomiting, and sweating.
- Other associated symptoms are diaphoresis, exertional dyspnea, or dyspnea at rest. Presyncope or syncope, palpitations, generalized anxiety, and depression are other features indicative of poor cardiac function.

Physical: Cardiogenic shock is diagnosed after documentation of myocardial dysfunction and exclusion of alternative causes of hypotension, such as hypovolemia, hemorrhage, sepsis, pulmonary embolism, pericardial tamponade, aortic dissection, or preexisting valvular disease. Shock is present if evidence of multisystem organ hypoperfusion is detected upon physical examination.

- Patients in shock usually appear ashen or cyanotic and have cool skin and mottled extremities.
- Peripheral pulses are rapid and faint and may be irregular if arrhythmias are present.
- Jugular venous distention and crackles in the lungs are usually (but not always) present. Peripheral edema also may be present.
- Heart sounds are usually distant, and both third and fourth heart sounds may be present.

- The pulse pressure may be low, and patients are usually tachycardic.
- Patients show signs of hypoperfusion, such as altered mental status and decreased urine output.
- A systolic murmur is generally heard in patients with acute mitral regurgitation or ventricular septal rupture.
- The associated parasternal thrill indicates the presence of a ventricular septal defect, whereas the murmur of mitral regurgitation may be limited to early systole.
- The systolic murmur, which becomes louder upon Valsalva and prompt standing, suggests hypertrophic obstructive cardiomyopathy (idiopathic hypertropic subaortic stenosis).

Approach to the initial clinical evaluation of a patient in shock

Shock is identified in most patients based on findings of hypotension and inadequate organ perfusion, which may be caused by either low cardiac output or low systemic vascular resistance (SVR).

Circulatory shock can be subdivided into 4 distinct classes

Hypovolemic shock

- Hypovolemic shock results from loss of blood volume caused by gastrointestinal bleeding, extravasation of plasma, major surgery, trauma, and severe burns.

Obstructive shock

- Obstructive shock results from impedance of circulation by an intrinsic or extrinsic obstruction. Pulmonary embolism, dissecting aneurysm, and pericardial tamponade all result in obstructive shock.

Distributive shock

- Distributive shock is caused by conditions producing direct arteriovenous shunting and is characterized by decreased SVR or increased venous capacitance because of the vasomotor dysfunction. These patients have high cardiac output, hypotension, high pulse pressure, low diastolic pressure, and warm extremities with good capillary refill. Such findings upon physical examination strongly suggest a working diagnosis of septic shock.

Cardiogenic shock

- Cardiogenic shock characterized by primary myocardial dysfunction causes the heart to be unable to maintain adequate cardiac output. These patients demonstrate clinical signs of low cardiac output, with adequate intravascular volume. The patients have cool and clammy extremities, poor capillary refill, tachycardia, narrow pulse pressure, and low urine output.

Medical Care:

Initial management includes fluid resuscitation to correct hypovolemia and hypotension, unless pulmonary edema is present.

Central venous and arterial lines are often required.

Swan-Ganz catheterization and continuous percutaneous oximetry are needed. Correction of electrolyte and acid-base abnormalities, such as hypokalemia, hypomagnesemia, and acidosis, are essential.

Hemodynamic support

- Dopamine, norepinephrine, and epinephrine are vasoconstricting drugs that help maintain adequate blood pressure during life-threatening hypotension and help preserve perfusion pressure for optimizing flow in various organs.
- In patients with inadequate tissue perfusion and adequate intravascular volume, initiation of inotropic and/or vasopressor drug therapy may be necessary. Dopamine increases myocardial contractility and supports the blood pressure; however, it may increase myocardial oxygen demand. Dobutamine may be preferable if the systolic blood pressure is higher than 80 mm Hg and has the advantage of not affecting myocardial oxygen demand as much as dopamine.
- If the patient remains hypotensive despite moderate doses of dopamine, a direct vasoconstrictor (eg, norepinephrine) should be started at a dose of 0.5 mcg/kg/min and titrated to maintain an MAP of 60 mm Hg.

Vasopressor supportive therapy:

- Dopamine is a precursor of norepinephrine and epinephrine and has varying effects according to the doses infused.

- Norepinephrine is a potent alpha-adrenergic agonist with minimal beta-adrenergic agonist effects. Norepinephrine can increase blood pressure successfully in patients who remain hypotensive following dopamine.
- Epinephrine can increase the MAP by increasing the cardiac index and stroke volume, along with an increase in SVR and heart rate. Epinephrine may increase oxygen delivery and consumption and decreases the splanchnic blood flow. Administration of this agent is associated with an increase in systemic and regional lactate concentrations. The use of epinephrine is recommended only in patients who are unresponsive to traditional agents.

Inotropic supportive therapy

- Dobutamine (sympathomimetic agent) is a beta1-receptor agonist, although it has some beta2-receptor and minimal alpha-receptor activity.
- Phosphodiesterase inhibitors (PDIs), currently inamrinone (formerly amrinone) and milrinone, are the PDI inotropes that have proved valuable.

Thrombolytic therapy

- Although thrombolytic therapy (TT) reduces mortality rates in patients with acute MI, its benefits for patients with cardiogenic shock secondary to MI are disappointing.
- Patients who are unsuitable for invasive therapy should be treated with a thrombolytic agent in the absence of contraindications.

Intra-aortic balloon pump

- The use of the IABP reduces systolic left ventricular afterload and augments diastolic coronary perfusion pressure, thereby increasing cardiac output and improving coronary artery blood flow.
- The IABP is effective for the initial stabilization of patients with cardiogenic shock. However, an IABP is not definitive therapy.

Ventricular assist devices

Distributive Shock

- Shock may be defined as a state in which alterations in tissue perfusion result in end-organ dysfunction.
- Distributive shock is characterized by hypotension (systolic blood pressure <90 mm Hg) due to a severe reduction in systemic vascular resistance (SVR), with normal or elevated cardiac output in most instances.
- Septic shock is the most commonly encountered form of distributive shock.
- Other causes of distributive shock include systemic inflammatory response syndrome (SIRS) due to noninfectious inflammatory conditions; toxic shock syndrome (TSS); anaphylaxis; drug or toxin reactions, including insect bites, transfusion reaction, and heavy metal poisoning; addisonian crisis; hepatic insufficiency; and neurogenic shock due to brain or spinal cord injury.

Pathophysiology:

- Decreased tissue perfusion in distributive shock results primarily from arterial hypotension caused by a reduction in SVR.
- In addition, a reduction in effective circulating plasma volume often occurs due to a decrease in venous tone and subsequent pooling of blood in venous capacitance vessels, and loss of intravascular volume into the interstitium due to increased capillary permeability also occurs.
- Finally, primary myocardial dysfunction often is present as manifested by ventricular dilatation, decreased ejection fraction (despite normal stroke volume and cardiac output).
- Tumor necrosis factor-alpha (TNF-alpha), interleukin (IL)-1b, and IL-6 act synergistically with other cytokines and phospholipid-derived mediators to produce the complex alterations in vascular and myocardial function, which leads to maldistribution of blood flow.

History:

- Patients with shock frequently present with dyspnea or respiratory distress, mental status changes, and obtundation.

- Patients with septic shock or SIRS may have prior complaints suggesting infection or inflammation of the respiratory tract, urinary tract, or abdominal cavity.
- Streptococcal TSS is associated with recent soft tissue injury, surgery, pharyngitis, and nonsteroidal anti-inflammatory drug (NSAID) use.
- Staphylococcal TSS still is observed most commonly in women who are menstruating, but it also is associated with cutaneous infections, postpartum and cesarean section wound infections, and focal staphylococcal infections, such as abscess, empyema, pneumonia, and osteomyelitis.

Physical:

Cardinal features of distributive shock include the following:

- Hypotension - With systolic blood pressure less than 90 mm Hg or a reduction of 40 mm Hg from baseline
- Heart rate - Greater than 90 beats per minute
- Respiratory rate - Greater than 20 breaths per minute
- Extremities - Frequently are warm with bounding pulses and increased pulse pressure (systolic minus diastolic blood pressure)

Pneumonia
Urinary tract infection
Intraabdominal infection or acute abdomen
Anaphylaxis
Toxic shock syndrome
Adrenal insufficiency

A pulmonary artery (PA) catheter should be considered when potential benefit from information obtained outweighs potential adverse consequences.

PA catheter measurements may be useful in differentiating shock due to state of low cardiac output (hypovolemic, cardiogenic, extracardiac obstructive) from distributive shock in certain patients.

Pulmonary Artery Catheter Findings in Common Shock States

Diagnosis	**Pulmonary Capillary Wedge Pressure**	**Cardiac Output**
Cardiogenic shock*	Increased	Decreased
Extracardiac obstructive shock 1. Pericardial tamponade† 2. Pulmonary embolism	 Increased Normal or decreased	 Decreased Decreased
Hypovolemic shock	Decreased	Decreased
Distributive shock 1. Septic shock 2. Anaphylactic shock	Normal or decreased Normal or decreased	Increased or normal Increased or normal

*In cardiogenic shock due to a mechanical defect such as mitral regurgitation, forward cardiac output is reduced though the measured cardiac output may be unreliable. Large V waves commonly are observed in the pulmonary capillary wedge tracing in mitral regurgitation.
†The hallmark finding is equalization of right atrial mean, right ventricular end-diastolic, PA end-diastolic, and pulmonary capillary wedge pressure.

TREATMENT

Medical Care: all patients with shock should be admitted to an ICU.

- Vital signs and fluid intake and output should be measured and charted on an hourly basis. Adequate intravenous access should be obtained.
- A central venous access device should be considered if vasoactive drug support is required.
- Placement of PA and arterial catheters should be considered.
- All patients should be treated prophylactically against thromboembolic disease, gastric stress ulceration, and pressure ulcers of the skin.
- The 2 primary goals of treatment in patients with distributive shock are to reverse the initiating cause of shock (treat infection) and to stabilize the patient hemodynamically.
    - Oxygen should be administered immediately by mask.
    - In all patients with suspected sepsis, empiric antibiotic therapy should be initiated immediately.
- 0.4 mg/kg IV q12h for 48 h with first dose administered with or just before antibiotics.

Initial hemodynamic support should be in the form of fluid resuscitation. Crystalloid fluids, such as 0.9% NaCl or lactated Ringers solution, should be infused rapidly in 250- to 500-cc boluses, with frequent reassessment of blood pressure, extremities, skin turgor, and urine output to determine response to therapy.
If the blood pressure fails to improve after 2-3 L of rapid crystalloid infusion or after reaching the target pulmonary capillary wedge pressure, vasoactive drug therapy should be initiated with dopamine.
If an adequate hemodynamic response is not achieved with dopamine infusion rates of 15-20 mg/kg/min or if excessive tachycardia or tachyarrhythmias develop, norepinephrine (Levophed) or phenylephrine (Neo-Synephrine) may be added to or substituted for dopamine.
Dobutamine may be added to the therapeutic regimen when cardiac output is low, recognizing that this drug acts primarily as a positive inotropic agent and may further decrease SVR.
Vasoactive Drugs in Sepsis and Usual Hemodynamic Responses

Drug	Dose	Cardiac Output	Blood Pressure	Systemic Vascular Resistance
Dopamine*	2.5-20 mcg/kg/min	+	+	+
Norepinephrine†	0.05-2 mcg/kg/min	+	++	++
Epinephrine	0.05-2 mcg/kg/min	++	++	+
Phenylephrine	2-10 mcg/kg/min	-	++	++
Dobutamine‡	2.5-10 mcg/kg/min	+	+/-	-

*Dopamine is the usual drug of first choice. At doses >10 mcg/kg/min, effects are similar to norepinephrine. Tachycardia may limit use.
†Norepinephrine may be effective when dopamine is inadequate to increase blood pressure. Evaluate for hypovolemia or low cardiac output if norepinephrine fails to increase blood pressure adequately.
‡Dobutamine is useful when low blood pressure is due to decreased cardiac output. Dobutamine may further lower blood pressure due to peripheral vasodilatation.
Patients with distributive shock should be evaluated thoroughly to identify a potential nidus of infection. Surgical drainage or debridement should be performed promptly.

PLASTIC SURGERY

WOUND HEALING: Normal wound healing comprises a combination of regeneration and repair. Three mechanisms are involved:

- ***epithelialization,***
- ***wound contraction, and***
- ***extracellular matrix synthesis***.

During repair, a complex chain of events eventually leads to the formation of a scar. The process requires: phagocytosis, chemotaxis, mitogenesis, and the synthesis of collagen and extracellular matrix components. In certain circumstances, the cellular processes that contribute to repair become unregulated, leading to excessive scarring in the form of hypertrophic scars and keloids.

TYPES OF HEALING:

There are four general types of wound healing:

1. Primary,
2. Delayed primary,
3. Secondary,
4. Healing that occurs in partial-thickness wounds.

Primary Healing: when wound is closed within hours of its creation.

- The wound edges are reapproximated directly using sutures or by some other mechanical means.
- Collagen metabolism provides long-term strength to the wound when normal synthesis, deposition, and cross-linking of the collagen occur.
- Matrix metalloproteinase enzymes regulate collagen and extracellular matrix degradation and allow for remodeling of the wound, leaving a relatively narrow scar.
- Epithelialization provides coverage of the wound surface and acts as a barrier from bacterial invasion.

*Delayed Primary Healing: C*ontaminated wound is left open to prevent wound infection.

- The skin and subcutaneous tissues are left unopposed and closure is performed after the normal host defenses are allowed to debride the wound.
- After 3 to 4 days, local phagocytic cell recruitment into the wound has occurred and angiogenesis has begun.
- Inflammatory cells are present that destroy contaminating bacteria.
- The wound edges are approximated following a delay of several days.
- Collagen metabolism is undisturbed and tensile strength develops as if closure had been immediate.

Secondary Healing: an open full-thickness wound is allowed to close by both wound contraction and epithelialization.

- The wound decreases in size by contraction. (myofibroblast is thought to play a key role). The cells appear in the wound on approximately the 3rd day after wounding and increase in number to a maximal level between 10th and 21st day.
- They disappear as contraction is completed.

Healing of Partial-Thickness Wounds

- Partial-thickness wounds, which involve the epithelium and the superficial portion of the dermis, heal mainly by epithelialization.
- Epithelial cells within the dermal appendages, hair follicles, and sebaceous glands replicate to cover the exposed dermis.
- There is minimal collagen deposition and an absence of wound contraction.

OVERVIEW: The process of wound healing occurs as a sequential cascade of phagocytosis, chemotaxis, mitogenesis, collagen synthesis, and the synthesis of other matrix components.

Tissue Injury

- Tissue injury initiates the process of bleeding, coagulation, inflammation, cell replication, angiogenesis, epithelialization, and matrix synthesis.
- Tissue injury is characterized by microvascular injury and therefore extravasation of blood into the wound.
- Injured vessels constrict rapidly and the coagulation cascade is activated in order to limit the blood loss.
- Vasoactive amines and other mediators are released by inflammatory cells, which contribute to the leak of plasma and proteins into the wound and allow effector cells to enter.

Coagulation

- Coagulation leads to hemostasis. Platelets trapped in the clot are essential for hemostasis as well as for a normal inflammatory response. The alpha granules of the platelets contain growth factors, including platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-b), and platelet factor IV. These proteins initiate the wound-healing cascade by attracting and activating fibroblasts, endothelial cells, and macrophages. The platelets also contain dense bodies that store vasoactive amines, e.g. serotonin, that increase microvascular permeability.
- The end product of both the intrinsic and extrinsic coagulation pathways is fibrin.
- Fibrin is essential to early wound healing because it provides the matrix.

Early Inflammation

- The next phase of healing, inflammation, begins with the activation of complement and the initiation of the classical molecular cascade, which leads to infiltration of the wound with granulocytes within 24 to 48 hours of injury.
- the granulocytes begin to adhere to the endothelial cells in the adjacent blood vessels by a process called margination, and begin to actively move through the vessel wall, a process known as diapedesis.
- The major function of granulocytes is to remove bacteria and foreign debris from the wound, thereby helping to prevent infection.

Late Inflammation

- Macrophages are the most important cells present in the healing wound and appear to act as the key regulatory cells for repair.
- Circulating monocytes and tissue macrophages, when depleted, cause severe alterations in wound healing with poor debridement, delayed fibroblast proliferation, inadequate angiogenesis, and poor fibrosis.
- Once the circulating monocyte passes through the blood vessel wall and into the wound, it is considered a wound macrophage.
- Between 48 and 72 hours after wounding, macrophages represent the predominant cell type within the wound.
- The macrophage functions as a phagocytic cell as well as being the primary producer of growth factors responsible for both the production and proliferation of the extracellular matrix (ECM) by fibroblasts, proliferation of smooth muscle cells, and proliferation of endothelial cells resulting in angiogenesis.
- The lymphocyte is the last cell to enter the wound during the inflammatory phase (>72 hours after wounding).

Fibroblast Migration/Collagen Synthesis

- Successful healing requires the migration of mesenchymal cells into the wound. Stimulated by growth factors, fibroblasts migrate into the wound through the ECM.
- By 7 days, they are the predominant cell type in the wound.
- At 5 to 7 days after wounding, the fibroblasts begin synthesizing collagen, which increases in a linear fashion for 2 to 3 weeks.
- Collagens provide strength and integrity for all tissues.
    - Type I collagen is the major structural component of bones, skin, and tendons.

- Type II collagen is found predominantly in cartilage.
- Type III collagen is found in association with type I collagen in varying ratios depending on the type of tissue.
- Type IV collagen is found in the basement membrane.
- Type V collagen is found in the cornea.

Angiogenesis

- Angiogenesis is the process of forming new blood vessels and is ongoing throughout the previously mentioned phases of wound healing.
- Platelets enter the wound in the earliest phase of repair and secrete, among others things, TGF-b, which indirectly promotes angiogenesis and attracts macrophages.
- The platelets also secrete PDGF, which attracts macrophages and granulocytes and promotes angiogenesis.

Epithelialization

Mitosis of epithelial cells begins 48 to 72 hours after injury.
The rate of epithelial coverage is increased if the wound does not need debridement, if the basal lamina is intact, and if the wound is kept moist.
Several growth factors modulate epithelialization. E.g. Epidermal growth factor (EGF), basic FGF and keratinocyte growth factor (KGF).

Remodeling Phase

Collagen synthesis and breakdown equilibrate to a steady state approximately 21 days after wounding.
There is ongoing collagen synthesis and collagen breakdown as the ECM is continually remodeled.
Collagen degradation is achieved by specific matrix metalloproteinases
Fibronectins are matrix molecules that are involved in wound contraction, cell-cell and cell-matrix interaction, cell migration, collagen matrix deposition, and epithelialization. They act as a scaffold for collagen deposition.

ABNORMALITY:

Excessive Wound Healing

- Hypertrophic scars and keloids are forms of excessive healing.
- Hypertrophic scars are defined as those that remain within the borders of the original scar, whereas keloids extend beyond the original scar margins.
- Wounds that cross skin tension lines, in thick skin or in susceptible locations such as the earlobe, presternal, and deltoid regions, are more prone to abnormal healing.
- Hypertrophic scars generally begin to develop in the weeks after injury, whereas keloids can develop up to 1 year later.
- Histologically, mucinous ground substance is present in large amounts in keloids, but fibroblast density is less than in hypertrophic scars.

The nonsurgical management of keloids:

1. Physical: Examples of physical forms of treatment include radiotherapy, ultrasound, cryotherapy, pressure, and laser.
2. Pharmacologic: intralesional steroids

Cleft Lip Palate

1. Epidemiology

- Cleft lip and palate represents the second most frequently occurring congenital deformity (after clubfoot deformity).
- 1/700 overall incidence for facial clefting.
- Clefting more common in Asians (1/400) and less common in African American (1/2000)
- Clefts can be unilateral or bilateral; Left side more common for unilateral
- Syndromic clefting accounts for 50-60% pts Cleft lip, cleft palate or both affects approximately 1 in 750.

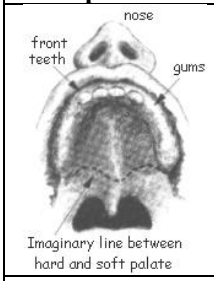
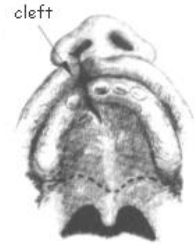
Embryology

- Weeks 5 & 6: Maxillary processes grow medially & fuse with frontonasal process
    a. Failure here > cleft lip +/- primary (anterior) palate
- Weeks 7 & 8: Tongue descent, migration & fusion of palatal shelves
    a. Failure here > cleft secondary (posterior) palate (Pierre-Robin, & other)

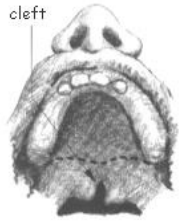
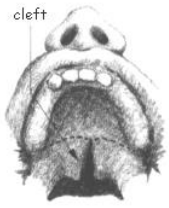
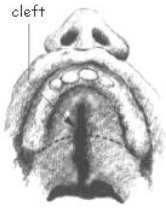
Anatomy

- The palatine processes of the maxilla and horizontal lamina of the palatine bones form the hard palate.
    - Its blood supply is mainly from the greater palatine artery.
    - The nerve supply is via the anterior palatine and nasopalatine nerves.
- The soft palate is a fibromuscular shelf made up of several muscles attached like a sling to the posterior portion of the hard palate.
    - It closes off the nasopharynx by tensing and elevating, thereby contacting Passavants ridge posteriorly.
    - The soft palate consists of the tensor veli palatini, the levator veli palatini, the musculus uvulae, the palatoglossus, and palatopharyngeus muscles.
    - CN V supplies the tensor veli palatini, while CN IX and CN X innervate the others.
    - The levator veli palatini is the primary elevator of the palate.

Examples of Unilateral and Bilateral Cleft Lip

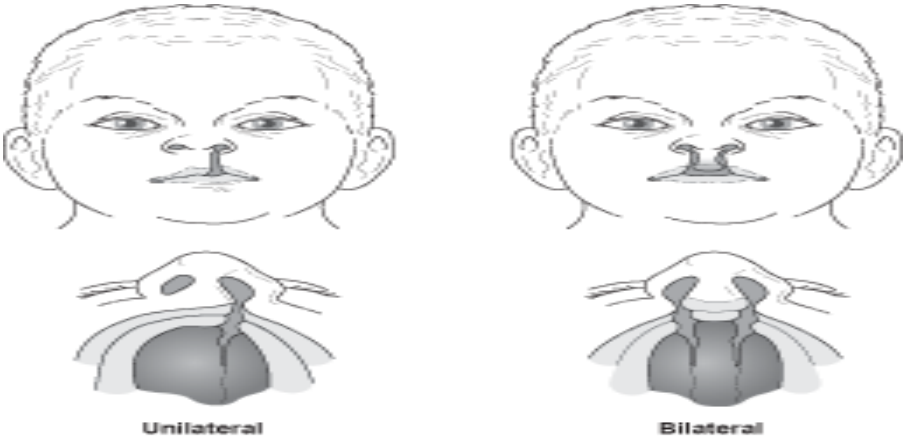
		
Normal roof of mouth	One-sided cleft lip	Two-sided cleft lip

Examples of cleft palate

			
Cleft of back of soft palate	Complete cleft of soft palate	Cleft of soft and hard palates	Complete cleft of lip and palate

2. Etiologies

- Teratogens: ethanol (FAS), anti-convulsants, steroids, chemo, excess Vita A
- Maternal / intra-uterine conditions: infant of diabetic mom, amniotic bands
- Chromosomal abnormalities, monogenic causes (AR, AD, XL)
- Unknown



Cleft lip and palate

Genetics

- Nonsyndromic inheritance of facial clefting is multifactorial.
- Familial inheritance of both cleft lip and palate occurs with varying frequency, depending on whether a parent or sibling is affected.
    - For cleft lip with or without cleft palate, the risk rate for future offspring is 2% with only one parent affected, 4% with only one sibling affected, 9% with two siblings affected, and 10-17% with one parent and one sibling affected.
    - For cleft palate alone, the risk rate for future offspring is 7% with only one parent affected, 2% with only one sibling affected, 1% with two siblings affected, and 17% with one parent and one sibling affected.
- Chromosome aberrations such as trisomy D and E have increased incidence of clefts.
- More than 200 recognized syndromes may include a facial cleft as a manifestation.
    - Common syndromes with cleft palates include Apert's, Stickler's and Treacher Collins. Van der Woude's and Waardenberg's syndromes are associated with cleft lip with or without cleft palate.

3. Diagnosis -- Newborn Physical Exam

- Inspect lip & oropharynx
- Palpate palate with gloved finger (submucous cleft is not visible, but can be felt in bony palate underlying mucous membrane. This diagnosis is often missed until later childhood when speech problems arise.

4. Newborn Feeding

- Isolated cleft lip rarely causes feeding problems
- Cleft lip & palate or palate alone may require special nipples, occluders.

5. Surgical Treatment

- Cleft lip: "Rule of Tens" -- ten weeks, ten pounds, hemoglobin of 10
- Cleft palate: around 1 year, before speech develops
    a. Subsequent surgical revisions required as child grows
    b. Palatal repair- repaired at approximately 9-12 months
    c. Secondary repair- if needed- repaired at approximately 4-6 years
    d. Alveolar cleft- repaired at 8-10 years
    e. Final repair- if needed repaired at 14-16 years

6. Associated Problems in Childhood

- ENT problems: often requires ear tubes

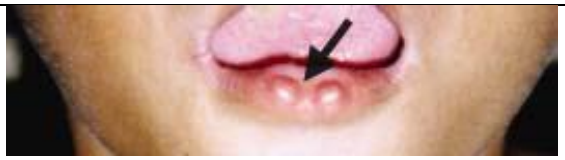
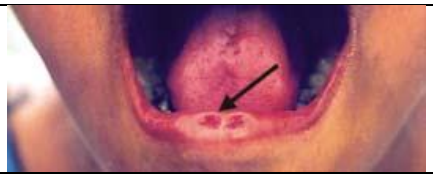
a. Hearing loss (cleft palate): Cleft palate is very often associated with eustachian tube dysfunction due to an abnormal insertion of the levator and tensor veli palatini muscles into the posterior margin of the hard palate. In addition to middle ear effusion, the patients also appear to have an increased incidence of cholesteatoma (7%).
b. Indications for myringotomy and tube insertion include a significant conductive hearing loss or persistent middle ear effusion, recurrent otitis media, or tympanic membrane retraction.

- Speech problems, often speech therapy (cleft palate): It is estimated that 75% of patients have velopharyngeal competence following primary cleft palate surgery, and this can be increased to 90-95% with directed secondary procedures.
- Dental problems, usually orthodontics
- Multi-disciplinary cranio-facial teams address child's multiple needs
- **Airway problems:** may arise in children with cleft palates, especially those with concomitant structural or functional anomalies. eg, Pierre-Robin sequence is the combination of micrognathia, cleft palate, and glossoptosis.

Van der Woude Syndrome (VWS)

About three percent of people with a cleft have VWS. VWS is inherited in an autosomal dominant pattern. Features of VWS include:

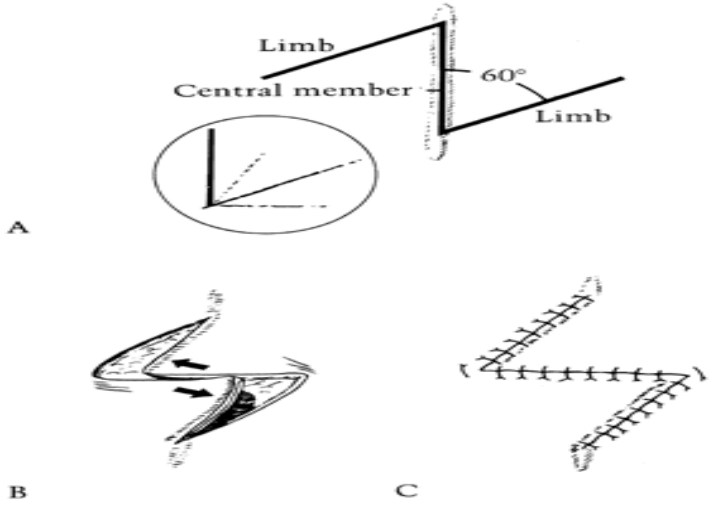
- Mounds or depressions (pits) on the lower lip
- Cleft lip, with or without cleft palate
- Cleft palate alone
- Missing teeth

	
Lip mounds in patient of Van der Woude Syndrome	Lip pits in patient with Van der Woude Syndrome

PRINCIPLE OF PLASTIC SUREGRY:

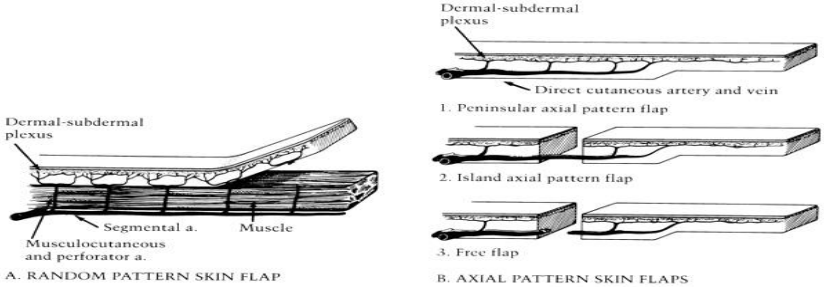
Geometric Principle of the Z-Plasty

- The Z-plasty is an ingenious principle that can be applied to revise and redirect existing scars or to provide additional length in the setting of scar contractor.
- The Z-plasty involves the transposition of two triangular flaps.
- The limbs of the Z must be equal in length to the central limb but can extend at varying angles (from 30–90 degrees) depending on the desired gain in length.
- The classic Z-plasty has an angle of 60 degrees and provides a 75% gain in length of the central limb by recruiting lateral tissue.



SKIN FLAPS:

- Unlike a graft, a flap has its own blood supply.
- Flaps are usually needed for covering recipient beds that have poor vascularity; reconstructing the full thickness of the eyelids, lips, ears, nose, and cheeks; and padding body prominences (i.e., for bulk and contour).
- A skin flap consists of skin and subcutaneous tissue that are transferred from one part of the body to another with a vascular pedicle or attachment to the body being maintained for nourishment.
- If the flap is pedicled, it is important that the pattern is cut to include the base of the flap and that it is made a little longer and wider than needed.
- The pattern is then tried again, being certain each time that it is shifted so that the base is held in a fixed position and not allowed to shift with the flap.
- The final pattern must be larger than needed, particularly its length, to avoid undue tension and kinking.
- Planning a transposition or rotation flap requires special attention to ensure that the most distal part of the flap is of sufficient length.



RANDOM & AXIAL FLAPS

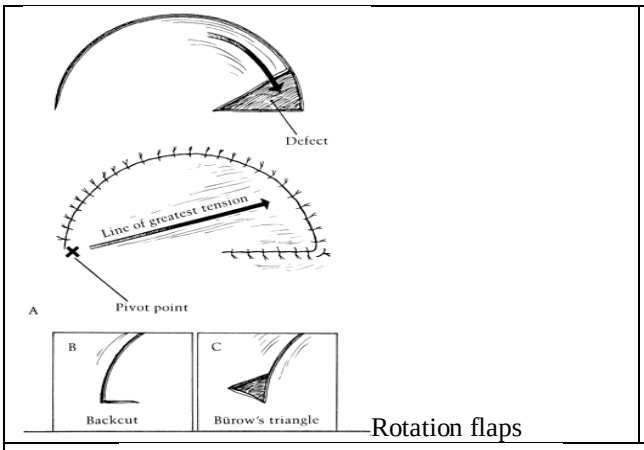
Local skin flaps are of two types:

- Flaps that rotate about a pivot point (rotation, transposition, interpolation flaps)
- Advancement flaps (single-pedicle advancement, V-Y advancement, Y-V advancement, and bipedicle advancement flaps).

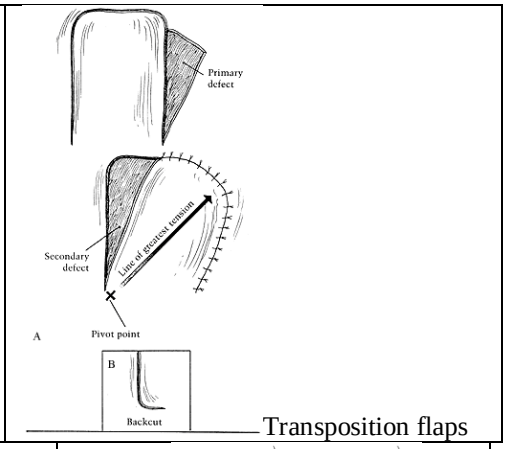
Flaps Rotating About a Pivot Point

- Rotation, transposition, and interpolation flaps have in common a pivot point and an arc through which the flap is rotated.
- The radius of this arc is the line of greatest tension of the flap.

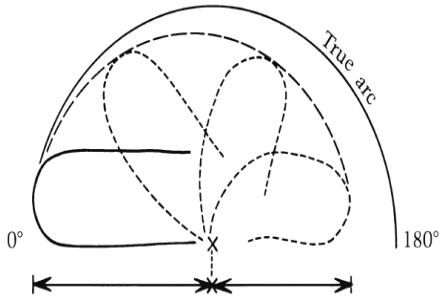
- The rotation flap is a semicircular flap of skin and subcutaneous tissue that rotates about a pivot point into the defect to be closed.
- A flap that is too tight along its radius can be released by making a short back-cut from the pivot point along the base of the flap.
- A triangle of skin (Burow's triangle) can be removed from the area adjacent to the pivot point of the flap to aid its advancement and rotation.
- The transposition flap is a rectangle or square of skin and subcutaneous tissue that also is rotated about a pivot point into an immediately adjacent defect.
- Bilobed flap: The key to a successful bilobed flap is an area of loose skin to permit direct closure of the secondary flap defect.



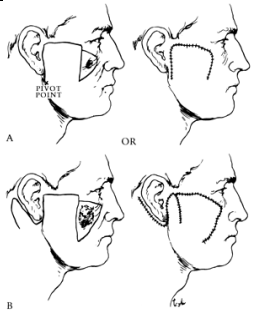
Rotation flaps



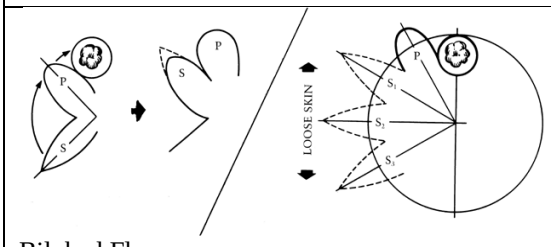
Transposition flaps



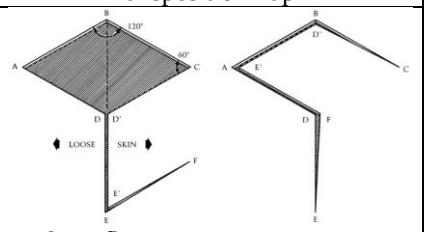
-
- Rotational flap



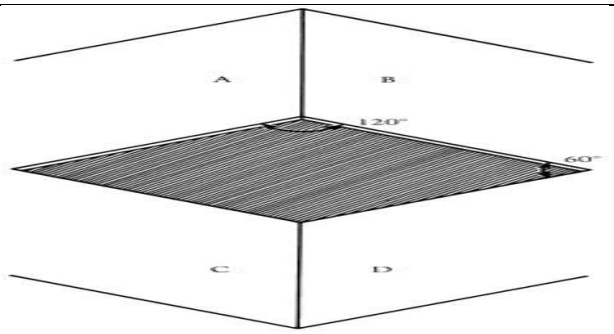
- B
- Transposition flap



Bilobed Flap



Limberg flap

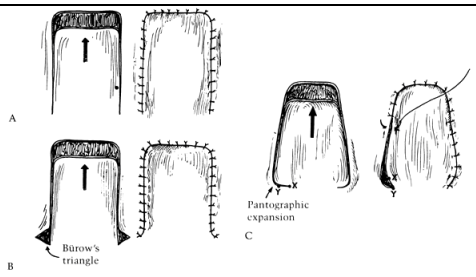


Four Limberg flap

- The Limberg flap is another transposition flap. This flap, like the bilobed flap and the Z-plasty, depends on the looseness of adjacent skin.
- A Limberg flap is suitable only for closure of rhomboid defects with angles of 60 and 120 degrees.
- With the Limberg flap, the sides are of the same length as the short axis of the rhomboid defect.

Advancement Flaps

- All advancement flaps are moved directly forward into a defect without any rotation or lateral movement.
- Modifications are the single-pedicle advancement, the V-Y advancement, and the bipedicle advancement flaps.
- The single-pedicle advancement flap is a rectangular or square flap of skin and subcutaneous tissue that is stretched forward.
- Advancement is accomplished by taking advantage of the elasticity of the skin and by excising Burow's triangles lateral to the flap.



Advancement

V-Y advancement

- This V-Y technique can be used to lengthen such structures as the nasal columella, eliminate minor notches of the lip, and, in certain instances, close the donor site of a skin flap.

SKIN GRAFTING

Skin grafts are divided into 2 major categories: ***full-thickness skin grafts (FTSGs) and split-thickness skin grafts (STSGs). STSGs may be subdivided into thin (0.008- to 0.012-mm), medium (0.012- to 0.018-mm), and thick (0.018- to 0.030-mm) grafts.***

STSGs are most commonly used when:

- Cosmesis is not a primary concern or when the defect to be corrected is of a substantial size that precludes the use of an FTSG.
- Coverage of chronic unhealing cutaneous ulcers, temporary coverage to allow observation of possible tumor recurrence, surgical correction of depigmenting disorders with the use of suction blister grafts to line cavities such as the orbit, and coverage of burn areas to accelerate wound healing and to reduce fluid loss.

The use of FTSGs is indicated:

- In defects in which the adjacent tissues are immobile or scarce.
- If that adjacent tissue has premalignant or malignant lesions and precludes the use of a flap.
- Specific locations for FTSGs include the nasal tip, helical rim, forehead, eyelids, medial canthus, concha, and digits.
- Other indications for the use of FTSG include punch grafting for hair transplantation and minigrafting (punch grafting) for the surgical correction of depigmenting conditions.

Contraindications: Contraindications to the use of STSGs include the need to place the graft in areas where good cosmesis or durability is essential or where significant wound contraction could compromise function.

The use of FTSGs is contraindicated when the recipient bed, due to lack of reasonable vascular supply, cannot sustain the graft. Using an FTSG on avascular tissues, such as exposed bone or cartilage, most often leads to graft necrosis.

Uncontrolled bleeding in the recipient bed is another contraindication to the placement of an FTSG because hematoma and/or seroma formation under the graft compromises graft survival.

Split-thickness skin grafts

An appropriate donor sites are anterior, lateral, or medial part of the thigh; the buttock; or the medial aspect of the arm. For larger defects, a large, flat donor surface is ideal for harvesting an STSG.

Full-thickness skin grafts

Common donor locations for FTSGs include areas of preauricular and postauricular, conchal bowl, supraclavicular, upper eyelid, nasolabial fold, axillary, antecubital, and inguinal fold skin.

Wound contracture is more common in STSGs than in FTSGs, and it can lead to cosmetic and functional problems.

SWELLINGS:

Dermoid Cyst

Dermoid cysts a solitary, or occasionally multiple, hamartomatous tumor. The tumor is covered by a thick dermislike wall that contains multiple sebaceous glands and almost all skin adnexa. Hairs and large amounts of fatty masses cover poorly to fully differentiated structures derived from the ectoderm.

In addition to the skin, dermoid cysts can be intracranial, intraspinal, or perispinal. Intra-abdominal cysts, such as cystic tumors of the ovary or omentum, occur as well.

Causes:

- Dermoid cysts are true hamartomas.
- Dermoid cysts occur when skin and skin structures become trapped during fetal development.
- Histogenetically, dermoid cysts are a result of the sequestration of skin along the lines of embryonic closure.

History:

- Dermoid cysts that are congenital and localized on the neck, head, or trunk are usually visible at birth.
- Intracranial, intraspinal, or intra-abdominal dermoid cysts may be suspected after specific or nonspecific neurologic or gynecologic symptoms occur.

Treatment: Surgical excision is the treatment of choice in any localization.

Lipoma

Lipomas are adipose tumors that are often located in the subcutaneous tissues of the head, neck, shoulders, and back. These slow-growing, nearly always benign, tumors usually present as nonpainful, round, mobile masses with a characteristic soft, doughy feel. Rarely, lipomas can be associated with syndromes such as hereditary multiple lipomatosis, adiposis dolorosa, Gardner's syndrome, and Madelung's disease. **Hereditary multiple lipomatosis**, an autosomal dominant condition is found most frequently in men, is characterized by widespread symmetric lipomas appearing most often over the extremities and trunk. **Gardner's syndrome**, an autosomal dominant condition involving intestinal polyposis, cysts, and osteomas. **Madelung's disease**, or benign symmetric lipomatosis, refers to lipomatosis of the head, neck, shoulders, and proximal upper extremities. Persons with Madelung's disease, often men who consume alcohol, may present with the characteristic "horse collar" cervical appearance. **Dercum's disease**, or

adiposis dolorosa, which is characterized by the presence of irregular painful lipomas most often found on the trunk, shoulders, arms, forearms, and legs. Dercum's disease is five times more common in women, is often found in middle age, and has asthenia and psychic disturbances as other prominent features.
There are also variants such as angiolipomas, neomorphic lipomas, spindle cell lipomas, and adenolipomas. Most lipomas are best left alone, but rapidly growing or painful lipomas can be treated with excision of the tumor.

Hemangioma

A haemangioma is a benign (overgrowth of blood vessels in the skin. It is due to proliferating endothelial cells. Ten percent of babies develop one or more haemangiomas. Over 80% occur on the head and neck area. They can grow for up to 18 months before they start regressing. This regression is known as involution and can take as long as 3-10 years.

Haemangioma is compressible because it consists of multiple blood-filled vascular spaces. Other compressible swellings are lymphangiomas, aneurysms, pharyngeal pouch, saphena varix, varicocoele, pneumatocoele, laryngeocoele, tracheocoele and hernias.
The commonest site of a haemangioma is head and neck region.
It affects internal organs also like liver and spleen.
Different types of haemangioma are:
1. Capillary Haemangioma : Port wine stain, Strawberry angioma, Salmon patch, Spider naevi
2. Venous Haemangioma (Cavernous haemangioma)
3. Arterial Haemangioma (Circoid aneurysm)
The commonest complication of a haemangioma is Haemorrhage.

Types of haemangiomas

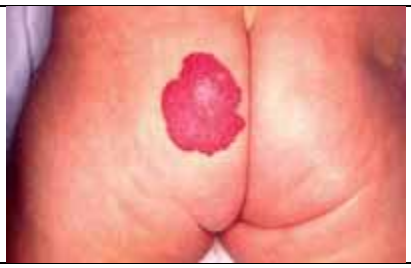
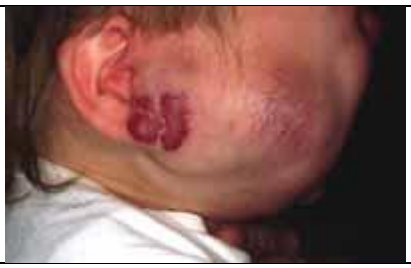
There are basically two main types of haemangiomas, capillary and cavernous. Capillary haemangiomas (superficial angiomatous naevi) affect the blood vessels in uppermost layers of the skin whilst cavernous haemangiomas (subcutaneous angiomatous naevi) are more deeply set in the dermis and subcutis. In some cases, both types of haemangiomas may occur together (mixed angiomatous naevi).

Capillary haemangioma

The capillary haemangioma or superficial angiomatous naevus is most commonly known as a strawberry haemangioma (strawberry birthmark, capillary naevus, haemangioma simplex). It is more common in premature babies and may appear when the baby is a few days or weeks old and rapidly grows over a few months. The eventual size varies from a tiny dot to several centimetres in diameter. Occasionally haemangiomas bleed or ulcerate, but this is rarely serious.

As most strawberry birthmarks disappear without any treatment by themselves over 5-7 years, treatment is rarely indicated.

If the birthmark grows over the eye, nose or mouth it could interfere with the breathing or feeding problems. Possible treatment includes oral steroids ***or laser therapy***. Interferon is no longer advised because it has been associated with the development of cerebral palsy in a few infants.

	
Strawberry haemangioma	Mixed capillary and cavernous haemangioma

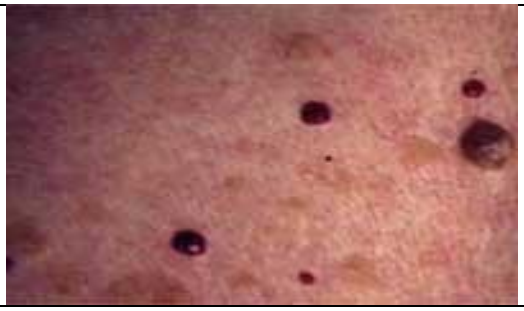
Cavernous haemangioma

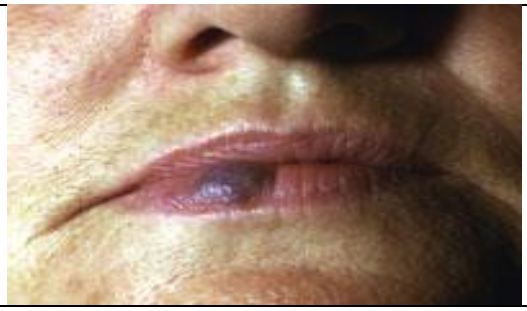
This type of birthmark is caused by overgrown blood vessels deep within the skin, resulting in a bluish swollen-up appearance. They may also grow and then get smaller, sometimes in conjunction with a strawberry mark.
The Kasabach-Merritt syndrome is also known as haemangioma-thrombocytopaenia syndrome. It is a rare complication of a rapidly growing cavernous haemangioma in the first few months of life. A defect of blood clotting (coagulopathy) is marked by anaemia, low platelet count and prolonged bleeding. The bleeding is thought to result from trapping and destruction of the platelets and depletion of circulating clotting factors. The coagulopathy is treated with special blood transfusions, and generally oral steroids to reduce the size of the haemangioma. The rapid growth of the haemangioma may also result in heart failure.

Other haemangiomas
The haemangiomas described below are all very rare conditons.

Type	Features
Verrucous haemangioma	Haemangiomas that also show an overgrowth and thickening of skin cells May be a single lesion or group occurring most often on the legs Do not resolve spontaneously and may need to be surgically excised
Eruptive neonatal haemangiomatosis	Multiple capillary haemangiomas present at birth or develop with first few weeks of life If only the skin is involved the disorder is called benign eruptive neonatal haemangiomatosis: these usually resolve spontaneously over time If lesions are also present on internal organs of the body (e.g. GI tract, lungs, brain, eyes) this is called disseminated eruptive neonatal haemangiomatosis: death generally occurs within the first few months of life A newborn with multiple haemangiomas present must be investigated thoroughly for haemangiomas on internal organs
Ulcero-mutilating haemangiomatosis	Rare disorder of multiple haemangiomas that form ulcers that lead to severe tissue damage
Acquired multiple haemangiomatosis	Large numbers of haemangiomas appear in childhood or adulthood on the skin and internal organs, particularly the skeleton, brain and liver Lesions persist indefinitely but are usually free of symptoms or complications

Haemangiomas arising in adults
Small capillary spots are called ***Campbell de Morgan lesions*** (also known as cherry angiomas), and appear most often around the midtrunk. They increase in number from about the age of 40. Their cause is unknown. They can be simply removed by diathermy or laser, but are usually left alone.
Angiomas are common on the face, particularly around the mouth. On the lip they are known as Venous Lakes, and are bluish in colour. No treatment is generally required.





Campbell de Morgan spots	Venous lake

Investigations
Haemangiomas are usually diagnosed clinically and no investigations are necessary. However, when there is uncertainty about the diagnosis or whether underlying tissues are affected, an ultrasound scan is often performed. Characteristically, a haemangioma has a firm lobular structure with vessels separating the lobules.
In more complicated cases it may be necessary to perform Magnetic Resonance Imaging (MRI) or angiography to help plan treatment.
Treatment of a cavernous haemangioma: Different lines of treatment are:
1. Injection of a sclerosant material (commonest material used is Ethanolamine oleate.)
2. Embolization injection (materials used are Gelfoam, alcohol foam & silicon particles)
3. Surgical excision
4. Laser radiation

CARCINOMA OF THE SKIN
Skin cancers are the most common forms of cancer.
Basal cell cancers account for nearly two thirds of skin cancer cases, while squamous cell cancers account for 10% of skin cancers.
RISK FACTORS
UV radiation, specifically 280-320 nm UV-B, is the most important risk factor for the development of skin cancer.
An increased risk is associated with geographic latitude; individuals who live closest to the equator have an increased risk for the development of skin cancer.
Less common risk factors include exposure to soot (scrotal SCCA in chimney sweeps noted by Sir Percivall Pott in 1775), tar, polycyclic aromatic hydrocarbons, arsenic pesticides, and pharmaceuticals.
Certain viral factors are also proposed to increase risk for the development of skin cancer (eg, human papilloma virus [HPV]).
Skin trauma (eg, burns, chronic ulcers) and ionizing radiation also contribute to skin cancer risk.

CLINICAL FEATURES
Presentation
- Erythematous, ulcerated, crusting lesion
- Area of persistent ulceration
- Hyperkeratotic patch
- Opaque nodule with or without ulceration
- Actinic keratosis (a premalignant condition that may develop into SCCA)

PATHOLOGY AND HISTOLOGIC VARIANTS
The current pathologic designations for premalignant and malignant skin lesions of squamous epithelial origin are squamous cell carcinoma-in-situ and SCCA.
Bowen disease of the skin and erythroplasia of Queyrat of the penis are clinical expressions of squamous cell carcinoma-in-situ.
Full-thickness involvement of the epidermis by cells with atypical and dysplastic features characterizes squamous cell carcinoma-in-situ.
Features include loss of orderly maturation as cells progress from basal to superficial layers; significant variability in nuclear size, shape, and staining between neighboring cells; mitoses at higher than expected levels; multinucleation; and dyskeratosis, hyperkeratosis, and parakeratosis.
Lesions with features that fall short of full-thickness involvement are characterized as actinic (solar) keratosis.

By definition, SCCA is a malignant squamous neoplasm in which the cells have penetrated the epithelial basement membrane and invaded the dermis for a variable distance.
Variants of SCCA are named according to their architectural features, including:
Spindle cell type/ adenoid type/ and verrucous type.
The spindle cell variant has large vesicular nuclei, indistinct cytoplasmic borders, and a spindled pattern, often resembling dermal sarcomas.
The adenoid (acantholytic) variant consists of nests of squamous cells with pseudoglandular formations secondary to central acantholysis.
Verrucous carcinomas are both exophytic and endophytic. The exophytic component displays papillomatosis, hyperkeratosis, and parakeratosis. The endophytic component manifests as acanthotic extensions of rete pegs with rounded appearance.

DIAGNOSIS

- Punch biopsy
- incisional biopsy
- Excisional biopsy

TREATMENT

High-risk tumors display the following characteristics:

- Size greater than 2 cm/ Depth greater than 4 mm/ Histology - Poorly differentiated/ Rapid growth/ Etiology - Burn, scar, and chronic ulcer/ Immunosuppressed patients/ Anatomic site - Scalp, nose, lip, eyelid, and ear (The ear is the primary site for aggressive tumor behavior.)/ Perineural invasion/ Recurrent lesions
    1. Surgical excision and primary closure occur under local anesthesia. The standard treatment includes 4- to 6-mm margins for 95% nonrecurrence rate.
    2. Mohs micrographic surgery offers better cure rates for lesions associated with high-risk factors. The surgery is performed using sequential excisions and histologic examination of the entire surgical margin. Subsequent excisions are performed only of the areas with persistent disease.
    3. Radiation is reserved for unusual cases.
    4. Topical chemotherapy with 5-fluorouracil may be useful for certain patients.

Risk factors for metastatic disease to regional lymph nodes include primary site tumor greater than 2 cm, depth greater than 6 mm, rapid growth, immunocompromised host state, anatomic site (eg, ear, temple, lip), and perineural invasion.
General guidelines for regional control include the following:

- Scalp, forehead, temple, and auricle may drain to paraparotid or intraparotid lymph nodes and to deep cervical nodes.
- Neck dissection is not usually indicated for patients with N0 necks. Monitor these patients, especially for the first 2 years. Rarely, prophylactic radiation to the neck is considered.
- Metastatic disease to the parotid region requires parotidectomy in conjunction with neck dissection.
- If cancer involves the skin or a scar from a previous excision or biopsy, include these areas in the surgical specimen.
- Preserve the facial nerve, unless the nerve is invaded directly by a tumor. If the nerve is resected, make every attempt to reconstruct the nerve using primary anastomosis, cable graft, or hypoglossal transfer.
- Patients who have distal metastatic disease do poorly. Combination surgery, radiation, and chemotherapy may benefit selected patients.

Head and Neck Cancer

Squamous cell carcinoma represents more than 90% of all head and neck cancers.

Pathophysiology

Squamous cell carcinoma is thought to arise from keratinizing or malpighian epithelial cells. The hallmark of squamous cell carcinoma is the presence of keratin or "keratin pearls" on histology. These are well-formed desmosome attachments and intracytoplasmic bundles of keratin tonofilaments.
Morphologically, it is variable and may appear as plaques, nodules, or verrucae.
These in turn may be scaly or ulcerated, white, red, or brown.
Verrucous carcinoma has a more favorable prognosis because of infrequent nodal and distant metastasis.

TNM clinical classification
T Primary tumor

- Tis Preinvasive cancer (carcinoma in situ)
- T0 No evidence of primary tumor
- T1 Tumor 2 cm or less in greatest dimension
- T2 Tumor more than 2 cm but not more than 4 cm
- T3 Tumor more than 4 cm
- T4 Tumor with extension to bone, muscle, skin, antrum, neck, etc
- Tx Minimum requirements to assess primary tumor cannot be met

N Regional lymph nodes

- N0 No evidence of regional lymph node involvement
- N1 Evidence of involvement of movable homolateral regional lymph nodes
- N2 Evidence of involvement of movable contralateral or bilateral regional lymph nodes
- N3 Evidence of involvement of fixed regional lymph nodes
- Nx Minimum requirements to assess the regional nodes cannot be met

M Distant metastases

- M0 No evidence of distant metastases
- M1 Evidence of distant metastases
- Mx Minimum requirements to assess the presence of distant metastases cannot be met

Staging

- Stage 1 T1 N0 M0
- Stage 2 T2 N0 M0
- Stage 3 T3 N0 N1 M0
- Stage 4 T1 T2 T3 T4 N1 M0 Any T N01N1 M0 Any T N2 N3 M0 Any N M1

RELEVANT ANATOMY
The oral cavity is defined as the area extending from the vermilion border of the lips to a plane between the junction of the hard and soft palate superiorly and the circumvallate papillae of the tongue inferiorly. This region includes the buccal mucosa, upper and lower alveolar ridges, floor of the mouth, retromolar trigone, hard palate, and anterior two thirds of the tongue. The lips are the most common site of malignancy in the oral cavity and account for 12% of all head and neck cancers, excluding nonmelanoma skin cancers. Squamous cell carcinoma is the most common histologic type, with 98% involving the lower lip. This predilection to the lower lip has been attributed to sun exposure. Next most common sites in order of frequency are the tongue, floor of the mouth, mandibular gingiva, buccal mucosa, hard palate, and maxillary gingiva.

Tumor site and lymphatic drainage

- Anterior tongue to subdigastric, submaxillary, or midjugular nodes
- Floor of mouth to subdigastric, submaxillary, or midjugular nodes
- Gingival to jugulodigastric, submaxillary, or midjugular nodes
- Buccal mucosa to submaxillary, preparotid, or jugular nodes
- Hard palate to submaxillary or jugulodigastric

TREATMENT

Several methods for treatment of cancer of the head and neck are acceptable, including surgery, radiotherapy, chemotherapy, and combinations of these.

Radiotherapy

- Nearly all patients with advanced disease require adjuvant radiotherapy, preoperatively or postoperatively. Radiation dosage in excess of 6000 cGy is recommended with a boost to areas of high risk.
- Indications for radiotherapy include a bulky tumor with significant risk of recurrence (T3 and T4), histologically positive margins, and perineural or perivascular invasion of tumor.
- For the neck, indications for radiotherapy include elective treatment of the N0 neck not treated surgically where risk of micrometastasis is high, gross residual tumor in the neck following neck dissection, multiple positive lymph nodes, and extranodal extension of tumor.

Chemotherapy

Bleomycin with or without electroporation has been used. Cisplatin is another chemotherapeutic drug of choice for head and neck cancers.

Surgical therapy

Surgical resection remains the criterion standard for treatment of head and neck cancer. Management of all but the earliest confirmed neck metastases is best achieved with surgical removal.

Neck dissection

Regardless of the site of the primary tumor, the presence of a single lymph node in either the ipsilateral or contralateral side of the neck reduces the 5-year survival rate by 50%.

Modified neck dissection is designed to preserve the spinal accessory nerve, the great auricular, and the sternocleidomastoid muscle. The jugular vein and submandibular gland also have been preserved.

In addition, successful results can be achieved through less than complete lymph node removal, selectively removing only those lymph node levels likely to be involved by metastases.

Classic radical neck dissection was described by Crile in 1901 and includes removal of all 5 levels of cervical lymph nodes en bloc down to the deep muscular fascia. This removal includes the sternocleidomastoid muscle, submandibular gland, jugular vein, and spinal accessory nerve. This operation remains the best procedure for definitive control of neck disease. Radical neck dissection can be combined with resection of the primary cancer and postoperative radiation therapy.

has pain and difficulty lifting his or her arm.

roduces a unique thymidine kinase. This viral enzyme preferentially phosphorylates the prodrug ganciclovir, a guanine nucleoside analogue, to produce a metabolite that, after cellular phosphorylation, is incorporated into replicating DNA, inhibiting DNA polymerase and ultimately killing the cell. This therapy is most effective in treating cancer cells growing in tissues where normal cells are not proliferating.

Many phase I and II trials are being pursued, and may ultimately provide nontoxic, tumor-specific, locally and regionally active, and biologically active injectable modalities that add therapeutic advantages to the existing treatment of head and neck cancers.

Basal cell carcinoma

There are four main clinical types of basal cell carcinoma: nodular, superficial, morpheaform, and pigmented.

Nodular basal cell carcinoma, the most common type, is a waxy, semitranslucent papule or nodule. The border is often pearly and rolled, and telangiectasias course over the surface of the lesion. Eventually, central ulcerations (rodent ulcers) develop.

Superficial basal cell carcinoma usually occurs as a slightly raised, pink or red, scaly, focally crusted plaque with a threadlike border.

Morpheaform basal cell carcinoma appears as an ivory plaque with overlying telangiectasias. This lesion may be more difficult to treat than other basal cell cancers.

Pigmented basal cell carcinoma is similar to the nodular and superficial variants but has brown or black pigmentation.It may be difficult to differentiate from melanoma.

MALIGNANT MELANOMA

Melanoma is a malignancy of pigment-producing cells (melanocytes) occurring in the skin, eyes, ears, GI tract, leptomeninges of the central nervous system (CNS), and oral and genital mucous membranes. Melanoma accounts for only 4% of all skin cancers.

Consider lesions exhibiting these features to be potential melanomas:

- Asymmetry
- Border notching
- Color variegation with black, brown, red, or white hue
- Diameter >6 mm

Types of Malignant Melanoma

There are four main types of melanoma

- Superficial spreading melanoma
- Nodular melanoma
- Lentigo Maligna melanoma (also sometimes called Hutchinson's melanotic freckle)
- Acral lentiginous melanoma

These four main types make up 90% of all diagnosed malignant melanoma.

Superficial spreading melanoma

This is the most common type of melanoma (65-70%). They are most common in middle aged people. To start with, they have a radial growth phase (grows in a horizontal plane, along, just above and below the dermo-epidermal junction) and is clinically macular or only slightly elevated. The melanoma will not become dangerously at risk of spreading until it begins to grow downwards into the deeper layers of skin and beyond. Most common on the trunk in men and women and on the legs in women

Nodular melanoma

About 1 in 4 melanomas (25%) are of this type. It is also found most often in middle aged people and ***in parts of the body only exposed to the sun.*** So it is most often found on the ***chest or back.*** Nodular melanomas are often very dark brownish black or black in colour. The depth of the lesion appears to correlate with the prognosis of the patient, and nodular melanoma is less often amenable to definitive treatment than is the superficial spreading variety.

Lentigo maligna melanoma

About 1 in 10 melanomas (10%) are this type. Lentigo MM is most common ***in elderly people.*** It appears in areas of skin that get a lot of sun exposure, so is ***commonest on the face.*** This type of melanoma grows very slowly, so it may be gradually getting bigger over several years. This lesion may grow for years as an in-situ tumor before developing the more aggressive vertical growth phase. In situ precursor lesion usually large (>3 cm diameter), existing for a minimum of 10-15 years, with dermal invasion characterized by development of dark brown-to-black macular pigmentation or raised blue-black nodules

Acral lentiginous melanoma

This type is most commonly found on the ***palms and soles or around the big toenail.*** It can also grow under the nails. It is much more common on the feet than on the hands.

Other types of melanoma

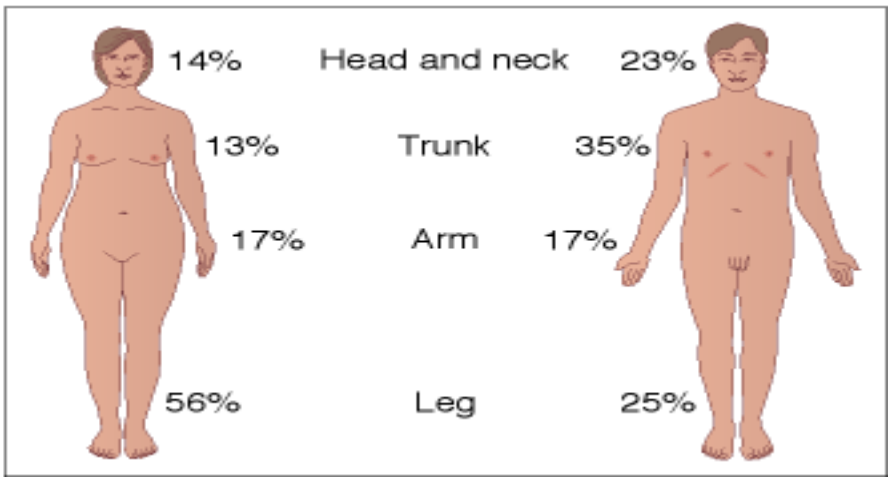
Melanoma can occur anywhere in the body, including in the internal organs. One area where melanoma does occur is eye. Rare melanoma variants (<2% of melanomas) include the following:

- Desmoplastic/neurotropic melanoma
- Mucosal (lentiginous) melanoma
- Malignant blue nevus
- Melanoma arising in a giant congenital nevus
- Melanoma of soft parts (clear cell sarcoma)

Amelanotic melanoma (<2% of melanomas) characteristics are as follows:

- Nonpigmented and appearing clinically as pink or flesh colored.
- Most commonly occurs in the setting of melanoma metastasis to the skin, presumably because of the inability of these poorly differentiated cancer cells to synthesize melanin pigment

The five year survival for tumours <0.75 mm is 95-99%, 0.76-1.49 mm is 80-90%, 1.5-3.99 mm is 60-75%, >4.0 mm is <50%.



Melanomas in men are most common on the back. In women, the commonest site is the legs.

- Two genodermatoses, ***xeroderma pigmentosum and familial atypical mole melanoma syndrome***, confer a 500-fold or greater relative risk of developing melanoma.
- arise from preexisting nevi; 1% of all cancers
- 30-40% mortality
- metastases: latent period of 2-20 years (most commonly 2-5 years)
    - lymphadenopathy
        - in 23% with level II + IV
        - in 75% with level V
    - bone (11-17%)
        - often initial manifestation of recurrence; poor prognosis
        - axial skeleton (80%); ribs (38%)
    - lungs (70% at autopsy)
        - ***most common site of relapse; most common cause of death***
    - liver (58% at autopsy): may be calcified, necrotic
    - spleen (1-5%): solid or cystic
    - bowel + mesentery (8%): mostly in small bowel
    - kidney (35%); adrenals (50%); subcutis

Clark staging:

- level I: all tumor cells above basement membrane (in situ)
- level II: tumor extends to papillary dermis
- level III: tumor extends to interface between papillary and reticular dermis
- level IV: tumor extends between bundles of collagen of reticular dermis
- level V: tumor invasion of sucutaneous tissue (87% metastases)

Breslow staging:

- thin: < 0.75 mm depth of invasion
- intermediate: 0.76 - 3.99 mm depth of invasion
- thick: > 4 mm depth of invasion

Malignant melanoma: gallium imaging
>50% sensitivity for primary and metastatic sites:

- 73% sensitivity if lesion is > 2 cm

- 17% sensitivity if < 2 cm

Surgical Care: Surgery is the primary mode of therapy for localized cutaneous melanoma.

Surgical margins for primary melanoma

- Surgical margins of 5 mm currently are recommended for melanoma in situ, and margins of 1 cm are recommended for melanomas up to 1 mm in depth (low-risk primaries).
- Randomized prospective studies show that 2-cm margins are appropriate for tumors in the intermediate-risk group (1-4 mm in Breslow depth), although 1-cm margins have been proposed for tumors of 1- to 2-mm thickness.
- Margins of at least 2 cm are recommended for cutaneous melanomas greater than 4 mm in thickness (high-risk primaries) to prevent potential local recurrence in or around the scar site.

Elective lymph node dissection

- Prophylactic lymph node dissection for primary cutaneous melanoma of intermediate thickness initially was believed to confer a survival advantage on patients with tumors 1-4 mm in depth. Subsequent clinical trials have shown no survival benefit for elective lymphadenectomy for melanomas of varying thicknesses on the extremities and marginal melanomas.

Sentinel lymph node biopsy/dissection

- Lymphatic mapping and sentinel node biopsy effectively have solved the dilemma of whether to perform regional lymphadenectomy (in absence of clinically palpable nodes) in patients with thicker melanomas (≥1 mm in depth).
- The sentinel node is examined for the presence of micrometastasis on both routine histology and with immunohistochemistry; if present, a therapeutic completion lymph node dissection is performed.
- A negative sentinel node biopsy prevents the morbidity associated with an unnecessary lymphadenectomy, since the histology of the sentinel node is characteristic of the entire nodal basin.

Melanoma surgery

Resection margins

- Until recently history rather than controlled trials have dictated practice
- Handley (1907)
  - Hunterian Lecture based on one case.
  - Recommended 5 cm margin
- Butterworth and Klaude (1934)
  - Found microscopic lymphatic invasion to 3 cm
  - Recommended 5 cm resection margins
- Olson (1966)
  - Trial of resection 1 cm vs. 3 cm resection margins
  - Identical local recurrence rate but still recommended 5 cm margin !
- WHO Melanoma Group (1990)
  - Randomised controlled trial of 1 cm vs. 3 cm resection margins
  - Resection margins did not influence survival
- Generally accepted resection margins based on clinical appearance are:
  - Impalpable lesions - 1 cm margin
  - Palpable lesion - 2 cm margin
  - Nodular lesion -3 cm margin

Regional lymphadenectomy

- 20% clinically palpable nodes are histologically negative
- 20% palpably normal nodes have occult metastases
- Therapeutic lymph node dissection provides regional control and prognostic information
- No improvement in survival
- For tumours <0.75 mm thick - 90% cured by local excision alone

- For tumours >4.0 mm thick - 70% have distant metastases at presentation
- For these two groups lymphadenectomy provides no added survival benefit
- Lymphadenectomy for 'intermediate' thickness tumours controversial

Morbidity of lymphadenectomy

- Lymphoedema (26%)
- Seroma (23%)
- 'Functional deficit' (8%)
- Wound Infection (5%)
- Persistent pain (5%)

Adjuvant Therapy

- Patients at high risk of recurrence should be considered for systemic adjuvant therapy
- Patients include those with:
    - Primary tumour > 4 mm thick
    - Resectable positive locoregional lymph nodes
- No standard adjuvant therapy exists
- Interferon α2b has shown promising results
- Shown to increase disease-free and overall survival

Isolated limb perfusion

- Intra-arterial chemotherapy
- Commonly used agents - ***melphalan +/- TNF-alpha***
- Used with ***hyperoxygenation***
- Hyperthermia with a temperature of 41-42 °C
- Perfusion generally last about 1 hour
- Usually combined with lymphadenectomy

Indications

- Intransit metastases
- Irresectable local recurrence
- Adjuvant therapy for poor prognosis tumours
- Palliation to maintain limb function

TOTAL PARENTERAL NUTRITION (TPN)

ASSESSMENT OF THE PATIENT (Prior to initiation of TPN)

Method of assessment	Moderately malnourished	Severely malnourished
Ideal Weight	60-80%	<60%
Creatinine Height Index (24 Hrs urinary creatinine ×100 / Ideal for height & sex)	60-80	<60
S. Albumin (mg/dl)	2.1-3	<2.1
S. Transferrin (mg/dl)	100-150	<100
TLC (cmm)	800-1200	<800
Delayed Hypersensit. Index *	1	0
Prognostic Nutritional index #	40-50	>50

* Delayed hypersensitivity index quantitates the amount of induration elicited by skin testing with a common antigen such as candida, trychphyton or mumps.
Induration grade: 0= < 0.5 cm.; 1= .5 cm. 2= 1cm.
PMI % = 158-1.66 × albumin (gm/l) – (0.78 × triceps skin fold in mm.)- (2 × transferrrin gm/l) – 5.8 × delayed hypersensitivity index)

REQUIREMENTS TO BE CALCULATED.
After assessing the nutritional status of the patient, requirement is calculated in terms of:
A: Fluid requirement B: Energy Requirement
C: Protein or AA requirement D: Mineral & Vitamin.
A: FLUID REQUIREMENT:
Normal Daily fluid requirement:
Infants: 120ml/kg body weight. Adults: 40ml/lg body weight.
For each 0C rise of Temp. add 200 ml/day.
Abnormal losses are added to daily requirements.

B: ENERGY REQUIREMENT:
Patients BASAL ENERGY EXPENDITURE (BEE) is calculated using HARRIS BENEDICT EQUATION.
For women: 655.10 + 9.56 (W) + 1.85 (H) - 4.68 (A) Kcal/day
For men: 665.47 + 13.75 (W) + 5 (H) - 6.76 (A) Kcal/day
W= wt. In Kg. H= height in cm. A= age in years.
To the BEE should be added:

- A value of 20% of BEE for a pt. without significant metabolic stress.
- 50% of BEE for patients with marked stress like sepsis and trauma.
- 100% of BEE for pt. with severe stress like >40% burn.

Harris Benedict equation is based on the data related to healthy subjects. So it may not correctly assess the caloric need of a hospitalized malnourished patient. Here assessment of ***Resting energy expenditure*** is a better guide.

- Men REE: (789 × BSA) + 137
- Women REE: (544 × BSA) + 414

BSA is Basal surface area.
A factor of 20% above REE estimates the need of most of the hospitalized patients, and 40-100% above REE for >40% burn.
C: PROTEIN AND AMINO-ACIDS REQUIREMENT:
Recommended dietary protein allowance:

- In non-stressed patients = 0.8 gm/kg body wt./day.

- Catabolic patients require = 1.2-1.7 gm/kg body wt./day

Protein balance = Protein intake – protein loss
Protein loss = 24 hrs. Urine urea nitrogen (g) × 6.25.
6.25 Gm of protein = 1 Gm of nitrogen.
Calorie to nitrogen ratio should be 100-150: 1 (To minimize protein catabolism).
D: MINERALS & VITAMIN REQUIREMENT.
The parenteral requirement of some of the vitamins may be higher than the enteral requirements, due to:

- The micronutrients are delivered into the systemic rather than portal system thereby by-passing the liver and rapidly excreted by the kidneys.
- Many patients requiring TPN have large GUT losses that results in Na, CL, K, and bicarbonate wasting and also loss of divalent cations and vitamins.
- The tubing and exposure to the oxygen and light can also absorb and destroy vitamins (eg. Vit. A) before it reaches the patient.

PRESCRIBING PARENTERAL NUTRITION: - Steps are:
Step I: Calculate patient's expenditure for caloric need & protein need.
Step II: identify appropriate amount of Dextrose/ Fat Calorie and amount of amino acids to supply nitrogen acid.
Step II: Order necessary electrolyte, mineral, vitamins & trace elements.
Step IV: Calculate fluid need in which TPN will be given.

Step I: Already described.
Step II:

Dextrose-

- In TPN concentrated Dextrose or Glucose is the most commonly prescribed caloric source.
- Dextrose provide 3.4% Kcal/gm.
- Thus 500 ml of 50% Dext. Supplies 850 Kcal.
- The basic conc. Of dext. is final solution = 20-25% dextrose.

Fat-

- Fat is needed to prevent essential fatty acids deficiency and also as a source of non-protein calories.
- Fat provides 9 Kcal/gm.
- Its available as 10% & 20% emulsion providing 1.1 & 2 Kcal/ml.
- Thus 500 ml of 10% fat emulsion = 500 × 1.1 = 550 Kcal.
- 500 ml of 20% fat emulsion = 500 × 2 = 1000 Kcal.

Crystalline Amino Acids: As protein source.

- Proteins are not provided for calories but to provide nitrogen for protein catabolism.
- 6.25 gm of protein contain 1 gm of nitrogen.
- The basic solution of TPN contains final conc. of 3-5% amino acid
- Thus 500 ml of 10% AA = 4.63 gm of N+ or 28.9 gm of proteins

Electrolytes and mineral are provided for maintenance and to for acute loss, should include: Na+, K+, Ca++, Mg+, Cl-, Po4—
Trace elements given daily are:

- 0.8 mg Manganese.
- 1 mg Copper.
- 4 mg of Zinc.
- 10 mg Chromium.

Adequate Vitamin supplementation should be done intravenously. Following vitamins have to be given I.M. as they are unstable in hyperalimentation solution.
Vit. K = 10 mg IMI / Week.
Folic acid = 5 mg / week

Vit B12 = 1 mg / month

3 In 1 TPN solution: combine glucose fat AA and other additives in One bag for infusion over 24 hours.

Advantages:

- Decreased risk of infection Due to less manipulation/ Cost saving/ Time saving
- Using a glucose, and fat calorie source provides a more physiologic solution > reduced co2 production.
- In this solution up to 40% kcal may be given as fat.

EXAMPLE: ordering TPN for 70 kg man, 170 cm height

Step I: Calculate caloric and nitrogen needs.

BSA = 1.8

REE = 7.89 × BSA + 137 = 789×1.8-137= **1557 Kcal.**

20% increment: Final REE = 1867 Kcal.

Calculated caloric requirement = 1867 Kcal.

Nitrogen requirement: 70 × 1.3 gm protein = 91 gm protein.

91 gm / 6.25 = 14.5 gm of nitrogen.

Calculated nitrogen need = 14.65 gm NT.

Step II: Ordering solution for 24 hrs. administration.

- 800 ml of 50% dextrose. = 1360 Kcal
- 500 ml of 10% fat. = 550 Kcal
- 900 ml of 10% AA = 15.1 gm N+

Step II: Add electrolyte mineral vitamins.

The starting infusion rate should be 50-100 ml / hr depending to patients cardiovascular and renal status. This rate gives 1200-2400 Kcal / day.

The increase should be 25-50 ml / hr. every day to allow kidney and pancreas to adjust to increased osmolality and glucose level.

SPECIFIC FORMULATIONS IN SPECIFIC DISESE STATE:

I: TPN in patients with Renal Failure:

- Patients in ARF not requiring dialysis require Concentrated TPN, (eg. Glucose-10%, Fat-20%, AA-10%), to reduce fluid load yet to provide adequate calories to prevent catabolism.
- Nitrogen conc. should be less.
- After regular dialysis is established protein content can be liberalized to provide 1-1.5 gm protein / kg / day.

II: In hepatic failure:

- Here ureagenesis is impaired with accumulation of toxic nitrogenous compounds eg. Ammonia
- Thus TPN is started with a reduced load of protein (0.7 gm/kg)
- Solution should contain more of branched chain AA and less of aromatic AA.
- Such solution appears to improve encephalopathy though it may not improve survival dictated by underlying liver failure.

III: In cardiac or respiratory failure.

- Fluid and Na+ restriction is indicated in CCF.
- In respiratory failure, a TPN solution may provide benefit, which contains higher percentage of calories as fat. (Fat has a lower RQ then carbohydrate; .07:1, thus less likely to lead to hypercapnia.)
- 40% of non-protein calories are given as fat if hypercapnia impairs respiratory functions.

EFFECTS OF TPN ON GUT FUNCTIONS:

ORGAN	EFFECT OF TPN
STOMACH	Delayed gastric emptying. Increased acid secretion
PANCREAS	Decreased enzymes and bicarbonate
SMALL BOWEL	Increased Weight, DNA, Enzymes

LIVER	**Increased Liver Chemistry. Steatosis, Cholestosis**
GALL BLADDER	**Increased incidence of ball stones**

MONITORING THE PATIENT ON TPN:

A: CLINICAL DATA TO BE CHECKED DAILY

1. Patient's sense of well being, symptoms suggesting fluid overload, high or low blood glucose.
2. Patient's strength as judged by graded activity, getting out of bed, walking stairs, climbing and weight measurement.
3. Vitals; Temp. BP, PR, RR.
4. Fluid balance: input vs. output.

5.Delivery equipment of TPN nutrition.

B: LABORATORY DATA TO BE MONITORED

Urine quantitation glucose	Four times daily
Blood Glucose, Na+, K+, Cl-, HCO3--, BUN	Daily until glucose infusion load & patient are stable.
S. albumin, Transferrin, LFT, S. creatinine, Ca++, PO4--, Mg++	Base line then twice weekly
Prothombin time	Base line then weekly

Nitrogen balance: N+ intake – (UUN + NUN).

UUN= Urine urea N+, NUN= Non urea and insensible losses.

C: INDIRECT CALORIMETERY:

To find out how the body is utilizing the caloric intake. It measures the respiratory quotient (RQ)

RQ > 1 Indirect Lipogenesis

RQ = 1 Carbohydrate Utilization

RQ= 0.74-0.85 Mixed fuel utilization.

RQ= 0.7 Fat utilization

COMPLICATIONS OF TPN

It can be broadly classified into 3 categories.

A: Mechanical.

B: Infectious.

C: Metabolic.

A: MECHANICAL COMPLICATIONS.

Arise either due to wrong placement of catheter or due to maintenance of venous access.

- Development of pneumo, hydro, hemo, or chylothorax.
- Injury to subclavian artery or brachial plexus.
- Malposition of catheter leading to arrhythmias.
- Air embolism or catheter embolism.
- Thrombophlebitis or thrombosis of SVC.
- Slipping of catheter, or hub detachment.

In order to avoid these complications following steps should be taken:

- *Catheter position must be confirmed by X-ray before hypertonic solution is infused.*
- *Minimal handling of the catheter*
- *Daily check arm of the patient for edema.*

B: INFECTION: Catheter sepsis is confirmed if;

- The catheter tip and blood cultures are positive for the same organism.
- Fever disappears/ decreases within 24 hrs of catheter removal.
- No other source of infection is identified.

One of the earliest sign of systemic sepsis is sudden development of glucose intolerance (with or without temp increase), in a pt. who previously has been maintained on TPN.
Sepsis is more likely with double or triple lumen tube.

METABOLIC COMPLICATIONS IN TPN

Nutrient Excess	Presentation
Glucose	Hyperglycemia, Polyuria (*)+polydipsia + Hyperosmolar non ketotic hyperglycemia
Amino acids	Hyperammonia in patients with liver disease, Azotemia in liver failure
Calcium	Hypercalcemia, Pancreatitis, renal stones
Vitamin D	Hypercalcemia, Osteopenia, long bone pains
NUTRIENT DEFICIENCY	
Copper	Neutropenia, Anaemia, Scorbutic bone lesions, decreased ceruloplasim, Microcytic anaemia.
Zinc	Nasolabial and perineal acrodermatitis, Alopecia, decreased cell function, decreased alkaline phosphatase.
Chromium	Glucose intolerance, Peripheral neuropathy.
Selenium	Myalgia, Cardiomyopathy, Decreased glutathion peroxidase.
Molybdenum	Amino acid intolerance, tachycardia, techypnoea, central scotoma, irritability, decreased uric acids.
Essential fatty acids	Eczymoid dermatitis, alopecia
Vitamin A (#)	Night blindness, Decreased dark field adaptation.
Biotin	Dermatitis, alopecia, hypotonia.
Thiamin	Wernick's encephalopathy

* Normal rate of glucose utilization in a normal adult is = 0.4-1.2 g/kg/hr.
# Requirement of Vit. E. is directly proportional to dietary fat.
Hypophosphatemia: Develops if phosphorus has not been added in amount adequate to meet the requirements for the metabolism of infused glucose and amino acids. The result is an extra vascular to intracellular shift of phosphate.
Signs and symptoms: paresthesia, confusion, convulsion and death.
Associated with Hypophosphatemia is a reduction in erythrocytic 2,3-diphosphoglycerate leads to increased affinity of Hb for oxygen hence, less O2 is released to peripheral tissue.

Early metabolic problem specially in elderly and debilitated patients including fluid overload producing CHF and glucose overload leading to stimulation of insulin secretion which causes intracellular shift of Phosphorus and potassium with resultant depletion of phosphorus and potassium leading to ***arrhythmias, cardiopulmonary function and neurological symptoms.***
To avoid these complications TPN should be started slowly and monitored carefully.
Late metabolic complications include ***cholestatic liver disease with bile sludging and gall stones***. The exact cause of liver disease is not understood but appears to be linked to the lack of enteral nutrition, the disease is less likely if some enteral feeding is continued.
Hyperosmolar non-ketotic hyperglycemia develops either if the hypertonic solutions are administered too rapidly or if the patient has impaired glucose tolerance. This is particularly common in latent diabetics and in patients following severe surgical stress or trauma.
Treatment of the condition consists of volume replacement, administration of insulin, electrolyte abnormality to be corrected.

COMPLICATIONS OF TPN (SUMMARY)

	Metabolic	Infectious	Mechanical
First 24 hrs.	Fluid overload Hyperglycemia Hypophosphatemia Hypokalemia		Cephalad displacement.
First 2 weeks	Cardio-pulm. Failure Hyper osmolar non-ketotic Hyperglycemia Electrolyte imbalance Acid-base imbalance	Catheter induced sepsis	Catheter extrusion Air embolism
After 3 months	Essential fatty acid def. Zn, Cu, Cr, Se, Mo, def. Iron def. Vit. Def. TPN induced liver disease. TPN induced metabolic bone Disease.	Catheter induced sepsis.	# or tear in catheter. Displacement of catheter hub with blood loss or air embolism

ONCOLOGY

The Cell Division Cycle

1. The General Strategy of the Cell Cycle.
   - For a typical mammalian cell, the cell cycle is divided into two major periods: mitosis, the process of nuclear division, and interphase, which comprises the time between successive mitosis. In early mitosis (i.e. prophase and prometaphase) the nuclear envelope breaks down, the contents of the nucleus condense into visible chromosomes, and the cell's microtubules reorganize to form the mitotic spindle. Then, the cell seems to pause at metaphase, in which the duplicated chromosomes are aligned on the mitotic spindle, poised for segregation. At this point, the cell "can decide" whether to stop cell division or not, however, past metaphase, there is no return and the process is taken till two daughter cells form. Anaphase marks the beginning of chromosome segregation, which will be followed by telophase and eventually, by cytokinesis, the separation of the two cells by division of the plasma membrane. This marks the end of the mitotic period, also known as the M phase. The M phase may last only for ~ 1hr, the other ~23 hr the cell spends in interphase. Towards late interphase is when the DNA is replicated.
   - The portion of interphase in which DNA replication occurs is known as the S phase (S=synthesis). Cells in S phase can be recognized by supplying them with 3H-thymidine, which only gets incorporated into DNA, or with bromo-deoxyuridine (BrdU), a T analog that can be recognized with a specific antibody. The interval between the completion of mitosis and the start of S phase is called G_1 phase (G=gap). During G_1 the cell monitors its environment and its own size, then, decides at the appropriate time to enter S phase. G_1 is by far the most variable cycle period timewise among different types of cells. Cells in G1, if they have not committed themselves to DNA replication, can enter G_0 (G zero), in which the cycle stalls with no S phase. G_0 can last from days to years and is typical of fully differentiated cells. After the S phase and before mitosis, cells are in G_2 phase. G1, S, G2 and M are the traditional subdivisions of the standard cell cycle.
   - There is an independent cell cycle control system made up of proteins that are different from the effector proteins that directly perform mitosis, G_1, DNA replication, or G_2. Brakes that can stop the cycle at specific checkpoints (a.k.a restriction points) regulate the control system. At checkpoints, feedback signals conveying information about the effector processes, or extracellular signals, can delay progress of the control system itself, so as to prevent it from triggering the next effector process before the previous one is finished. The two major checkpoints occur at G_1, just before entry into S phase, and at G_2 shortly before mitosis. There is an additional checkpoint before the exit from mitosis that corresponds to the point of no return at metaphase. In yeast this checkpoint is call Start. This is also the point where cells enter G_0 if the conditions are appropriate.

- The G_2 checkpoint senses unreplicated DNA, which generates a signal that leads to cell cycle arrest, unless DNA replication is complete. Progression through the cycle is also stopped at the G_2 checkpoint in response to DNA damage, such as that resulting from irradiation.
- DNA damage arrests the cycle at G_1 too, which allows time for repair before going into the S phase. At G_1, damaged DNA induces the rapid synthesis of the p53 protein, which then signals cell cycle arrest. Mutations in the p53 gene are the most common genetic alterations in human cancers, illustrating the critical importance of cell cycle regulation in the life of multicellular organisms.
- The checkpoint at metaphase monitors the alignment of chromosomes on the mitotic spindle, thus ensuring that a complete set of chromosomes is distributed accurately to the daughter cells.
- The cell-cycle control system is based on two families of proteins: the cyclin-dependent protein kinases (Cdk) and the cyclins. Cyclins bind and activate Cdk's, which phosphorylate selected proteins on Ser/Thr residues thereby inducing downstream effector cell cycle processes. There are mitotic cyclins, which bind Cdk molecules during G_2 and are required for entry during mitosis, and G1 cyclins, which binds to other Cdk molecules during G_1 and are required for entry into S phase. The cyclic assembly, activation, and disassembly of cyclin-Cdk complexes are the pivotal events that drive the cell cycle.

2. Regulators of Cell Cycle Progression.
    - MPF: a Dimer of Cdc2 and Cyclin. Experiments have led to the identification of the first cell cycle regulator, M phase-promoting factor (MPF). Further studies showed that MPF could also promote the G_2-to-M phase transition in mitotic cells.
    - Temperature-sensitive mutants that were defective in cell cycle regulation were isolated from two species of yeasts, *S. serevisiae and S. pombe.* These were called cdc (for cell division cycle) mutants. They showed arrest at specific points in the cycle. For example, cdc28 mutant in *S. cerevisiae* was arrested at Start, and S. *pombe* cdc2 mutant was arrested at the G2-M transition. These two genes turned out to encode for the same protein kinase (called Cdc2), which was the first evidence for protein phosphorylation in cell cycle control. The human homologue was later isolated and shown to complement the yeast mutations, indicating the high level of conservation in the control mechanism across species.

G1 Cell Cycle Regulation in Oncogenesis and Macromolecular Delivery

Growth factor stimulation of a resting G0 cell to enter the early G1 phase of the cell cycle and transition across the G1 restriction point into the late G1 phase, followed by entrance into S phase and DNA synthesis, requires the coordinated efforts of multiple cyclin:Cdk complexes and an increased metabolism. Previous research has demonstrated the roles of tumor-suppressor genes in the regulation of cell cycle progression, specifically the G1 phase of the cell cycle. An important negative regulator of G1 cell cycle progression at the restriction point is pRB, the product of the retinoblastoma tumor-suppressor gene. pRB targets cellular transcription factors, such as members of the E2F family. E2F transcription factors are involved in driving the expression of genes involved in DNA synthesis after transition through the restriction point into late G1. Transition across the restriction point irrevocably commits a cell to continue through the rest of the cell cycle. This key growth regulatory checkpoint balances the appropriate requisite level of metabolism with growth factor stimulation.

Phosphorylation on 16 cyclin-dependent kinase (Cdk) consensus sites by G1 cyclin:Cdk complexes regulates pRB. In G0 cells, pRB is unphosphorylated and does not associate with E2F transcription factors, suggesting that this form is inactive. As cells progress into early G1, pRB becomes hypophosphorylated on Cdk sites and associates with E2Fs. At the restriction point, pRB becomes inactivated by hyperphosphorylation on Cdk sites and E2Fs are released. Due to continued Cdk activity, pRB remains hyperphosphorylated through S, G2, and M phases. Thus, in response to growth factor stimulation, pRB is differentially regulated by cyclin:Cdk complexes in early and late G1. Although the *RB* gene is genetically altered in a low percentage of human malignancies (<1 percent), the $p16^{INK4a}$, and cyclin D1, Cdk4, and Cdk6 proto-oncogenes are mutated in most, if not all, human malignancies.

Serum Tumor Markers

Monoclonal antibodies are used to detect serum antigens associated with specific malignancies. These tumor markers are most useful for monitoring response to therapy and detecting early relapse. With the exception of prostate-specific antigen (PSA), tumor markers do not have sufficient sensitivity or specificity for use in screening.

- Cancer antigen (CA) 27.29 is used to follow response to therapy in metastatic breast cancer. Carcinoembryonic antigen is used to detect relapse of colorectal cancer.
- CA 19-9 may be helpful in establishing the nature of pancreatic masses.
- CA 125 is useful for evaluating pelvic masses in postmenopausal women, monitoring response to therapy in women with ovarian cancer, and detecting recurrence of this malignancy.
- Alpha-fetoprotein (AFP), a marker for hepatocellular carcinoma.
- Beta subunit of human chorionic gonadotropin (b-hCG) is an integral part of the diagnosis and management of gestational trophoblastic disease.
- Combined AFP and b-hCG testing is an essential adjunct in the evaluation and treatment of nonseminomatous germ cell tumors, and in monitoring the response to therapy.
- PSA is used to screen for prostate cancer and to detect recurrence of the malignancy.

To date, no tumor marker has demonstrated a survival benefit in randomized controlled trials of screening in the general population. Nevertheless, tumor markers can play a crucial role in detecting disease and assessing response to therapy in selected groups of patients.

Conditions Associated with Elevated Tumor Marker Levels

Tumor marker	***Normal value***	***Primary tumor(s)***	***Additional associated malignancies***	***Benign conditions***	***Level wherebenign disease is unlikely***	***Sensitivity***
CA 27.29	<38 units per mL	Breast cancer	Colon, gastric, hepatic, lung, pancreatic, ovarian, and prostate cancers	Breast, liver, and kidney disorders, ovarian cysts	>100 units per mL	Elevated in 33% of early-stage breast cancers and 67% of late-stage breast cancers
CEA[3,4]	<2.5 ng per mL in nonsmokers <5 ng per mL in smokers	Colorectal cancer	Breast, lung, gastric, pancreatic, bladder, medullary thyroid, head / neck, cervical, and hepatic cancers, lymphoma, melanoma	Cigarette smoking, peptic ulcer, IBD, pancreatitis, hypothyroidism, cirrhosis, biliary obstruction	>10 ng per mL	Elevated in less than 25% of early-stage colon cancers and 75% of late-stage colon cancers
CA 19-9[5]	<37 units per mL	Pancreatic and biliary tract cancers	Colon, esophageal, and hepatic cancers	Pancreatitis, biliary disease, cirrhosis	>1,000 units per mL	Elevated in 80% to 90% of pancreatic cancers and 60% to 70% of biliary tract cancers*
AFP[6]	<5.4 ng per mL	Hepatocellular carcinom	Gastric, biliary, and pancreatic cancers	Cirrhosis, viral hepatitis,	>500 ng per mL	Elevated in 80% of hepatocellular

		a, nonseminomatous germ cell tumors		pregnancy		carcinomasNonseminomatous germ cell tumors: see b-hCG below
b-hCG[7,8]	<5 mIU per mL	Nonseminomatous germ cell tumors, gestational trophoblastic Dis	Rarely, gastrointestinal cancers	Hypogonadal states, marijuana use	>30 mIU per mL[7]	AFP or b-hCG elevated in 85% of nonseminomatous germ cell tumors; elevated in only 20% of early-stage nonseminomatous germ cell tumors
CA 125[9-11]	<35 units per mL	Ovarian cancer	Endometrial, fallopian tube, breast, lung, esophageal, gastric, hepatic, and pancreatic cancers	Menstruation, pregnancy, fibroids, ovarian cysts, PID, cirrhosis, ascites, pleural / pericardial effusions, endometriosis	>200 units per mL[11]	Elevated in about 85% of ovarian cancers; elevated in only 50% of early-stage ovarian cancers
PSA[12-14]	<4 ng /mL for screening Undetectable level after radical prostatectomy	Prostate cancer	None	Prostatitis, benign prostatic hypertrophy, prostatic trauma, after ejaculation	>10 ng per mL[12]	Elevated in more than 75 percent of organ-confined prostate cancers[14]
CA = cancer antigen; CEA = carcinoembryonic antigen; AFP = alpha-fetoprotein; b-hCG = beta subunit of human chorionic gonadotropin; PSA = prostate-specific antigen. **--The greatest possible sensitivity is 95 percent, given that 5% of the population have Lewis-null blood type and are unable to produce the antigen.* *Information from references 1 through 14.*						

Cancer Antigen 27.29

- Cancer antigen (CA) 27.29 is a monoclonal antibody to a glycoprotein (MUC1) that is present on the apical surface of normal epithelial cells. CA 27.29 is highly associated with breast cancer.
- CA 27.29 also can be found in patients with benign disorders of the breast, liver, and kidney, and in patients with ovarian cysts.
- However, CA 27.29 levels higher than 100 units per mL are rare in benign conditions.

- Because of superior sensitivity and specificity, CA 27.29 has supplanted CA 15-3 as the preferred tumor marker in breast cancer.
- The CA 27.29 level is elevated in approximately one third of women with early-stage breast cancer (stage I or II) and in two thirds of women with late-stage disease (stage III or IV).
- CA 27.29 lacks predictive value in the earliest stages of breast cancer and thus has no role in screening for or diagnosing the malignancy.

Carcinoembryonic Antigen

- Carcinoembryonic antigen (CEA), an oncofetal glycoprotein, is expressed in normal mucosal cells and overexpressed in adenocarcinoma, especially colorectal cancer.
- Benign conditions with higher CEA levels include cigarette smoking, peptic ulcer disease, inflammatory bowel disease, pancreatitis, hypothyroidism, biliary obstruction, and cirrhosis. Levels exceeding 10 ng per mL are rarely due to benign disease.
- Fewer than 25 percent of patients with disease confined to the colon have an elevated CEA level. Sensitivity increases with advancing tumor stage: CEA values are elevated in approximately 50 percent of patients with tumor extension to lymph nodes and 75 percent of patients with distant metastasis. The highest values (above 100 ng per mL) occur with metastasis, although poorly differentiated tumors are less likely to produce CEA.
- CEA is not useful in screening for colorectal cancer or in the diagnostic evaluation of an undefined illness.
- CEA levels typically return to normal within four to six weeks after successful surgical resection.
- The major role for CEA levels is in following patients for relapse after intended curative treatment of colorectal cancer.

Cancer Antigen 19-9

- Elevated levels of CA 19-9, an intracellular adhesion molecule, occur primarily in patients with pancreatic and biliary tract cancers.
- This tumor marker has a sensitivity and specificity of 80 to 90 percent for pancreatic cancer and a sensitivity of 60 to 70 percent for biliary tract cancer.
- Benign conditions such as cirrhosis, cholestasis, cholangitis, and pancreatitis also result in CA 19-9 elevations, although values are usually less than 1,000 units per mL.
- Patients with Lewis-null blood type do not produce CA 19-9. Thus, about 5 percent of persons are unable to produce this antigen.
- The antigen has no value in screening because its positive predictive value is < 1 %.

Alpha-Fetoprotein

- Alpha-fetoprotein is the major protein of fetal serum but falls to an undetectable level after birth.
- The primary malignancies associated with AFP elevations are hepatocellular carcinoma and nonseminomatous germ cell tumors.
- Other gastrointestinal cancers occasionally cause elevations of AFP, but rarely to greater than 1,000 ng per mL.
- Patients with cirrhosis or viral hepatitis may have abnormal AFP values, although usually less than 500 ng per mL.
- Pregnancy also is associated with elevated AFP levels, particularly if the pregnancy is complicated by a spinal cord defect or other abnormality.
- AFP levels are abnormal in 80 percent of patients with hepatocellular carcinoma.

Beta Subunit of Human Chorionic Gonadotropin

The beta subunit of human chorionic gonadotropin (b-hCG) normally is produced by the placenta. Elevated b-hCG levels most commonly are associated with pregnancy, germ cell tumors, and gestational trophoblastic disease. False-positive levels occur in hypogonadal states and with marijuana use.

AFP and b-hCG Levels in Germ Cell Tumors and Gestational Trophoblastic Disease		
Tumor	*AFP elevation*	*b-hCG elevation*
Seminoma and dysgerminoma	Never*	Occasional, minimal

Embryonal cell carcinoma	Yes	Yes
Choriocarcinoma	No	Yes
Yolk sac tumors	Yes	No
Teratoma	No	No
Gestational trophoblastic disease†	No	Yes

AFP = alpha-fetoprotein; b-hCG = beta subunit of human chorionic gonadotropin.
**--Any detectable AFP indicates the presence of a nonseminomatous component; in this situation, the malignancy should be treated as a nonseminomatous germ cell tumor.*
†*--Gestational trophoblastic disease is not a germ cell tumor; rather, it is a rare gynecologic malignancy related to pregnancy.*

Both AFP and b-hCG play crucial roles in the management of patients with nonseminomatous germ cell tumors. The AFP or b-hCG level is elevated in 85 percent of patients with these tumors, but in only 20 percent of patients with stage I disease. Hence, these markers have no role in screening.

In patients with extragonadal disease or metastasis at the time of diagnosis, highly elevated AFP or b-hCG values can be used in place of biopsy to establish a diagnosis of nonseminomatous germ cell tumor. AFP values in excess of 10,000 ng per mL or b-hCG levels above 50,000 mIU per mL at initial diagnosis portend a poor prognosis, with a five-year survival rate of 50 percent. Similarly staged patients with lower AFP and b-hCG levels have a cure rate higher than 90 percent.

Following AFP and b-hCG levels is imperative in monitoring response to treatment in patients who have nonseminomatous germ cell tumors. Patients with AFP and b-hCG levels that do not decline as expected after treatment have a significantly worse prognosis. AFP or b-hCG elevation is frequently the first evidence of germ cell tumor recurrence; a confirmed elevation should prompt reinstitution of therapy.

The b-hCG level is used to diagnose gestational trophoblastic disease, a rare neoplastic complication of pregnancy. The b-hCG value is followed to assess response to treatment and to detect relapse in a manner similar to that for germ cell tumor.

Cancer Antigen 125

CA 125 is a glycoprotein normally expressed in coelomic epithelium during fetal development. This epithelium lines body cavities and envelopes the ovaries.

Elevated CA 125 values most often are associated with epithelial ovarian cancer. CA 125 levels are elevated in about 85 percent of women with ovarian cancer, but in only 50 percent of those with stage I disease. Higher levels are associated with increasing bulk of disease and are highest in tumors with nonmucinous histology. Multiple benign disorders also are associated with CA 125 elevations, presumably by stimulation of the serosal surfaces.

Annual ultrasound examination and CA 125 screening have been advocated for women with hereditary ovarian cancer syndromes.

CA 125 has been used as an adjunct in the diagnosis of pelvic masses. In postmenopausal women with asymptomatic palpable pelvic masses, CA 125 levels higher than 65 units per mL have a positive predictive value of 98 percent for ovarian cancer. Because premenopausal women have more benign causes of elevated CA 125 levels, testing for the marker is less useful in this population.

Prostate-Specific Antigen

Prostate-specific antigen (PSA) is a glycoprotein produced by prostatic epithelium. The PSA level can be elevated in prostate cancer, prostatitis, benign prostatic hypertrophy, and prostatic trauma, as well as after ejaculation.

In men with prostatitis, PSA levels return to normal within eight weeks of symptom resolution. Waiting 48 hours after ejaculation to measure the PSA level has been recommended. Digital rectal examination does not elevate PSA levels above normal values. In men who have been taking finasteride (Proscar) for more than six months, reported PSA levels should be doubled to accurately reflect true values.

In prostate cancer, the positive predictive value of PSA levels greater than 4 ng per mL is 20 to 30 percent and rises to 50 percent when PSA levels exceed 10 ng per mL. Nevertheless, 20 to 30 percent of men with prostate cancer have PSA levels within normal ranges.

In patients with PSA values between 4 and 10 ng per mL, the PSA velocity and percentage of free PSA have been helpful in making clinical decisions. A velocity of 0.75 ng per mL per year is predictive of cancer. When less than 10 percent of PSA is unbound, the positive predictive value for prostate cancer is 55 percent, compared with 8 percent when more than 25 percent of PSA is unbound.

PSA levels predict the presence of metastatic disease. Patients with newly diagnosed prostate cancer and PSA levels below 20 ng per mL rarely have osseous metastasis (lower than 2 percent). In addition, CAT scanning is unnecessary in men with PSA levels below 25 ng per mL.

Cancer of Unknown Primary

Confusion exists about the value of tumor markers in a patient with cancer of unknown primary. Unfortunately, most tumor markers are too nonspecific for this purpose. However, with adenocarcinoma in older men, significant PSA elevations have sufficient specificity to make the diagnosis of prostate cancer.

In poorly differentiated tumors, AFP and b-hCG levels should be ordered. Marked elevations of these tumor markers signify the presence of an extragonadal germ cell tumor. In women with peritoneal carcinomatosis or malignant ascites, treatment for ovarian cancer is instituted if the CA 125 level is elevated.

Tumor Markers In Common Use

		Use of tumor marker			
Tumor marker	*Primary tumor(s)*	*Screening*	*Diagnosis*	*Follow-up after primary treatment*	*Monitoring of treatment response*
CA 27.29[1]	Breast cancer	No	No	Consider in patients at high risk for recurrence; obtain CA 27.29 level every 4 to 6 months.	Helpful
CEA[16]	Colorectal cancer	No	No	In patients at high risk for recurrence, obtain CEA level every 2 to 3 months for at least 2 years.	Very helpful
CA 19-9[5]	Pancreatic cancer, biliary tract cancer	No	Selected pancreatic masses	No	Helpful
AFP[8,20,41]	Hepatocellular carcinoma, nonseminomatous germ cell tumor	No*	Poorly differentiated cancer of unknown primary; patients with cirrhosis and a liver mass	In patients treated for nonseminomatous germ cell tumor, obtain AFP and b-hCG levels every 1 to 2 months for 1 year, then quarterly for 1 year, and less frequently thereafter.	Essential in patients treated for nonseminomatous germ cell tumor; very helpful in patients treated for hepatocellular carcinoma
b-hCG[8,24,41]	Nonseminomatous germ cell tumor, gestational trophoblastic	No	Poorly differentiated cancer of unknown	Nonseminomatous germ cell tumor: In patients treated for gestational	Essential in patients treated for nonseminomatous

	disease		primary; gestational trophoblastic disease	trophoblastic disease, obtain b-hCG level once a month for 6 to 12 months.	germ cell tumor or gestational trophoblastic disease
CA 125[26,27,41]	Ovarian cancer	No†	Adjunct for diagnosis of pelvic mass in postmenopausal women; malignant ascites in women with cancer of unknown primary	Obtain CA 125 level every 3 months for 2 years, then less frequently.	Very helpful
PSA[12,39-41]	Prostate cancer	Yes	Adenocarcinoma of unknown primary; widely positive bone scan and prostate mass	Obtain PSA level every 6 months for 5 years, then annually. Any detectable PSA after radical prostatectomy indicates recurrence. 3 consecutive PSA elevations after radiation therapy indicate recurrence.	Very helpful
CA = cancer antigen; CEA = carcinoembryonic antigen; AFP = alpha-fetoprotein; b-*hCG = beta subunit of human chorionic gonadotropin; PSA = prostate-specific antigen.* **--Except in highly selected patients with nonalcoholic-induced cirrhosis.* †*--Except in heritable ovarian cancer syndromes.*					

Oncogene

An **oncogene** is a modified gene, or a set of nucleotides that codes for a protein, that increases the malignancy of a tumor cell. New research indicates that small RNAs 21-25 nucleotides in length called miRNAs can control expression of these genes by downregulating them.

The first oncogene was discovered in 1970 and was termed SRC (pronounced *SARK*). Src was in fact first discovered as an oncogene in a chicken retrovirus. Experiments performed by Dr G. Steve Martin of the University of California Berkeley demonstrated that the SRC was indeed the oncogene of the virus. In 1976 Drs. J. Michael Bishop and Harold E. Varmus of the University of California San Francisco demonstrated that oncogenes were defective proto-oncogenes, found in many organisms including humans. For this discovery Bishop and Varmus were awarded the Nobel Prize in 1989.

Proto-oncogene

A **proto-oncogene** is a normal gene that can become an oncogene, either after mutation or increased expression. Proto-oncogenes code for proteins that help to regulate cell growth and differentiation. Proto-oncogenes are often involved in signal transduction and execution of mitogenic signals, usually through its protein product. Upon *activation*, it (or its product) becomes a tumor inducing agent, an oncogene.

Activation

The proto-oncogene can become an oncogene by a relatively small modification of its original function. There are two basic activation types:

- A mutation within a proto-oncogene can cause a change in the protein structure, caused by

  - an increase in protein (enzyme) activity
  - a loss of regulation
  - the creation of a *hybrid protein*, through a chromosomal aberration during cell division. A distinct aberration in a dividing stem cell in the bone marrow leads to adult leukemia
- An increase in protein concentration, caused by
  - an increase of protein expression (through misregulation)
  - an increase of protein stability, prolonging its existence and thus its activity in the cell
  - a gene duplication, resulting in an increased amount of protein in the cell

Oncogene

Growth factors

Growth factors, or mitogens, are usually secreted by a few specialized cells to induce cell proliferation in paracrine, autocrine, or endocrine manner. If a cell that usually does *not* produce growth factors suddenly starts to do so (because it developed an oncogene), it will thereby induce its own uncontrolled proliferation (*autocrine loop*), as well as the proliferation of neighboring cells. In addition, abnormal growth of endocrine glands often cause ectopic production of growth hormones that have secondary effects on other parts of the body.

Protein kinases and related proteins

There are six known classes of protein kinases and related proteins that can become an oncogene:

- **Receptor tyrosine kinases** that become constitutively (permanently) active like the epidermal growth factor receptor (EGFR), platelet-derived growth factor receptor (PDGFR), and vascular endothelial growth factor receptor (VEGFR).
- **Cytoplasmic tyrosine kinases** like the Src-family, Syk-ZAP-70 family and BTK family of tyrosine kinases.
- **Regulatory GTPases**, for example, the Ras protein.
- **Cytoplasmic Serine/Threonine kinases and their regulatory subunits**, for example, the Raf kinase, and cyclin-dependent kinases (through overexpression).
- **Adaptor proteins in signal transduction**.
- **Transcription factors**.

Important Oncogenes

Numerous genes have been identified as proto-oncogenes. Many of these genes are responsible for providing the positive signals that lead to cell division. Some proto-oncogenes work to regulate cell death. As stated in the introduction to this section, the defective versions of these genes, known as oncogenes, can cause a cell to divide in an unregulated manner. This growth can occur in the absence of normal pro-growth signals such as those provided by growth factors. A key feature of oncogene activity is that a single altered copy leads to unregulated growth. This is in contrast with tumor suppressor genes which must BOTH be defective to lead to abnormal cell division.

The proto-oncogenes that have been identified so far have many different functions in the cell. Despite the differences in their 0normal roles, these genes all contribute to unregulated cell division if they are present in a mutant (oncogenic) form. The mutant proteins often retain some of their capabilities but are no longer sensitive to the controls that regulate the normal form of the protein. Selected oncogenes that have been associated with numerous cancer types are described in more detail on the pages that follow. To learn about a particular gene, choose from the list below.

- HER-2/*neu* (*erb*B-2): a growth factor receptor.
- *ras*: a signal transduction molecule
- *myc*: a transcription factor
- *src*: a protein tyrosine kinase.
- *hTERT*: an enzyme that functions in DNA replication.

Bcl-2: a membrane associated protein that functions to prevent apoptosis.

TRAUMA

Initial Evaluation of the Trauma Patient
The objectives of the initial evaluation of the trauma patient are (1) to stabilize the trauma patient, (2) to identify life-threatening injuries and to initiate adequate supportive therapy, and (3) to efficiently and rapidly organize either definitive therapy or transfer.

TRIAGE AND ORGANIZATION OF CARE

The objective of triage is to prioritize patients with a high likelihood of early clinical deterioration. When performing a triage with patients having different types of injuries, the priorities of the primary survey help to determine precedence (eg, a patient with an obstructed airway receives greater priority for initial attention than a relatively stable patient with a traumatic amputation).

INITIAL ASSESSMENT

The initial evaluation follows a protocol of primary survey, resuscitation, secondary survey, and either definitive treatment or transfer to an appropriate trauma center for definitive care.

Primary survey

Assessment of ABC: (Assessment and management occur simultaneously)

- **Airway** and cervical spine control
- **Breathing**
- **Circulation** with haemorrhage control.
- **Disability:** Brief neurological evaluation
- **Exposure:** Completely undress the patient.

AIRWAY: In trauma airway problems are due to:

ASSESSMENT

- look in the mouth/oropharynx; Stridor; Cyanosis; Level of consciousness

TREATMENT

- Administer 100% O2 in every case.
- Try chin lift, jaw thrust
- Oral airway
- Suction
- Intubation + Ventilation

BREATHING

LIFE THREATENING PROBLEMS

- Airway obstruction
- Tension/ Open pneumothorax
- Massive haemothorax
- Flail Chest

TREATMENT

Insert 12g cannula into second intercostal space mid clavicular line if tension pneumothorax is suspected. *If the patient is in extreme distress, suspect and treat for tension pneumothorax, prior to applying positive pressure ventilation*.

CIRCULATION

Hypovolemia is the commonest cause of shock in trauma
FLUIDS: Give colloids promptly and in large volumes. Resuscitate not only the BP and pulse but also the urinary output, peripheral return and gut.
BLOOD

LINES
ONGOING ASSESSMENT
OTHER CAUSES OF SHOCK IN TRAUMA
CARDIOGENIC

- Tamponade; Cardiac Contusion; Air Embolism; Acute Myocardial infarct

NEUROGENIC

- High cervical cord lesion; Decreased blood pressure, decreased heart rate and peripherally vasodilated

DISABILITY
Determine if there is any neurological deficit. Assess the GCS.

EXPOSE
Expose the patient
Perform log roll and examine the back
Attend to PR examination. This should be done prior to male catheterisation.

Resuscitation phase

During the primary survey, when making diagnoses and performing interventions, continue until the patient condition is stabilized, the diagnostic workup is complete, and resuscitative procedures and surgeries are complete.

Secondary Survey

Total Evaluation of Patient
Is patient ABC Stable? If yes, then go head to toe, front to back, over the whole patient looking for injuries/complications etc. Constantly reassess ABC's

1. Head and skull (including ears and oral cavity)
2. Maxillofacial injuries
3. Neck
4. Chest
5. Abdomen
6. Perineum/Rectum
7. Extremities
8. Complete neurological examination
9. Appropriate x-rays, laboratory tests, and special studies
10. "Tubes and fingers" in every orifice ie PV / PR.

MONITOR

- ECG
- BP
- O2 saturation
- Core temperature

INSERT

- Urinary catheter
- Gastric tube (Oro-gastric NOT Naso-gastric if head / facial injuries)

X-RAYS

- Cervical spine lateral initially and ensure C7 and Tl are visualised.
- Erect CXR
- Pelvis

BLOODS

- ABG - Remember acidosis is a sensitve indicator of the effectiveness of resuscitation. Repeat frequently.
- X match
- FBC

- UEC, LFT, AMY
- Blood Glucose

Head Trauma

TBI may be divided into 2 broad categories, closed head injury and penetrating head injury. The Glasgow Coma Score (GCS) is used to describe the level of consciousness of TBI patients. The GCS is divided into 3 categories, eye opening (E), motor response (M), and verbal response (V). The score is determined by the sum of the score in each of the 3 categories, with a maximum score of 15 and a minimum score of 3, as follows:

Glasgow Coma Scale

** Add up the score for 1, 2 and 3.			
1. Eyes	Open	Spontaneously	4
		To loud verbal command	3
		To pain	2
	No response		1
2. Best Motor Response	To verbal command	Obeys	6
	To painful stimuli	Localises pain	5
		Flexion—withdrawal	4
		Flexion—abnormal (decorticate rigidity)	3
		Extension (decerebrate rigidity)	2
		No response	1
3. Best Verbal Response		Oriented and converses	5
		Disoriented and converses	4
		Inappropriate words	3
		Incomprehensible sounds	2
		No response	1

GCS = E + M + V: **E + M + V = 3 to 15**

RELEVANT ANATOMY AND CONTRAINDICATIONS

The intracranial compartment is divided into 3 compartments by 2 major dural structures, the falx cerebri and the tentorium cerebelli. The tentorium cerebelli divides the posterior fossa or infratentorial compartment (the cerebellum and the brainstem) from the supratentorial compartment (cerebral hemispheres). The falx cerebri divides the supratentorial compartment into 2 halves and separates the left and right hemispheres of the brain. Both the falx and the tentorium have central openings and prominent edges at the borders of each of these openings. When there is a significant increase in ICP, the brain can slide through these openings within the falx or the tentorium, a phenomenon known as herniation. As the brain slides over the free dural edges of the tentorium or the falx, it frequently is injured by the dural edge.
Several types of herniation exist, as follows: (1) transtentorial herniation, (2) subfalcine herniation, (3) central herniation, (4) upward herniation, and (5) tonsillar herniation.

Transtentorial (2)

- herniation of uncus through tentorial hiatus.
- Signs:
    1. Compression of 3rd cranial nerve causing ipsilateral dilatation of pupil.
    2. Pyramidal tract compression causes contralateral hemiparesis.
    3. Lateral displacement of the brain stem causing an ipsilateral hemiparesis.
    4. Posterior cerebral artery kinking causing cerebral ischaemia / hemianopia.
    5. Brain stem compression resulting in deterioration of the level of consciousness leading to coma,

6. Hypertension and bradycardia (Cushing response and respiratory failure, which may be manifested as Cheyne-Stokes periodic breading pattern.)

Foramen magnum (4)

- Increased pressure within the posterior fossa will result in herniation of the cerebellar tonsils into the foramen magnum and compression of the medulla.
- Signs:
    1. If slowly progressing the patient may develop abnormal neck posture and a child may develop a neck tilt.
    2. Rapid respiratory failure.
    3. May cause abrupt limb paresis and sensory disturbance.

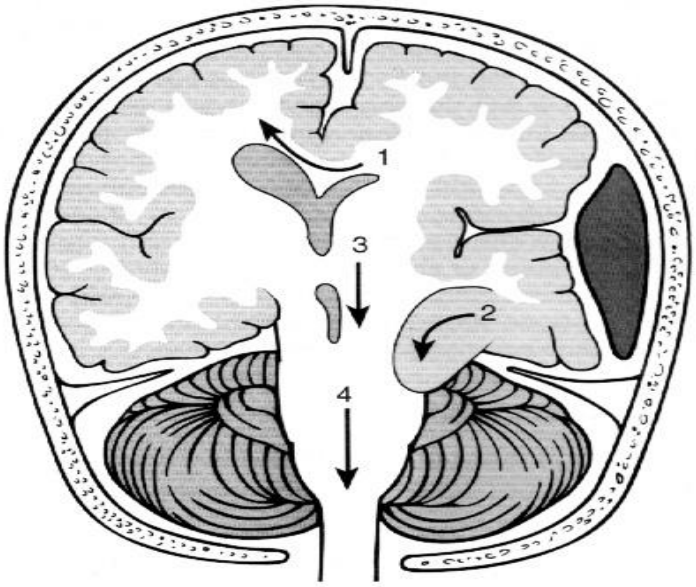


Fig. 3.3 Brain herniations. A lateral supratentorial mass will cause displacement of the lateral ventricles with (1) subfalcine herniation of the cingulate gyrus below the falx cerebri; (2) herniation of the uncus into the tentorial hiatus; (3) caudal displacement of the brain stem. Raised pressure within the posterior fossa may cause herniation of the cerebellar tonsils into the foramen magnum (4). (Adapted from Jennett and Teasdale 1981. Reproduced with permission.)

Transtentorial Herniation (Uncal Herniation)

Important structures running through the tentorial hiatus:

Midbrain, 3rd cranial N. and the posterior cerebral arteries.

Stage I

- Ipsilateral pupilary dilation & loss of its reaction to light and accommodation.
- Contralateral hemiperesis.

Stage II

- Contralatral pupillary dilatation

Stage III (Kernohans notch)

- Ipsilateral hemiparesis.
- Also, the posterior cerebral artery may be kinked or compressed, leading to a medial occipital infarct. It would result in homonymous hemianopia

Monro-Kellie Doctrine: Simple concept but vital for the understanding of intracerebral pathologies and dynamics. **Monro-Kellie doctrine states that the total intracranial volume is fixed because of the**

inelastic nature of the skull. The intracranial volume (V i/c) is equal to the sum of its components, as follows:

V i/c = V (Brain) + V (CSF) + V (Blood)

Intracranial Pressure

- Normal ICP <10mmHg (136 mm water)
- 20 mmHg < is abnormal.
- 40 mmHg < severe elevation.
- The higher the ICP after head injury the worst the outcome
- ICP value gets elevated at point of decompensation.
- When ICP starts going up the patient will rapidly decompensate and herniation is imminent

Signs of increased ICP:

- **Headache:**
- **Nausea and vomiting**, usually worse in the morning.
- **Drowsiness**. Important clinical sign not to be dismissed.
- **Papilloedema.**

1. Due to transmission of the pressure in the subarachnoid sheath to the optic nerve.
2. "Filling in" of the optic cup and dilatation of the retinal veins.
3. Failure of the normal pulsations of the retinal veins.
4. Blurring of the disk margins.
5. Flame shaped haemorrhages along disk margins and alongside the vessels.
6. Optic atrophy may develop in long standing raised ICP.

- 6th nerve palsy, causing diplopia may occur in raised ICP due to stretching of the 6th nerve by caudal displacement of the brain stem." False localising sign"
- Bulging fontanelles in infant.

Cerebral Perfusion Pressure.

- The CPP is just as important as the intracranial pressure.

CPP= Mean Arterial Blood Pressure - ICP

- CPP 70mmHg> is generally associated with a poorer outcome.

Cerebral Blood Flow.

- Normal: 50mL/100g of brain/minute.
- Below a CBF of 20 to 25 mL/100g/min, the EEG activity gradually disappears.
- Around 5 mL/100g/min there is cell death or irreversible brain damage.
- Autoregulation between 50 and 160mmHg mean pressure.
- Autoregulation is impaired in head injured patients

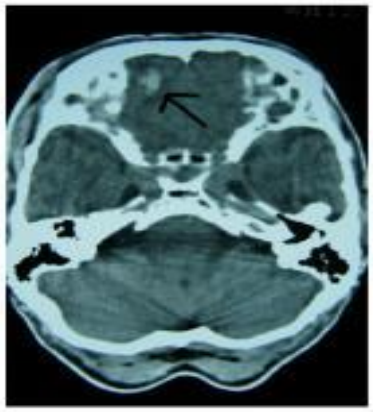
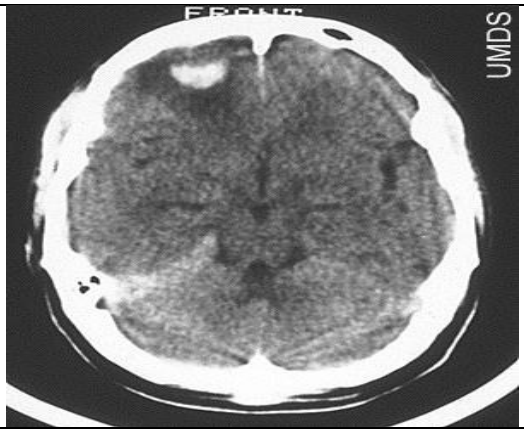
IMAGING STUDIES:

***Skull x-rays*:** are used occasionally in the evaluation of penetrating head trauma to provide a rapid assessment of the degree of foreign body penetration in nonmissile penetrating head injuries (eg, stab wounds) or in gunshot wounds to screen for retained intracranial bullet fragments.

CT scan

- A CT scan is the diagnostic study of choice in the evaluation of TBI.
- The standard CT scan for the evaluation of acute head injury is a noncontrast scan, from the base of the occiput to the top of the vertex in 5-mm increments.
- Each intracranial structure has a characteristic density, which is expressed in Hounsfield units. On this scale, CSF has a density of (+) 4 to (+) 10 units, white matter has a density of (+) 22 to (+) 36 units, and gray matter has a density of (+) 32 to (+) 46 units. Extravascular blood has a density of (+) 50 to (+) 90 units, and calcified tissue and bone have a density of (+) 800 to (+) 1000 units.

- Extra-axial hematomas include epidural (extradural) and subdural hematomas. Epidural hematomas are located between the inner table of the skull and the dura. They typically are **biconvex** in shape. **Epidural hematomas usually are caused by injury to an artery, although 10% of epidural hematomas may be venous in origin**.
- Subdural hematomas are located between the dura and the brain. **Their outer edge is convex, while their inner border is usually irregularly concave. Subdural hematomas usually are venous in origin**, although some subdural hematomas are caused by arterial injuries. The classic cause of a posttraumatic subdural hematoma is an injury to one of the bridging veins that travel from the cerebral cortex to the dura.
- Intra-axial hematomas are defined as hemorrhages within the brain parenchyma. These hematomas include **intraparenchymal hematomas, intraventricular hemorrhages, and subarachnoid hemorrhages.** Subarachnoid hemorrhages that occur because of trauma typically are located over gyri on the convexity of the brain. The subarachnoid hemorrhages that occur as the result of a ruptured cerebral aneurysm usually are located in the subarachnoid cisterns at the base of the brain.

	
Frontal contusions on head CT scan (arrow)	There is a focal area of haemorrhagic contusion in the right frontal lobe, with surrounding low density due to infarction or oedema. This is a frequent location for a contre-coup injury following a blow to the back of the head.

MRI: Although MRI provides extraordinary anatomic detail, it is not commonly used to evaluate acute head injuries because of its long acquisition times and the difficulty in obtaining MRIs in persons who are critically ill. **MRI is superior to CT scan in identifying diffuse axonal injury (DAI) and small intraparenchymal contusions.**

Contusions

- The contusions occurring under the point of impact are called coup contusion.
- The centre coup contusions occur opposite the impact site.
- The most common site of contusion are the under surface of the frontal & temporal poles.

Diffuse Brain Injuries

- Concussion: A "classical concussion" is an injury that results in loss of consciousness. The loss of consciousness is transient and reversible.

DAI (Diffuse axonal injury)

These patients remain in deep coma for prolonged period.

Skull Fracture

Diagnosis

- The basal fractures are not usually picked up on plain x-rays and are readily shown by axial CT.
- Also helpful are the clinical signs of basal skull fracture.

Anterior Fossa fractures

- Epistaxis.
- Rhinorrhea.
- Anosmia
- "Panda eyes" or "raccoon eyes".

Middle cranial Fossa

- 'Battle sign'
- CSF otorrhea
- Severe hearing loss & vertigo.
- Diabetes insipidus or SIADH

TREATMENT

Medical therapy: The treatment of head injury may be divided into the treatment of closed head injury and penetrating head injury.

Closed head injury

Mild head injury

Most head injuries are mild head injuries. Many of these patients require only minimal observation after they are assessed carefully, and many do not require radiographic evaluation. These patients may be discharged if a reliable individual can monitor them.

Patients with mild head injuries typically have concussions. A concussion is defined as physiologic injury to the brain without any evidence of structural alteration. As many as 30% of patients who experience a concussion develop postconcussive syndrome (PCS). PCS consists of a persistence of any combination of the following after a head injury: headache, nausea, emesis, memory loss, dizziness, diplopia, blurred vision, emotional lability, and sleep disturbances. Fixed neurologic deficits are not part of PCS, and any patient with a fixed deficit requires careful evaluation.

Moderate and severe head injury

The treatment of moderate and severe head injuries begins with initial cardiopulmonary stabilization. After a thorough neurologic assessment,a CT scan of the head is obtained.

Most neurosurgeons consider any of the following as **indications for surgery** in patients with head injuries: ***extra-axial hematoma with midline shift greater than 5 mm, intra-axial hematoma with volume greater than 30 cc, an open skull fracture, or a depressed skull fracture with more than 1 cm of inward displacement. In addition, any temporal or cerebellar hematoma that is more than 3 cm in diameter is considered a high-risk hematoma because these regions of the brain are smaller and do not tolerate additional mass as well as the frontal, parietal, and occipital lobes. These high-risk temporal and cerebellar hematomas usually are evacuated immediately***

If no surgical lesion is present on the CT scan, treatment of the head injury begins. The first phase of treatment is to institute general measures. Once appropriate fluid resuscitation has been completed, **intravenous fluids** are administered to maintain the patient in a state of euvolemia or mild hypervolemia. The use of **anticonvulsants** in TBI is a controversial issue.

When treating elevated ICP, remember that the goal of treatment is to optimize conditions within the brain to prevent secondary injury and to allow the brain to recover from the initial insult.

CSF accounts for 2-3% of total intracranial volume. In adults, total CSF production is approximately 20 cc/hour or 500 cc/day. In many patients with TBI who have elevated ICP, a ventriculostomy may be placed and CSF may be drained. Removal of small amounts of CSF hourly can result in improvements in compliance that result in significant improvements in ICP.

Brain or tissue comprise 85-90% of the total intracranial volume. When significant brain edema is present, it causes an increase in the tissue component of the total intracranial volume and results in decreased compliance and increased ICP. Treatments for elevated ICP that reduce total brain volume include diuretics, perfusion augmentation (CPP strategies), metabolic suppression, and decompressive procedures.

Mannitol, an osmotic diuretic, is the most common diuretic used. Mannitol is a sugar alcohol that draws water out from the brain into the intravascular compartment. The standard dose ranges from 0.25-1 g/kg, administered every 4-6 hours. Other diuretics that sometimes are used in patients with TBI include furosemide, glycerol, and urea.

Management of severe head injury
Preempt measures to control ICP:

- Sedation with narcotics
- Paralysis with nm blockers
- Prophylactic anticonvulsants
- Mild hyperventilation
- Bolus mannitol

If no surgical lesions on CT or following the operation, shift the patient to ICU and direct intracranial pressure is recorded through a ventriculostomy catheter.

Normal supine ICP is 120 - 150 mm of CSF or 10 - 15 mm He.

Specific measures:

Mannitol

Mannitol does not easily cross the BB barrier and osmotically draws the extracellular water from brain.
Problems with Mannitol

- Significant osmotic diuresis can result in hypotension
- Accumulated mannitol may leak through BBB, leading to rebound intracranial hypertension.

CSF drainage

- Produces an immediate fall in ICP.

Hyperventilation

A rapid method of reducing ICP.
MOA - CSF alkalosis leads to localized vasoconstriction.
Excessive hyperventilation can produce significant vasospasm and hypoxia. So keep $PaC0_2$ approximately 30 mmHg.

Barbiturates

Act by reducing cerebral metabolic rate for **O2** and a coupled reduction in CBF However systemic hypotension and pulmonary failure may result. Presently, barbiturates are generally used when other medical managements have failed

Indications for surgery

1. Significant mass effect i.e. - displacement more than 5 mm.
2. Decline in the conscious state, focal neurological symptoms or ↑ ICP.

Surgery

Craniotomy (Preferred)
Craniectomy if the neurological deterioration is rapid and does not permit for a CT.

CSF rhinorrhoea

Initial management: conservative. If no improvement, surgery indicated.

Early and Late Posttraumatic Seizures

- Early (within the first week after injury)
- Late (after the first week after injury).

- Early PTSs are more common in children, usually focal and amenable to prophylaxis. Late PTS are more common in adults and usually GTCS.
- Treatment:
  - Early PTS: IV phenytoin (DOC).
  - Late PTS: Antiepileptic drugs (AEDs) do not influence the outcome.

Penetrating trauma

The treatment of penetrating brain injuries involves 2 main aspects. The first is the treatment of the TBI caused by the penetrating object. Penetrating brain injuries, especially from high-velocity missiles, frequently result in severe ICP elevations which is identical to the treatment of closed head injuries.

The second aspect of penetrating head injury treatment involves debridement and removal of the penetrating objects.

Head injury in children

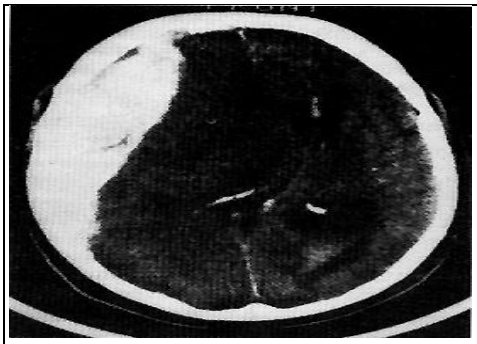
Head injuries in children differ from head injuries in adults in several ways. Children tend to have more diffuse injuries than adults, and traumatic intracerebral hematomas are less common in children than in adults. In addition, early posttraumatic seizures are more common in children than in adults.

SUBDURAL HAEMATOMAS

- Subdural haematomas may be classified into acute, subacute and chronic.

1. **Acute subdural haematoma** - less than 3 days. Hyper dense (**white on CT**)
2. **Subacute subdural haematoma** - 4-21 days. Isodense (**similar to brain on CT**)
3. **Chronic subdural haematoma** - more than 21 days. Hypo dense (**dark on CT**)

- Occur much more frequently from tearing of **bridging veins.**
- May be associated with arterial lacerations on the brain surface.
- Subdural haematomas normally cover the e**ntire surface** of the hemisphere.



Acute Subdural.
Up to 1/3 of patients have a **lucid period**. Majority are drowsy/ comatosed. Arousable patients may complain of unilateral headache and frequently have a slight **enlarged pupil on that side** (5-10% contralateral). Brain damage more severe, prognosis worse than for extradural haematomas. Bilateral in about 1/3 of cases, compared to 3% in extradural haematomas.

Chronic Subdural haematoma.

- Preceding trauma less clear.
- 20-30% give no history of preceding trauma (esp. elderly patients with bleeding diathesis).
- History stretching weeks or month of:

1. Slowed thinking.
2. Confusion.
3. Changes in personality.
4. seizures.
5. +/- mild hemiparesis.
6. Fluctuation in the level of consciousness may occur.
7. May be bilateral.
8. Initially usually diagnosed as stroke, brain tumor, drug intoxication, depression, and senile or other dementia.

- Patient may present with "spells" of hemiparesis of aphasia lasting for 10min and indistinguishable from TIA's
- CT: Low-density mass over convexity of the hemisphere 2-6 weeks after the initial bleed, may show only a shift of the midline structures.
- LP- may cause worsening tissue shifts and should be avoided but if done will demonstrate **xanthochromia +variable RCC's**

Treatment

- Glucocorticoids alone may suffice **in some cases**.
- Surgical evacuation is most often successful.
- Pseudomembranes that grow from the dura and encapsulate the region require surgical resection to prevent recurrent fluid accumulation.
- Small haematomas are largely resorbed and only organising membrane remains, which may become calcified in time.

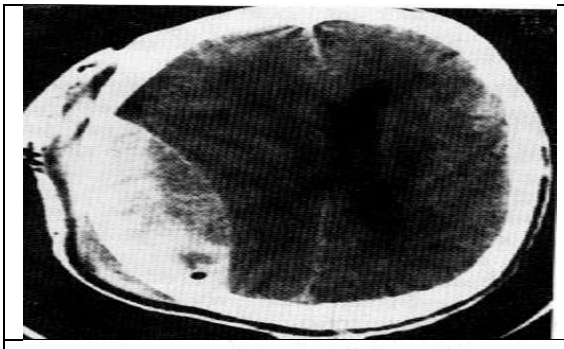
Extradural Haematomas.

- **Young age group** as the dura can more easily be striped away from bone.
- A fracture overlies the haematoma in nearly all (95%) adults and most (75%) children.
- Features of increased ICP may develop:

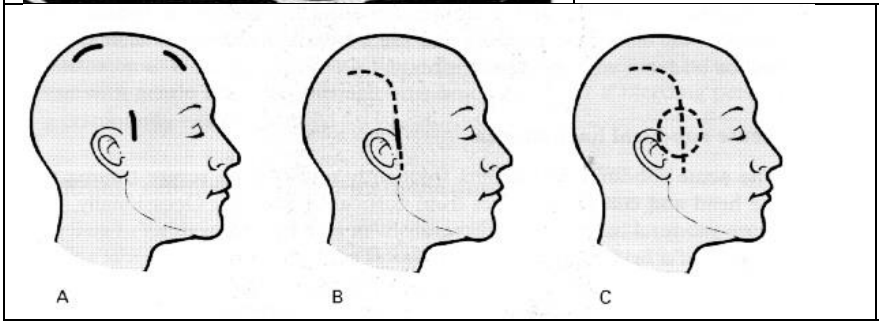
1. Headache
2. Deteriorating conscious state
3. Focal neurological signs (dilated pupil, hemiparesis)
4. Change in vital signs.

Treatment

- **Urgent CT** as soon as the diagnosis is suspected.
- In a rapidly deteriorating patient an **infusion of mannitol or frusemide** may be useful to buy to for the patient to be rapidly transferred to the operating theatre.
- It is a surgical emergency and **Urgent evacuation** is needed.
- Prognosis is excellent if haematoma is drained early.
-



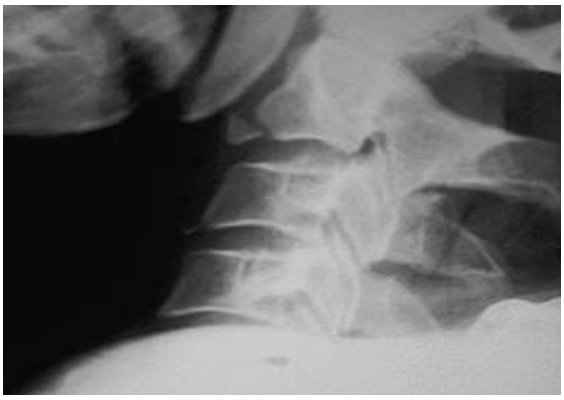
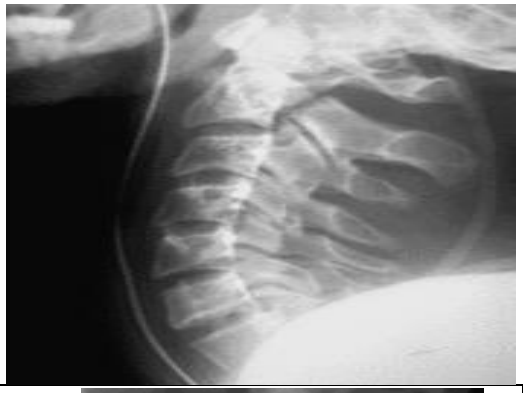
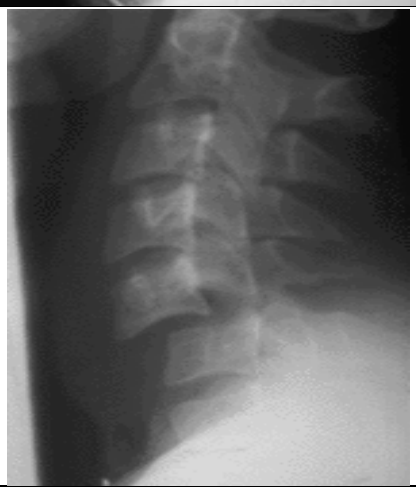
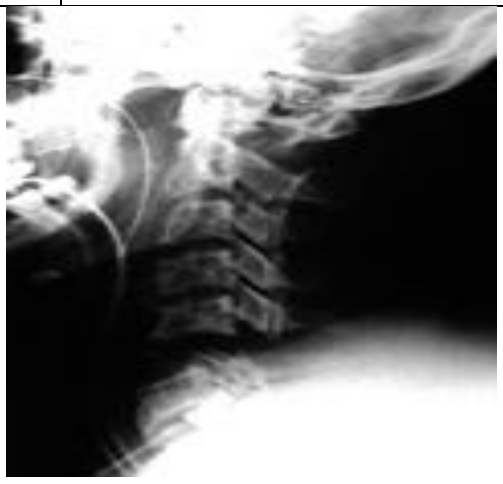
Most common cause of an extradural is a **torn middle meningeal artery but also extradural veins, the superior sagital veins, transverse sinus or posterior meningeal artery**.



Surgical access to the brain.

Cervical Spine

- All patients with head trauma or maxillofacial trauma should be presumed to have an unstable cervical spine injury until positively excluded.
- Absence of neurological deficit does not exclude cervical spine injury.
- Examination of the c-spine is impaired in comatosed patients.

	This injury is known as **extension teardrop fracture**. This injury is secondary to a hyperextension mechanism and usually involves the **second cervical vertebrae**. It is seen most often in the elderly. This injury is potentially unstable.
	This is known as a **hangman's fracture** and consists of **fractures through the pedicles of C-2** (traumatic spondylolithisis of the axis). The injury occurs with hyperextension and commonly, following car accidents. In this patient with little displacement, the anterior and longitudinal ligaments are intact and the injury is relatively stable. With marked anterior displacement, the ligaments are ruptured and the injury is unstable.
	
This is an injury known as a **bilateral facet dislocation**. This injury occurs with hyperflexion (car accident or dive into pool, etc). The injury is quite unstable and the patient is virtually always a quadraplegic (poor prognosis). Treatment in the ED consists of supportive care, high dose steroids, and placement of a halo. Traction is placed until the	C5/C6 dislocation, fracture

fracture is reduced.	

Chest Trauma

The major pathophysiologies encountered in blunt chest trauma involve derangements in the flow of air, blood, or both in combination. Blunt trauma commonly results in chest wall injuries (eg, rib fractures). Direct lung injuries, such as pulmonary contusions, are frequently associated with major chest trauma and may impair ventilation by a similar mechanism. Shunting and dead space ventilation produced by these injuries can also impair oxygenation. Space-occupying lesions; pneumothoraces, hemothoraces, and hemopneumothoraces, interfere with oxygenation and ventilation by compressing otherwise healthy lung parenchyma.

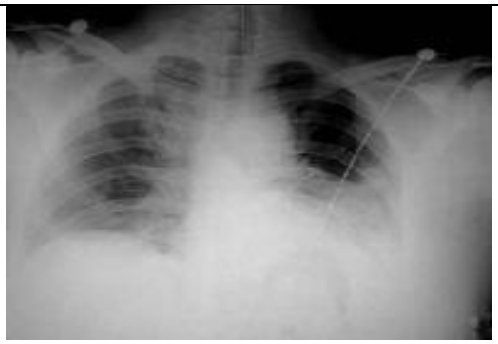
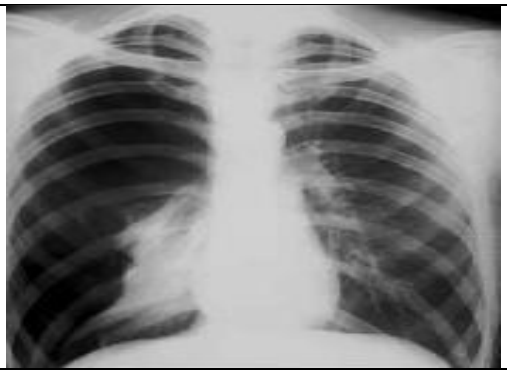
Primary survey chest injuries	Secondary survey chest injuries
• Airway obstruction • Tension pneumothorax • Open pneumothorax • Massive haemothorax • Pericardial tamponade	• Pulmonary contusion • Myocardial contusion • Aortic disruption • Traumatic diaphragmatic hernia • Tracheobronchial disruption • Oesophageal disruption

Lab studies

Complete blood cell count; Arterial blood gas; Serum chemistry profile; Coagulation profile; Serum troponin levels (Troponin is a protein specific to cardiac cells. Elevated serum troponin I levels correlate with the presence of echocardiographic abnormalities in patients with possible blunt cardiac injuries.

Imaging studies

Chest radiographs: A CXR is an important in the diagnosis of many conditions, including chest wall fractures, pneumothorax, hemothorax, and injuries to the heart and great vessels (eg, enlarged cardiac silhouette, widened mediastinum). *Tension pneumothorax should be immediately decompressed before obtaining a CXR.*

	
Left hemothorax in a patient with rib fractures.	Right-sided pneumothorax due to a stab wound.

Chest CT scan: Chest CT scans are more sensitive than CXRs for the detection of injuries such as pulmonary contusions.

Thoracic ultrasound: Pericardial effusions or tamponade can be recognized, as can hemothoraces associated with trauma.

Chest injury: Rib fractures

Rib fractures are the most common blunt thoracic injuries. Physical findings include local ***tenderness and crepitus*** over the site of the fracture. Rib fractures do not require surgery. Pain relief and the establishment

of adequate ventilation are the therapeutic goals. If a fractured rib lacerates an intercostal artery or other vessel, it requires surgical control.

Flail chest

*When **3 or more consecutive ribs are fractured in 2 or more places,** a free-floating, unstable segment of chest wall is produced. This is called flail chest. Physical examination reveals **paradoxical motion** of the flail segment.* The chest wall moves inward with inspiration and outward with expiration. Endotracheal intubation and ***positive pressure mechanical ventilation*** is treatment of choice. Various operations have been devised for correcting flail chest. These include the application of external fixation devices or the placement of plates or pins for internal fixation.

Chest x-ray will show	**Indications of intubation are:**
• Multiple rib fractures • Underlying lung contusion • Hemopneumothorax	• Significant other injuries (ISS >50) • Respiratory rate more than 35 per min • Partial pressure oxygen less than 8.0 kPa • Partial pressure carbon dioxide greater than 6.6 kPa • Vital capacity less than 12 ml / kg • Right to left shunt of more than 15%

Pneumothorax

Pneumothorax is most frequently caused when a fractured rib penetrates the lung parenchyma. Physical examination demonstrates ***decreased breath sounds and hyperresonance*** to percussion over the affected hemithorax. All patients with pneumothoraces due to trauma need a tube thoracostomy. The chest tube is connected to a collection system and placed to water seal.

Hemothorax

The accumulation of blood within the pleural space can be due to bleeding from the chest wall (eg, lacerations of the intercostal or internal mammary vessels attributable to fractures of chest wall elements) or to hemorrhage from the lung parenchyma or major thoracic vessels. Most hemothoraces are associated with a ***decrease in breath sounds and dullness to percussion over the affected area.*** Hemothoraces are evacuated using tube thoracostomy. Large, clotted hemothoraces may require an operation for evacuation to allow full expansion of the lung and to avoid the development of other complications such as fibrothorax and empyema. Thoracoscopic approaches can also be used.

Points to remember:

- Pleural cavity can hold up to 3 litres of blood.
- One litre may accumulate before apparent on chest x-ray (angles are obliterated at 500 ml).
- 90% due to injury to internal mammary or intercostal vessels.
- 10% from pulmonary vasculature.
- Bleeding usually stops when lung re-expanded.
- Most require no more than simple chest drainage.

Indications for surgery:

Indications for emergency room thoracotomy	***Indications for urgent thoracotomy***
• Acute pericardial tamponade unresponsive to cardiac massage • Exsanguinating intra-thoracic haemorrhage • Intra-abdominal haemorrhage requiring aortic cross clamping • Need for internal cardiac massage	• Chest drainage >1500 ml or >200 ml per hour • Large unevacuated clotted haemothorax • Developing cardiac tamponade • Chest wall defect • Massive air leak despite adequate drainage • Proven great vessel injury on angiography • Proven oesophageal injury

	• Proven diaphragmatic laceration • Traumatic septal or valvular injury of the heart

Open Pneumothorax: This injury is commonly caused by penetrating mechanisms but may occur with blunt thoracic trauma. Patients are typically in respiratory distress. Examination reveals a chest wall defect that is larger than the cross-sectional area of the larynx. The affected side demonstrates a complete loss of breath sounds. The increased intrathoracic pressure can shift the contents of the mediastinum to the opposite side, decreasing the return of blood to the heart, leading to hemodynamic instability.
Treatment for an open pneumothorax consists of placing an occlusive dressing over the wound. A tube thoracostomy is then performed. After initial stabilization, wound debridement and closure is done.

Tension pneumothorax
With a tension pneumothorax, air continues to leak from an underlying pulmonary parenchymal injury, increasing pressure within the affected hemithorax. Patients are in respiratory distress, breath sounds are absent, and the hemithorax is hyperresonant. The trachea is deviated away from the side of the injury. The mediastinal contents are shifted away from the affected side. Immediate therapy for this life-threatening condition includes decompression of the affected hemithorax by ***needle thoracostomy***. A large-bore needle (ie, 14- to 16-gauge) is inserted through the second intercostal space in the midclavicular line. A tube thoracostomy is then performed.

Pericardial tamponade
- Haemopericardium prevents diastolic filling of the heart
- ***Classic signs are Beck's triad***
    - ***Hypotension***
    - ***Venous distension***
    - ***Muffled heart sounds***
- May be associated with pulsus paradoxus
- Chest x-ray shows a globular heart
- Unstable patient requires urgent thoracotomy
- In stable patient diagnosis can be confirmed by
    - Echocardiography/ Pericardiocentesis
- Subxiphoid pericardiotomy is both a diagnostic and therapeutic procedure.

Burn
The initial approach to the burn victim is the same as any trauma victim: Airway with C-spine control, Breathing, Circulation. Never assume the burn victim is merely burned. The burn victim may have been injured by an explosion or fall. Airway compromise or lung injury may be present. Shock is often present in severely burned patients. If airway burns are present, immediate intubation is wise. Once edema develops, intubation may be impossible, and even cricothyrotomy may not be successful due to upper tracheal edema. **Burns may be classified into six major groups:**

Scalds	Liquids 1. Splash type injury 2. Immersion injury Grease Steam
Contact Burns	
Fires	Flash Flame
Chemical	
Electrical	

Radiation

Burns are graded as first-, second-, third- or fourth-degree.

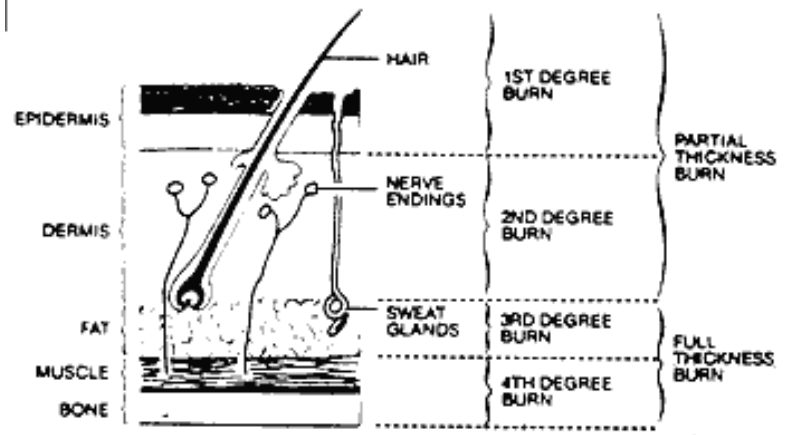


Figure 2. Cross Section of Skin

Depth of burns	Depth	Presentations
1st	Epidermis	Painful, dry, hyperemic (red) areas, blanches on pressure & no blisters.
2°(Superficial)	Epidermis and superficial dermis	Most Painful, hypersensitive, pink blanching , with bullae and blisters.
2nd (Deep 2°)	Epidermis and deep dermis	Painful, pale waxy , no blanching. Blisters are thick walled and few.
3rd	Full-thickness injury	Painless, insensate and dry.

For adults and children, the American Burn Association grades the level of care required for burns as follows:

Minor burns -- these can be managed on an outpatient basis:	**Moderate burns** -- these should be managed on an inpatient basis:	**Major burns** -- these require transfer to a specialized burn center:
• <10% total body surface area (TBSA) in an adult • <5% TBSA in young or elderly • <2% full thickness burn	• 10-20% TBSA burn in an adult • 5-10% TBSA in young or elderly • 2-5% full thickness burn • Suspected inhalation injury • Circumferential burn • Associated medical problem, e.g., diabetes	• >20% TBSA burns in adult • >10% TBSA burns in young or elderly • >5% full thickness burn • inhalation injury • Significant burn to face, eyes, genitalia or joints • Significant associated traumatic injury

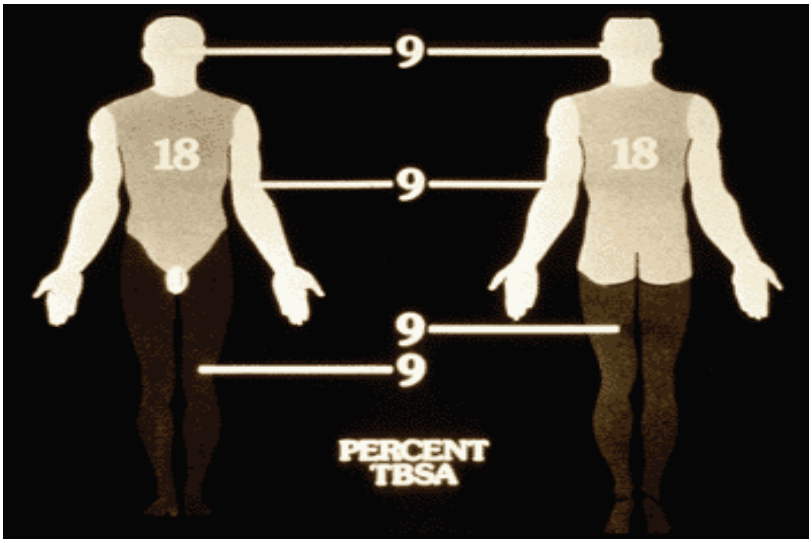
Superficial burns, those without blistering or evidence of deeper skin damage, are best managed simply with a lotion and antibiotics. Burns which have blistered (second-degree burns) should have large blisters, or blisters which have burst, débrided.

An antibiotic ointment is then applied. Traditionally, this has been **silver sulfadiazine.** This agent should be avoided on the face (ophthalmic bacitracin is a better choice), if there is a history of sulfa drug allergy, and in the very young, when there is a danger of kernicterus. The ointment is applied twice a day and covered with a gauze dressing.

Sometimes, patients with even superficial burns will develop infection in the burn. The typical organism is ***Streptococcus pyogenes*** and it is often highly sensitive to penicillin. Recently, however, *Staphylococcus aureus* has emerged as a common organism.

The first few hours after a **major burn** are associated with massive fluid shifts, resulting in profound shock if not corrected. Later, there is a hyperdynamic phase, as the body meets the increased metabolic demands placed upon it. Initially, the patient should be assessed in the usual fashion with attention paid to the airway, breathing and circulation. In cases of burns, breathing may be compromised by the presence of circumferential burns around the chest wall. These burns result in restriction of chest expansion and thus respiratory compromise. If this is the case, then an escharotomy should be considered. ***Escharotomy is the procedure of incising through the burnt tissue until healthy tissue is reached***. Escharotomies may also be limb saving procedures when there are circumferential burns around arms, legs or digits, compromising the circulation, unless the pressure is released. In general, escharotomies should be performed on the midlateral or medial aspects of limbs or digits in order to prevent joint exposure.

The '**rule of nines**' refers to a mechanism to evaluate the extent of the burns.



Rule of 9's: The major body areas are divided such that each area is a multiple of nine. The head represents 9% of the body surface, and each arm is 9%. The front of each leg (to the groin) is 9%, and the back 9%. The front of the torso is 18%, and the back is 18%.
The remaining 1.0% of the body surface area is allocated to the perineum. Another rule of thumb is that the palm of the hand represents 0.5% of the body surface area.
In children, the preferred method of assessment of the extent of the burn area is through the use of the **Lund-Browder chart**.
Formulae to calculate the fluid requirements of the burn victim:
Evans formula (1 ml/kg/% burn of 0.9% saline + 1 ml/kg/% burn colloid + 2L dextrose 5%) and the **Brooke formula** (same as above but 1.5 ml/kg/% burn of Lactated Ringer's and 0.5 ml/kg/% burn of colloid). However, the most widely accepted formula is the **Parkland formula**, which calls for 4 ml/kg/% burn of Lactated Ringer's solution. Half of this volume should be given in the first 8 hours after the burn, while the remaining 50% should be given over the next 16 hours. All of these formulae rely upon monitoring urine output as a guide to adequacy of fluid resuscitation. Urine output should be no less than 0.7ml/kg/hr. If urine output is inadequate, increase infusion by 200 ml in next hour.
Potassium is usually elevated 24-36 hours following the burn due to lysis of cells. After 72 - 96 hours, hypokalaemia may develop as cell membranes regain their integrity.
Burns 20% or greater carry a high incidence of paralytic ileus and Curling Ulcer.

Flame burns to the neck and chest may contribute to respiratory difficulties as the inelastic eschar of the anterior and posterior thorax inhibits respiratory efforts.
Escharotomies may be necessary

Management of Burns
An evaluation of the Airway, Breathing, and Circulation (the ABCs) should receive first priority.
Smoke inhalation causes more than 50% of fire-related deaths. Most injuries result from the inhalation of toxic smoke; however, super-heated air may rarely cause direct thermal injury to the upper respiratory tract. Patients who are breathing spontaneously and at risk for inhalation injury should be placed on high-flow humidified oxygen. These patients may have facial burns, singeing of the eyebrows and nasal hair, pharyngeal bums, carbonaceous sputum, or impaired mentation. A change in voice quality, stridorous respirations, or wheezing may be noted. The upper airway may be visualized by laryngoscopy, and the tracheobronchial tree should be evaluated by bronchoscopy. **Chest radiography is not sensitive for detecting inhalation injury.**
Patients who have suffered an inhalation injury are also at risk for carbon monoxide (CO) poisoning. The pulse oximeter is not accurate in patients with CO poisoning because only oxyhemoglobin and deoxyhemoglobin are detected. Co-oximetry measurements are necessary to confirm the diagnosis of CO poisoning. Patients exposed to CO should receive 100% oxygen using a nonrebreather face mask. Hyperbaric oxygen (HBO) therapy reduces the half-life of CO to 23 minutes. HBO is recommended for patients with COHb levels greater than 25%, myocardial ischemia, cardiac dysrhythmias, or neuropsychiatric abnormalities. HBO is also recommended for pregnant women and young children with COHb levels of 15% or greater.

Medical Treatment
Burn Assessment
After completion of the primary survey, a secondary survey should assess the depth and total body surface area (TBSA) burned.
First-degree burns involve the epidermis layer of the skin, but not the dermal layer. These injuries are characterized by pain, erythema, and lack of blisters. These burns heal without scar formation.
Second-degree burns are subdivided into superficial and deep partial-thickness burns.
Superficial partial-thickness burn injury involves the papillary dermis, containing pain-sensitive nerve endings. burn management, burns, burn Blisters or bullae may be present, and the burns usually appear pink and moist. These burn injuries heal with little or no scarring.
Deep partial-thickness burn injury damages both the papillary and reticular dermis. These injuries are painful and often appear white or mottled pink. Deep partial-thickness burns can produce significant scarring.
Full-thickness or third-degree burns involve all layers of the epidermis and dermis and may destroy subcutaneous structures. They appear white or charred. These burns are usually insensate because of destruction of nerve endings, but the surrounding areas are extremely painful. Third-degree burns are best treated with skin grafting to limit scarring.
Fourth-degree burns involve structures beneath the subcutaneous fat, including muscle and bone.
Estimation of TBSA burn is based upon the "rule of nines."

Assessment of Percentage of Burn Area	
Head	9%
Anterior Torso	18%
Posterior Torso	18%
Each Leg	18%
Each Arm	9%
Genitalia/perineum	1%

Agent	Spectrum of Activity	Advantage	Side effects
silver	Gram-positive, yeast, gram-	Well tolerated	Transient neutropenia

sulfadiazine MC agent	neg. except pseudomonas and Enterobacter cloacae.	Painless	Cannot use with sulfa allegy
mafenide acetate	Most gram + and gram -; No Staphylococcus coverage	Good eschar penetration Broadest spectrum	Pain Metabolicaci dosis. Hypokelimia
Silver nitrate	Effective against most of the gram-positive and granvnegative, yeast. Poor eschar penetration	Broad spectrum	Staining of tissue. Leaches electrolytes ↓Na, ↓K, ↓CI Methemoglobinemia (nitrates)

Management of Moderate to Severe Burns

Initial Fluid Resuscitation - The Parkland Formula

Initiation of fluid resuscitation should precede initial wound care. In adults, IV fluid resuscitation is usually necessary in second- or third-degree burns involving greater than 20% TBSA. In pediatric patients, fluid resuscitation should be initiated in all infants with burns of 10% or greater TBSA and in older children with burns greater than 15% or greater TBSA.

Two large-bore IV lines should be placed. Lactated Ringer's solution is the most commonly used fluid for burn resuscitation.

The Parkland formula is used to guide initial fluid resuscitation during the first 24 hours. The formula calls for 4 cc/kg/TBSA burn (second and third degree) of lactated Ringer's solution over the fast 24 hours. Half of the fluid should be administered over the first eight hours post burn, and the remaining half should be administered over the next 16 hours.

Urine output should be used as a measure of renal perfusion and to assess fluid balance. In adults, a urine output of 0.5-1.0 mL/kg/h should be maintained.

Full thickness injuries

All regenerative elements have been destroyed in these injuries, and healing only occurs from the edges and is associated with considerable contraction. All such injuries should therefore be excised and grafted unless they are < 1 cm in diameter in an area where function would not be compromised.

- Full thickness injuries have no regenerative elements left. Unless they are very small they will take weeks to heal and undergo severe contraction. They should be referred for surgery as early as possible.
- Deep dermal injuries are unlikely to heal within three weeks. The incidence of unsightly hypertrophic scarring rises from 33% to 78% if healing is delayed from three to six weeks. Therefore these injuries should also be excised and grafted within the first 5-10 days.
- Superficial wounds should heal by regeneration within two weeks. They should be cleaned, dressed, and reviewed on alternate days to optimise the wound healing environment.
- Clean wounds can be dressed with a non-adherent primary dressing and an absorbent secondary dressing such as gauze or Gamgee Tissue. Antimicrobial agents are added where infection is likely or heavy colonisation is evident on the dressings or invasive infection is suspected.

Electrical Burns

- ✓ Body part with small cross sectioned area (e.g extremely); tissue destruction is more
- ✓ Injury is mostly internal because the route of least electrical resistance follows nerves, blood vessels and muscles. Skin has relatively high resistance to electric current, and is therefore, mostly spared.
- ✓ Muscle is the major tissue through which the current flows, and thus it sustains the most **damage**
- ✓ Myoglobinuria common. Mx- vigorous hydration + mannitol + NaHC03.

High voltage injury:

- ✓ High tension (voltage) burns cause more damage.

- ✓ High voltage injuries cause direct damage to blood vessels and muscle necrosis with the rapid onset of compartment syndromes. Fasciotomy is required.
- ✓ Hyperkalemia due to extentive tissue necrosis may potentiate cardiovascular problems.
- ✓ Cardiac rhythm disturbances (esp. 1st 24 hrs); Cardiac arrest most likely at 50-60 cycles / sec. requiring cardiopulmonary resuscitation. Continuous cardiac monitoring is required for the first 24 hours.

Delayed complications

Neurologic deficits
Cataracts especially in H&N burns

Lightening injury

Unique cutaneous injury = serpiginous and arborizing pattern
Tympanic membrane injury
Lethal in about 1/3 case.

Chemical injury

- Acid bums less dngerous than alkali burns.
- Single most effective mean to decrease tissue damage is immediate irrigation with large quantities of water
- Use of neutralizing solution may accentuate tissue damage by generating heat.
- Hydrofluoric acid → highly corrosive
  i) Systemic absorption leads to hypocalcemia and life threatening arrhythmias as free fluoride combines with Ca.
  ii) Most effective treatment → calcium gluconate IV + irrigation of wound by copious 2.5% calcium gluconate gel
- Coal tar: Causes direct thermal injury. Immediate cooling by plain water and then cover with petroleum based ointment to solubilize the tar and facilitate its removal.

Cold injuries
Frostbite - freezing injury, tissue necrosis.
Treatment:

- Rapid rewarming of the frozen part in water bath at 40°C

Pernio, or chilblain, is the most common type of cold injury and develops after prolonged exposure to dry cold above freezing
"**Trench foot,"** occurs when a body part is exposed to a cold, wet environment. The symptoms are similar to those of chilblains, but the damage is usually more serious.
Immersion foot develops more slowly, after a few days to several weeks of immersion in cool or cold water at temperatures usually higher than those causing trench foot.

RENAL TRANSPLANTATION

HISTORY: Skin autografting in India during the sixth century BCE.
Gaspare Tagliacozzi's (1545-1599) text on the restoration of the nose, lips, and ears.
In 1906, Mathieu Jaboulay carried out the first attempts at human kidney transplantation.
Corneal and skin transplant developed during 2nd half of 19th century.
Jaboulay used pig and goat kidneys anastomosed to blood vessels of the arm of patients with chronic renal failure, which functioned for approximately 1 hour.
In 1911, Hammond and Sutton of Philadelphia performed the first human-to-human kidney transplant with transient success.
Alexis Carrel, improved the methods of vascular anastomosis and introduced **cooling** as a method of organ preservation in his work in Chicago. Later, Carrel found that he could successfully autograft dog kidneys; unfortunately, allografts invariably failed. Carrel suggested that "the principle of immunity" might explain this observation.

In 1942, Gibson and Peter Medawar, in their early experience with skin allografts in the treatment of burns sustained in World War II, noted that the second set of grafts from 1 donor is destroyed much faster than the first.
Surgeon Joseph Murray performed first successful human transplant in 1954 between identical twin brothers.

INDICATIONS AND CONTRAINDICATIONS

Chronic renal failure: Renal transplantation is the treatment of choice for patients with chronic renal failure from most causes.

Causes: ***Diabetes – 31%,*** Chronic glomerulonephritis – 28%, Polycystic kidney disease – 12%, Nephrosclerosis (hypertensive) – 9%, Systemic lupus erythematosus (SLE) – 3%, Interstitial nephritis – 3%

Renal tumors - Renal tumors (eg, Wilms tumor in children, renal cell carcinoma in adults) can be treated with transplantation.

CONTRAINDICATIONS TO SURGERY

- Cardiopulmonary insufficiency, Peripheral and cerebrovascular disease
- Active infection
- Morbid obesity
- Tobacco abuse
- Hepatic insufficiency
- Other factors that increase the risk associated with a major surgical procedure

Contraindications to immunosuppression

- Infection and malignancy are the primary medical conditions. Acute infections should be fully resolved at time of transplantation. HIV currently is an absolute contraindication in most programs.

Type of Malignancy	Duration
breast, colorectal cancer, melanoma, diffuse bladder carcinoma, and non-in situ ovarian cancer	5 years
In situ uterine carcinoma, some renal tumors (clear cell, Wilms', urothelioma), basal or Squamous cell skin carcinoma.	2 years
isolated nodules of Prostatic carcinoma and focal bladder carcinoma	1 year

Other relative contraindications

The risk of recurrent disease is not a contraindication to renal transplantation. Glomerulonephritides (eg, mesangiocapillary glomerulonephritis type 1, IgA nephropathy).
Focal and segmental glomerulosclerosis is associated with a highly variable rate of recurrence in the first allograft.
Nearly all patients with diabetes will show histologic evidence of diabetic nephropathy within 4 years. Increasingly, the treatment of choice for patients with type 1 diabetes and renal failure is combined kidney and pancreas transplantation or pancreas transplantation after kidney transplantation. At present, pancreas graft survival is slightly worse in "pancreas after kidney" transplants
The treatment of oxalosis is controversial; some studies favor intensive dialysis followed by combined liver and kidney transplantation.
Hemolytic uremic syndrome may recur following transplantation in response to cyclosporine-based or tacrolimus-based immunosuppression.

WORKUP

Infectious profile

- Hepatitis B and C serologies
- Epstein-Barr virus serologies (IgM and IgG)
- *Cytomegalovirus (CMV) serologies (IgM and IgG)*

- Varicella-zoster serologies (IgM and IgG)
- Rapid plasma reagin (RPR) test for syphilis
- HIV
- Purified protein derivative - TB skin test with anergy panel, when indicated

Urinalysis, urine culture, and cytospin (when indicated)

Other Tests:

Recipients of kidney transplants undergo an extensive immunological evaluation that There are 4 components of the immunologic evaluation.

ABO blood group determination: Transplantation across incompatible blood groups may result in humoral-mediated hyperacute rejection.

Human leukocyte antigen (HLA) typing: All transplant recipients are tissue typed to determine the HLA class I and class II loci. Six HLA antigens are determined. The kidney donors also are HLA typed, and the degree of incompatibility between the donor and recipient is defined by the number of antigens that are mismatched at each of the HLA loci.

Serum screening for antibody to HLA phenotypes

- Sensitization to histocompatibility antigens occurs when the recipient is sensitized because of receiving multiple blood transfusions, a previous kidney transplant, or from pregnancy.
- Transplantation of a kidney into a recipient that is sensitized against donor class I HLA antigens puts the recipient at high risk of developing hyperacute antibody-mediated rejection. All transplant candidates are screened to determine the degree of humoral sensitization to HLA antigens.

Crossmatching:. This immunologic test is conducted prior to transplantation. A negative crossmatch must be obtained prior to accepting a kidney for transplantation.

Histocompatability

The important histocompatability systems are ABO and HLA system

A and B substances are present on the endothelial cells and most individuals have the antibody to the RBC antigen they lack.

The major histocompatability antigen are the glycoprotein on the cell membrane and are encoded by the major histocompatibility complex (MHC) gene present on the short arm of the Chr. 6.

These agents are divided into class I and II. Class I antigen are HLA-A, HLA-B, and HLA-C, present on all nucleated cells and are detected by serotyping T Lymphocytes.

Class I antigen are HLA-DR, HLA-DQ, and HLA-DP. Present on B lymphocytes activated T Cells, Monocytes, Macrophages, dendritic cells and some endothelial cells and HLA-DR is detected serotypinf B lymphocytes (Testing for HLA-DQ and DP is not routinely done).

ORGAN DONATION

Living donation transplantations

Offers the advantage of optimal preparation for the recipient and donor.

Minimize the organ preservation time.

Laparoscopic and laparoscopy-assisted techniques has proven to be a major improvement to living donation.

If one of the kidney is better than the other, better one if left for donor.

Left kidney if preferred due to its long renal vein.

Flank incision is used most often and donor receives 25 gms of mannitol in 1 hour infusion at the beginning of the surgery to improve perfusion.

Cadaver donation

Allocation of cadaver donor grafts is based on a waiting list, with special priorities given to HLA zero mismatch pairings, pediatric recipients, and patients with a high PRA titer.

Most cadaver kidney grafts come from brain-dead, heart-beating cadavers.

Criteria for cadaver donor are: Ages 18 months to 55 years; no HT/DM or Malignancy (other than primary brain tumours and treated skin cancer); no generalized viral or bacterial infection; normal BUN and creatinine values and negative assay for syphilis, hepatitis, HIV and HTLV-I.

Goals of resuscitation for brain dead donor are systolic BP > 90 mm/Hg and urinary output > 0.5 ml/kg/Hr.
Absolute contraindications to cadaver donation include some active infection, including HIV, and extracranial malignancy.
Relative contraindications include poor renal function in the donor, positive hepatitis serologies, advanced donor age (especially if paired with hypertension or diabetes).
This procurement essentially involves perfusion of the involved organs with ice-cold (4°C) organ preservation solution. These solutions typically contain high levels of potassium to depolarize cell membranes. These solutions also may contain impermeant sugars to prevent cell swelling, albumin or dextrans to maintain osmolality and to prevent swelling of the extravascular extracellular fluid compartment, and free radical scavengers and agents (eg, allopurinol) to reduce reperfusion injury. The most commonly used preservation solution is UW solution (formulated at the University of Wisconsin).
To provide target cells for the crossmatch, lymphoid tissue (ie, lymph nodes, spleen) is obtained at the time of procurement.

PROCEDURES:
Pretransplant native kidney nephrectomy/nephroureterectomy:
Not a routine pretransplant procedure.
The native kidneys are left in place because they still may produce significant volumes of urine, secrete erythropoietin, and activate vitamin D.
Indication: large polycystic kidneys (Massive enlargement), significant proteinuria, and chronic reflux disease.
renal calculi, renal infection, hematuria
Pretransplant cholecystectomy: Symptomatic or asymptomatic gallstones.
Splenectomy: May be indicated as a protocol for ABO-incompatible kidney transplants.
Multiple random blood transfusions: Once, this was associated with improved, kidney transplant graft survival. Currently, there is no clinical benefit to transfusion, and the risk of sensitization is significant.

TECHNIQUE, POSTOPERATIVE MANAGEMENT
Gibson incision: A curvilinear incision in a lower quadrant of the abdomen (ie, Gibson incision), with division of the muscles of the abdominal wall and dissection of the preperitoneal space to expose the iliac vessels and the bladder. Then, the donor kidney's renal vessels are connected to the iliac vessels, typically with end-to-side anastomoses of a fine (5-0 or 6-0) permanent vascular suture.
Ureteroneocystostomy
The ureter is introduced into the bladder by creating a ureteroneocystostomy.
This may involve bringing the ureter through a tunnel in the bladder submucosa (Leadbeder-Politano) or by creating an anastomosis between the tip of the ureter and the bladder mucosa, then partially covering this with bladder muscularis (Lich).
Postoperative management
Management of the operative procedure: 0.45% Saline in 0-5% Dextrose at a rate equal to hourly output (often in the 250-500 cc/h range) plus insensible loss. With improving renal function, fluid balance must be maintained, hypertension management may need modification, and electrolyte abnormalities may require correction.
Immunosuppressive therapy: can be divided into 2 phases induction and maintenance. The induction immunosuppression should occur during and immediately following transplantation and again should be divided into antibody and nonantibody regimens. The typical antibody-based induction immunosuppression uses either monoclonal or polyclonal antibody preparations directed at T lymphocytes in combination calcineurin inhibitors (eg, cyclosporine, tacrolimus), antiproliferative agents (eg, azathioprine, mycophenolate), and steroids. Both nonantibody induction therapy and most forms of maintenance therapy dispense with the antibodies but use calcineurin inhibitors, antiproliferative agents, and steroids in various combinations.

Drug Category: *Antirejection induction agents* -- Induction immunotherapy consists of a short course of intensive treatment with intravenous agents. Antilymphocyte antibody induction therapeutics are varied and

include polyclonal antisera, mouse monoclonals, and so-called humanized monoclonals. Polyclonal antisera, such as antilymphocyte globulin (ALG), antilymphocyte serum (ALS), and antithymocyte globulin (ATG), are equine, goat, or rabbit antisera directed against human lymphoid cells.

1. Antithymocyte globulin, equine (ATGAM): Infection, leukopenia, and thrombocytopenia may occur; adverse reactions include fever, chills, malaise.
2. Daclizumab: Humanized monoclonal antibody that specifically binds to and blocks IL-2 receptor on surface of activated T cells.
3. Basiliximab: Chimeric monoclonal antibody that specifically binds to and blocks IL-2 receptor on the surface of activated T cells.
4. Antithymocyte globulin, rabbit (Thymoglobulin) -- A purified immunoglobulin solution produced by the immunization of rabbits with human thymocytes. Infection, leukopenia, and thrombocytopenia may occur; adverse reactions include fever, chills, malaise, headache.
5. Methylprednisolone: Steroids ameliorate delayed effects of immune reactions. Caution in active infection, diabetes, heart failure

Drug Category: *Maintenance Immunosuppression*: Maintenance immunosuppressive agents are required for the patient's entire life.

1. Prednisone: Immunosuppressant for treatment of autoimmune disorders; may decrease inflammation by reversing increased capillary permeability and suppressing PMN activity. Abrupt discontinuation of glucocorticoids may cause adrenal crisis; hyperglycemia, edema, osteonecrosis, myopathy, peptic ulcer disease, hypokalemia, osteoporosis, euphoria, psychosis, myasthenia gravis, growth suppression, and infections may occur with glucocorticoid use.
2. Azathioprine (Imuran) -- Active component of azathioprine is 6-mercaptopurine. Acts as purine analog that interacts with DNA and inhibits lymphocyte cell division. Risk of leukopenia and (rarely) liver dysfunction; caution with liver disease and renal impairment; hematologic toxicities may occur.
3. Cyclosporine: Calcineurin inhibitors that diminish IL-2 production in activated T cells. These agents bind to the intracellular immunophilin cyclophilin, interfering with the action of calcineurin, which inhibits nuclear translocation of the NFAT. Evaluate renal and liver functions often; may increase risk of infection and lymphoma.
4. Tacrolimus: Calcineurin inhibitor that diminishes IL-2 production in activated T cells. Binds to intracellular immunophilin and FKBP, interfering with the action of calcineurin, which inhibits nuclear translocation of the NFAT. Has nephrotoxic effects; tonic clonic seizures may occur.
5. Sirolimus: Inhibits lymphocyte proliferation by interfering with signal transduction pathways. Binds to immunophilin FKBP to block action of mTOR. May exacerbate hyperlipidemia and thrombocytopenia

COMPLICATIONS

Early postoperative complications include the following:

- Delayed graft function (DGF): DGF is rare with living donor grafts, probably because of the short cold ischemia time (CIT is the time between perfusion of the graft with ice-cold preservative solution and reperfusion with blood in the recipient. For cadaver kidneys, CIT remains the best predictor of DGF).
- Vascular-related and ureter-related complications:
  Renal artery thrombosis occurs in about 1% of transplants. Nephrectomy is generally indicated.
  Arterial stenosis occurs in 2-10% of cases, and is associated with the abrupt onset of hypertension. It can be suspected on the basis of Doppler ultrasound; confirmation generally requires angiography. Management of arterial stenosis is angioplasty and stent-placement.
  Venous thrombosis occurs in 0.5%-4% of cases. Thrombosis of the main renal vein has in rare instances been successfully treated with thrombolytic agents, though nephrectomy is generally required.

- Ureteral obstruction is the most common urinary tract problem associated with transplantation. Early obstruction may result from distal obstruction, clot, edema, or technical problems associated with the ureteroneocystostomy. When Foley catheter placement and expectant management does not resolve the problem, surgical revision of the ureteroneocystostomy over a stent may be required. Late obstruction, when not caused by external compression (lymphocele, pregnancy, etc.), is most typically associated with fibrosis. Management is typically by radiologic or cystoscopic stent placement and stricture dilatation.
- Urine leak can be suspected when a patient with good or improving graft function develops a fluid leak from the wound or abdominal pain or perineal swelling. Nuclear renal scan is probably the most sensitive test for urine leak. Small bladder leaks can often be managed by bladder decompression with a foley catheter. Larger leaks typically require exploration and repair.
- Lymphocele Leakage from perivascular lymphatic vessels can lead to significant collections of lymph between the lower pole of the transplanted kidney and the bladder. Sclerotherapy with 10% povidone-iodine solution may be successful in small unloculated collections but has a high rate of recurrence.The current standard of care is internal drainage of the lymphocele into the abdominal cavity. This is increasingly being done laparoscopically.
- Infections
- Allograft regection
  Hyper acute: An irreversible process that occurs immediately after renal revascularization and mediated by pre formed circulating antibodies.
  Accelerated rejection: It is mediated by humoral and cellular components, occurs within days and weeks and usually does not respond to antirejection treatment.
  Acute rejection: In the first year following transplantation, acute rejection is observed in approximately 25% of patients. Rejection usually is asymptomatic, or associatd with fever, increased BP, decreased output and pain at the graft site. Rejection usually presents as an unexplained rise in serum creatinine and can be confirmed with biopsy. Typical biopsy findings of acute cellular rejection include a lymphoplasmacytic infiltration of the renal interstitial areas with occasional penetration of the tubular epithelial by these cells. Renal scan shows increased graft size and decreased renal blood flow, GFR and tubular function. Most rejection episodes can be treated successfully with a short course of increased steroids or antilymphocyte antibody agents in some cases.
  Chronic rejection appears to have both immunologic and nonimmunologic components and characterized by gradual decline in renal function. As a broad classification for progressive graft failure, risk factors include initial poor function of the graft and a history of acute rejection episodes.

MEDIASTINUM

Mediastinum - that part of the thorax contained between the two pleural cavities.

Superior compartment - above the aortic arch

- Thyroid/ Aneurysms/ Oesophageal/ Neurogenic

Anterior - is bordered by the sternum anteriorly, the pericardium posteriorly and the mediastinal pleura laterally. (4 T's)

- Thymus/ Thyroid/ Teratoma (and other germ cell tumours)/ Terrible Lymphoma and other lymphoid diseases (sarcoid, Castlemann's NSCLC, SCLC)
- (also pericardial cyst and Morgagni hernia inferiorly)

Middle (visceral) compartment - from the anterior pericardium back to the pre-vertebral fascia and bounded by both pleura, includes the heart, trachea, main bronchi and oesophagus. (BLAB)

- Bronchogenic carcinoma/ Lymphoma/ Aneurysms (and other vascular, including cardiac tumours)/ Bronchogenic cyst

Posterior compartment - better referred to as the paravertebral sulci, includes those structures medial to the pleura but excluding the vertebral column. (NOBA)

- Neurogenic/ Oesophageal (duplication and para-oesophageal hernia)/ Bone/ Aneurysms

Presentation

Mediastinal tumours in children are usually symptomatic with respiratory symptoms such as cough, stridor and dyspnoes.

Malignant lesions are often accompanied by lethargy, fever, malaise and chest pain.

In adults many lesions are asymptomatic, found incidentally on routine chest radiographs. However, obstructive symptoms do occur when the tumour impresses on the superior vena cava, oesophagus or tracheo-bronchial tree and cardiac tamponade can be caused by large anterior compartment tumours. Invasion of phrenic, recurrent laryngeal or sympathetic chain nerves may cause breathlessness, hoarseness or Horner's syndrome.

Diagnosis

CT scan or MRI scan outline the exact site of the lesion and will give clues to the diagnosis, a ***variegated appearance suggesting teratoma***. Scans will also give an indication of malignant invasion of adjacent structures and pleural metastases which in the case of ***thymoma produce a "droplet" pattern***.

Fine needle aspiration cytology is frequently inadequate to differentiate thymoma from lymphoma and almost never provides enough tissue to differentiate between types of lymphoma. Mediastinoscopy, mediastinotomy via anterior mini-thoracotomy or thoracoscopy may be required to provide enough issue for the pathologist to make a full diagnosis. In patinets who are unstable due to compression or obstruction of a vital organ treatment with steroids, radiotherapy or chemotherapy may be commenced before a full diagnosis is obtained surgically.

Thymic tumours are associated with a number of ***paraneoplastic or "parathymic" syndromes.*** The rare paraganglionic neurogenic tumours may be functional in that they produce biogenic amines resembling phaeochromocytoma. Vanillylmandelic acid or homovanillic acid may be detectable in the urine. Haematological markers of germ cell tumours (beta-HCG and alpha feto-protein) should be sought.

Neurogenic tumours of the mediastinum

Neurogenic tumours account for 20-30% of all mediastinal tumours rising to 50-60% in children. Von Recklinhausen's neurofibromatosis is associated with an increased incidence of neurogenic tumours of all histological types.

Most tumours are benign neurilemmomas (also known as schwannomas) or ganglioneuromas (classification) and are completely cured by excision.

Treatment

- Benign – resection
- Complete resection also leads to high cure rates in the intermediate malignancy ganglioneuroblastoma and even frankly malignant neuroblastoma and paraganglionoma.
- Malignant schwannoma can rarely be excised completely and leads to death within a year of diagnosis: incompletely excised paraganglionoma usually proves fatal regardless of adjuvant therapy though survival is substantially longer.
- Neuroblastoma is more sensitive to chemotherapy and when used in combination with radiotherapy even incompletely excised tumours can achieve reasonable long-term survival.
- Radiotherapy can also reduce local recurrence of incompletely excised neurilemmoma, neurofibroma and ganglioneuroblastoma

Tumours of the thymus

The thymus is a bilobed lymphoid organ ***sited in the superior mediastinum*** in adults. It is relatively large at birth and enlarges to a maximal size during puberty. In adulthood, it regresses as its functional tissue is replaced by fatty connective tissue.

The thymus is thought to have a central role in the development of immune function.

There are three general categories of thymic tumours: thymoma, thymic carcinoma and tumours of other thymic elements. Thymomas are one of the ***most common mediastinal neoplasms - 90% are benign***.

Thymoma

Thymomas are of particular fascination because of their unusual para-neoplastic associations. The best known of these is myasthenia gravis but the number of syndromes associated with thymoma is extensive (Parathymic syndromes). The tumour contains both epithelial and lymphocytic elements which can also make differentiation from lymphoma difficult.

Types

Three main types are:

- ***Benign - the most common, accounting for 80-90% of thymomas***. Characterized by a diffuse ***proliferation of neoplastic thymic epithelial cells and an abundance of lymphocytes***. There is ***no capsular invasion***.
- Malignant type I - cytologic features are identical to the benign thymoma but with additional invasion of the capsule. Occasionally, there may be metastases to the lungs and bone.
- Malignant type II - known as thymic carcinoma. There is capsular invasion and cytologic pleomorphism. The tumour often resembles a squamous cell carcinoma.

Classification: Masoaka staging system categorises thymoma purely on encapsulation and invasion of local tissues, and the ***Muller-Hermelink morphological classification***.

Clinical features

- mean age of patients with thymomas is 50 years; rare in children where they are associated with a poor prognosis
- males : females = 1:1
- radiographic mass - most common in ***anterosuperior mediastinum***
- variable clinical presentation dependent upon the aggressiveness of the lesion. Basic patterns include:
    - asymptomatic
    - features attributable to local pressure effects e.g. cough, dyspnoea, dysphagia and superior venal caval obstruction
    - associated systemic disorders.

Associated conditions

- myasthenia gravis - the most common association but less often associated with more aggressive thymomas
- haematologic cytopenias e.g. aplastic anaemia
- hypogammaglobulinaemia
- collagen vascular diseases e.g. systemic lupus erythematous
- non-thymic malignancies

Di George syndrome

The DiGeorge syndrome is an example of a selective T-cell deficiency caused by the failure of development of the third and fourth pharyngeal pouches.

These pouches give rise to the following structures:

- Thymus/ parathyroids/ aortic arch / portions of the lips and ears

Consequently, DiGeorge syndrome may present with as immune deficiency state - usually T cells, but sometimes B cells, and also aberrant calcium metabolism, congential heart disease and abnormal facies.

Nezelof syndrome

Nezelof syndrome is congenital hypoplasia of the thymus with retention of normal parathyroid function. It should be contrasted to DiGeorge syndrome in which there is absence of the parathyroids.

Thymic Carcinoma

Thymic carcinoma is exceedingly rare and are of squamous histology and most have metastases at the time of diagnosis and follow an aggressive course.

Treatment consists of chemotherapy and radiotherapy appropriate to the corresponding histological type.

Parathymic Conditions

Neuromuscular	**Haematologic disorders**	**Immune deficiency disorders**
• Myasthenia gravis • Peripheral neuropathy • Polymyositis • Dermatomyositis	• Red cell aplasia • Pernicious anaemia • Erythrocytosis • Pancytopoenia • Autoimmune	• Acquired hypogammaglobulinaemia • T-cell deficiency syndrome • Auto-immune disorders • Systemic lupus erythematosus

	haemolytic anaemia • Leukaemia • Multiple myeloma	• Rheumatoid arthritis • Sjogren's syndrome • Scleroderma
Dermatologic disorders • Pemphigus • Lichen planus • Chronic mucosal candidiasis • Alopecia areata	**Endocrine disorders** • Multiple endocrine neoplasia • Cushing's syndrome • Thyrotoxicosis	**Miscellaneous** • Giant cell myocarditis • Nephrotic syndrome • Ulcerative collitis • Hypertrophic osteoarthropathy • Lymphoid interstitial pneumonitis

Dermoid (mediastinal)

Dermoid cysts arise from ectodermal tissue, whereas teratomas are germ cell tumours that contain ectodermal, mesodermal and endodermal tissue. These teratodermoid tumours occur in the mediastinum mainly in 20 to 30 year age group, ***most often in the anterior mediastinum***. ***In general, dermoids are cystic and benign, whereas teratomas are solid and malignant.***

Management

- thoracotomy may be considered for diagnosis and removal
- radiotherapy may may achieve long-term control in malignant teratoma

Germ cell tumours of the mediastinum

25% of anterior compartment mediastinal tumours are of germ cell origin and fall into three groups: benign teratoma, malgnant seminoma and nonseminomatous malignant germ cell tumours. They are due to primary tumours arising from residual germ cells which have migrated along the embryonic urogenital ridge. The malignant germ cell tumours, have a preponderance in males and are associated with chromosomal abnormalities such as Klinefelter's syndrome and other blood dyscrasias.

- Benign teratomas are cured by complete surgical excision.
- Seminomas are very radiosensitive and radiotherapy is the mainstay of treatment. Bulky tumours may respond to induction therapy with cisplatin, bleomycin and etoposide before radiotherapy.
- Non seminomatous tumours cisplatin based chemotherapy can produce complete remission in over 50% of cases. Surgery is indicated for residual disease in the mediastinum or for lung metastases if serum tumour markers have reverted to normal.

Cardiac tumours

Cardiac tumours are rare and ***most are benign. Myxomas, 90% of which occur in the left atrium, are the commonest of the benign tumours.***

Presentation

Cardiac tumours present with syncopal attacks due to obstruction of flow within cardiac chambers, valve incompetence due to impairment of valve closure, symptoms of embolisation, rarely arrythmia or constitutional symptoms such as fever, weight loss, finger clubbing, Raynaud's syndrome or myalgia.

Investigation

Echocardiography outilines the intracardiac disease Cardiac catheterisation is usually contraindicated because of the risk of inducing embolisation, unless coronary surgery is anticipated. CT scan will outline the extent of extracardiac disease.

There is no non-invasive method of distinguishing between a benign from malignant cardiac lesion. Therefore surgical exploration is required for any symptomatic or clinically suspicious intra-cardiac mass.

Treatment and prognosis

- Surgical resection by open heart surgery under cardio-pulmonary bypass is curative for the majority of atrial myxomas and other benign tumours.
- Malignant neoplasms are rarely cured with surgery alone though patients whose tumours have been resected have a median survival of twenty-four months compared to eleven months for patients with unresectable tumours.

VASCULAR DISEASES

Abdominal aortic aneurysms

- An AAA is an increase in aortic diameter by greater than 50% of normal (aortic diameter of greater than 3 cm diameter).
- More prevalent in elderly men. Male : female ratio is 4:1
- Risk factors – hypertension, peripheral vascular disease, family history (15-25%)
- Other causes of aortic aneurysms include:
    - Genetic: There is a familial tendency to aortic aneurysms. Connective tissue disorders such as Ehlers-Danlos syndrome and Marfan's syndrome.
    - Post-traumatic:
    - Arteritis, e.g.Takayasu disease, giant cell arteritis, and polychondritis.
    - Congenital malformation of the aorta (aneurysms tend to develop just beyond the narrowing of a coarctation of the aorta).
    - ***End-stage (tertiary) syphilis, which tends to affect the ascending aorta and arch of the aorta.***
    - Mycotic: infective (immunodeficiency, IV drug abuse, valve surgery).
- Degenerative aneurysms account for more than 90% of all infrarenal AAAs.
- Most cases of AAA begin below the renal arteries and end above the iliac arteries.
- They generally are spindle shaped (fusiform)

Natural history

- In general, AAAs gradually enlarges (0.2-0.8 mm/y) and eventually rupture.
- 5 year risk of rupture:
    - 5.0 – 5.9 cm = 25%
    - 6.0 – 6.9 cm = 35%
    - More than 7 cm = 75%

Pathophysiology:

- The aortic wall contains smooth muscle, elastin, and collagen arranged in concentric layers.
- The number of medial elastin layers from the proximal thoracic aorta to the infrarenal aorta is markedly reduced, with medial thinning and intimal thickening.
- Elastin is the principal load-bearing element in the aorta. Elastin fragmentation and degeneration are observed in aneurysm walls.
- It is coupled with the histological changes of this matrix protein in aneurysms.

Clinical features: 75% are asymptomatic

- Possible symptoms include
    - Epigastric pain
    - Back pain
    - Malaise and weight loss (with inflammatory aneurysms)
- Rupture presents with
    - Sudden onset abdominal pain
    - Hypovolaemic shock
    - Pulsatile epigastric mass
- Rare presentations include
    - Distal embolic features: may cause livedo reticularis (blue toe syndrome)
    - Acute aortic occlusion: Occasionally, small AAAs thrombosis, producing acute claudication.
    - Aorto-caval fistula (symptoms include tachycardia, congestive heart failure (CHF), leg swelling, abdominal thrill, machinery-type abdominal bruit, renal failure, and peripheral ischemia).

- Primary aorto-intestinal fistula (AAA may rupture ***into the fourth portion of the duodenum*** and present with a herald upper gastrointestinal bleed).

Indication for operation

- Rupture
- Symptomatic aneurysm; any size.
- Rapid expansion
- Asymptomatic > 6 cm – exact lower limit controversial.

Contraindications: COPD/ severe cardiac disease/ active infection/ and medical problems that preclude operative intervention. These patients may benefit best from endovascular stenting of the aneurysm. Severe life-threatening comorbidities include advanced cancer, end-stage lung disease, or cardiac disease.

Approach:

- Monitor patients if AAA is smaller than 4 cm with ultrasound every 6 months, offer surgical intervention if the aneurysm expands or becomes symptomatic.
- Patients with an AAA of 5-6 cm in diameter benefit from repair, especially if they have other contributing factors like hypertension, continued smoking, or COPD.
- For patients at higher risk, the threshold for repair may be 6-7 cm in diameter.

Pre-operative investigation

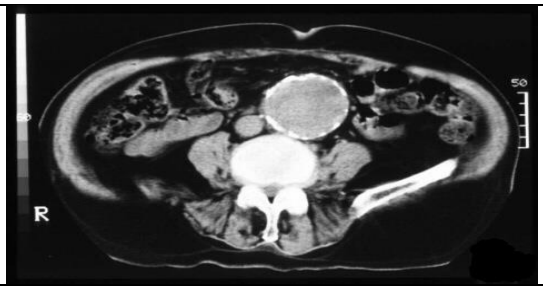
- Need to determine
  - Extent of aneurysm
  - Fitness for operation
- Ultrasound, conventional CT and more recently spiral CT
- Determines – aneurysm size, relation to renal arteries, involvement of iliac vessels
- ***Angiography: It is indicated only(not in all cases) when associated renal or visceral involvement, peripheral occlusive disease, or aneurysmal disease exists.***
- Most significant post op morbidity and mortality related to cardiac disease
- Cardiac revascularisation required in up to 10% of patients.

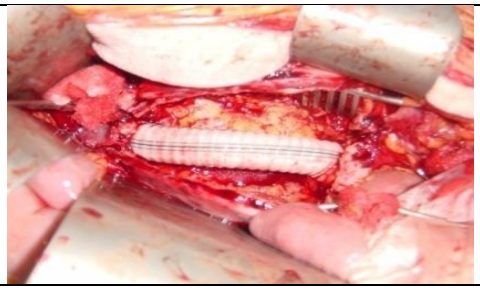
TREATMENT

Medical therapy: Smoking cessation/ aggressively control hypertension.

Surgical therapy: Operative approach is through the traditional open laparotomy approach or, by the placement of endovascular stents.

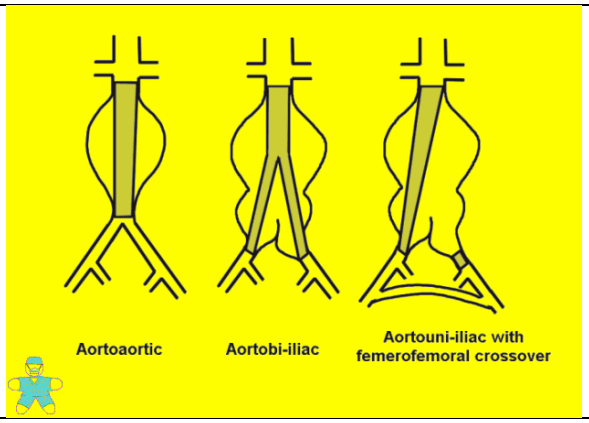
Prevention of distal embolization: The patient is heparinized prior to aortic cross clamping. ***If significant intraluminal debris, juxtarenal thrombus, or prior peripheral embolization exists, the distal arteries are clamped first,*** followed by aortic clamping.





Endovascular aneurysm repair

- Morbidity of conventional open aneurysm surgery related to:
  - Exposure of infra-renal aorta/ Cross clamping of aorta
- Endovascular repair achieved by transfemoral or transiliac placement of prosthetic graft
- Proximal and distal cuffs / stents anchor graft
- Exclude aneurysm from circulation
- Only ~40% of aneurysms suitable for this type of repair
- Major problem related to placement and leakage around stent



- Three main types of graft
  - Aorto-aortic
  - Bifurcated aorto-iliac
  - Aorto-uniiliac graft with femoro-femoral crossover and contralateral iliac occlusion

Complications

- Graft migration/ Endovascular leak/ Graft kinking/ Graft occlusion

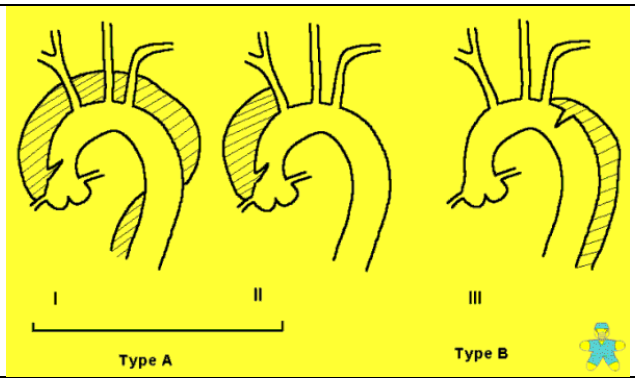
Aortic dissection

- **Commonest aortic emergency**
- Incidence is twice that of ruptured abdominal aortic aneurysm
- Most commonly seen between 50 and 70 years
- Associated with hypertension, Marfan's syndrome, bicuspid aortic valve

Pathology

- Intimal tear results in blood splitting the aortic media
- Rupture can occur back into the lumen or externally in pericardium/ mediastinum
- External rupture often results in fatal pericardial tamponade
- ***Commonest site of intimal tear is within 2-3 cm of aortic valve***
- Dissection can result in occlusion of aortic branches
- **Most commonly involved are renal, spinal, coronary or iliac arteries**

Classification



- Stanford - Type A and B depending on whether ascending or descending aorta involved
- DeBakey - Divided into Types I, II and III as above

Clinical features

- Usually presents with tearing chest pain radiating to back associated with collapse
- Examination may show
  - Reduced or absent peripheral pulsed
  - Soft early diastolic murmur
- Chest x-ray usually shows a widened mediastinum.
- If aortic branches occluded there may clinical evidence of
  - Acute renal failure

- Paraplegia
- Acute limb ischaemia
- Cerebrovascular accident
- Inferior myocardial infarction

Management

- All patients require urgent management of associated hypertension
- **Type A dissections usually require surgical intervention**
- Dissection excised and aorta replaced with graft
- Aortic valve is preserved if possible
- *An evolving CVA or established renal failure are contraindications to surgery*
- **Type B dissections may be treated without surgery**
- Requires fastidious blood pressure control
- Surgery should be considered if evidence of aortic expansion.
- Surgery for Type B dissections is associated with significant risk of paraplegia
- Without operation the prognosis for Type A dissections is poor
- 40% die within 24 hours and 80% die within 2 weeks

Popliteal artery aneurysms

- Defined as a popliteal artery diameter greater than 2 cm
- Account for 80% of all peripheral aneurysms
- 50% are bilateral. 50% are associated with an abdominal aortic aneurysm. 50% are asymptomatic
- Symptomatic aneurysms present with features of:
  - Compression of adjacent structures (veins or nerves)
  - Rupture
  - Limb iscahemia due to emboli or acute thrombosis
- **Treatment is by proximal and distal ligation**
- Revascularisation of the leg with a femoropopliteal bypass
- With a symptomatic popliteal aneurysm 20% patients will undergo an amputation

Arterial assessment

Clinical Assessment

Claudication

- Calf or thigh pain precipitated by exercise. Usually occurs after predictable distance. Relieved by rest
- Progression of symptoms is important - worsening or improvement
- Need to differentiate form spinal stenosis: Also cause exercise induced leg pain; Usually associated with neurological symptoms and relieved by spinal flexion
- Peripheral pulses can be present in patients with intermittent claudication

Critical limb ischaemia

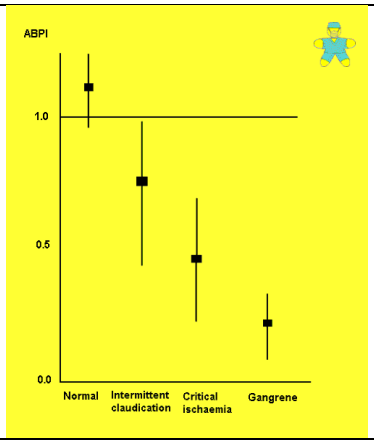
- Characterised by rest pain
- Occurs when foot is elevated (e.g. in bed)
- Improved with foot dependent
- May be associated with ulceration or gangrene
- Foot pulses are invariably absent

Non-invasive testing of arterial patency

Hand-held doppler

- Reflection of an ultrasound wave off a stationary object does not change its frequency. Reflection off a moving object results in a change of frequency
- The change in frequency is proportional to velocity or blood flow
- Hand held 8 MHz doppler probe is used to assess arterial system

- Can be used to measure arterial pressures (at rest and after exercise).
- In normal individual lower limb pressures are greater than upper limb
- Ankle-brachial pressure index (ratio of best foot systolic to brachial systolic Pr)
-



- Normal >1.0
- Claudication 0.4 -0.7
- Critical Ischaemia 0.1-0.4

- In normal individuals pressures do not fall flowing exercise
- In claudicants the ABPI falls and recovery is delayed
- In diabetic lower limb pressures are falsely elevated due to calcification in the vessel wall

Toe pressures

- Provides accurate assessment of distal circulation
- Not influenced by calcification in pedal vessels
- Normal toe pressures are 90-100 mmHg
- Toe pressure less than 30 mmHg suggests critical limb ischaemia

Duplex ultrasound

- Combined pulsed doppler and real time B mode ultrasound
- Allows imaging of vessels and any stenotic lesion.
- Flow and pressure wave form can be also be assessed
- Duplex ultrasound has sensitivity of 80% and specificity of 90%.

Pulse generated run off

- Proximal occlusion often causes poor filling of crural vessels on arteriography
- Rapid cycling of a proximal cuff generates arterial pulse wave
- P GR allows functional testing of distal arterial patency

Magnetic resonance angiography: No contrast required.

Invasive vascular assessmen

Angiography

- Usually performed using digital subtraction techniques
- Femoral artery is commonest site of venous access.
- Potential complications include
    - Contrast-related: Anaphylactic reaction/ Toxic reactions. Deterioration in renal function
    - Technique-related: Haematoma/ Arterial spasm/ Sub-intimal dissection/ False aneurysm/ Arteriovenous fistula/ Embolisation/ Infection

CT angiography

- Required intravenous contrast and ionising radiation
- Spiral CT and reconstruction can provide detailed images
- Particularly useful for the assessment of aneurysmal disease

Acute limb ischaemia

- Effects of sudden arterial occlusion depends on state of collateral supply

Aetiology of acute limb ischaemia

Embolism

- Left atrium in patients in atrial fibrillation
- Mural thrombus after myocardial infarct
- Prosthetic and diseases heart valves
- Aneurysm or atheromatous stenosis
- Tumour, foreign body, paradoxical

Thrombosis
Trauma
Dissecting aneurysm
Raynaud's Syndrome

Clinical features of limb ischaemia

- Clinical diagnosis depends on the 6 'p' s
    - Pain/ Paraesthesia/ Pallor/ Pulselessness/ Paralysis/ Perishing with cold
- ***Objective sensory loss requires urgent treatment***
- Need to differentiate embolism from thrombosis
- Important clinical features include
    - Rapidity of onset of symptoms
    - Features of pre-existing chronic arterial disease
    - Potential source of embolus
    - State of pedal pulses in contralateral leg

Management of acute ischaemia

Initial

- Heparinise & analgesia. Treat associated cardiac disease
- Treatment options are:
    - Embolic disease - embolectomy or intra-arterial thrombolysis
    - Thrombotic disease - intra-arterial thrombolysis / angioplasty or bypass surgery

Emergency embolectomy: Can be performed under either general or local anaesthesia

- Transverse artereotomy performed over common femoral artery
- Fogarty balloon embolectomy catheters used to retrieve thrombus
- If embolectomy fails - on-table angiogram and consider
    - Bypass graft or intraoperative thrombolysis

Intra-arterial thrombolysis:

- Arteriogram and catheter advanced into thrombus. Streptokinase 5000u/hr + heparin 250u/hr
- Alternative thrombolytic agents are urokinase/ tissue plasminogen activator (tPA).
- Repeat arteriogram at 6 -12 hours
- Advance catheter and continue thrombolysis for 48 hours or until clot lysis.
- Angioplasty of chronic arterial stenosis may be necessary

Buerger Disease (Thromboangiitis Obliterans)

Thromboangiitis obliterans is a nonatherosclerotic, segmental, inflammatory, vasoocclusive disease that affects the ***small and medium-sized arteries and veins*** of the upper and lower extremities. It is strongly associated with heavy tobacco use.

Male-to-female ratio = 3:1and majority of patients are aged 20-45 years.

History: Because a firm diagnosis of thromboangiitis obliterans is difficult to establish, a number of different diagnostic criteria have been proposed:

- Age younger than 45 years
- Current (or recent) history of tobacco use
- Presence of distal-extremity ischemia (indicated by claudication, pain at rest, ischemic ulcers, or gangrene) documented by noninvasive vascular testing
- Exclusion of autoimmune diseases, hypercoagulable states, and diabetes mellitus by laboratory tests

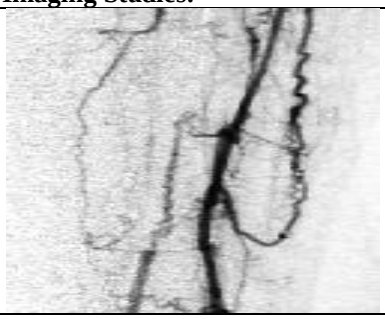
- Exclusion of a proximal source of emboli by echocardiography and arteriography
- Consistent arteriographic findings in the involved and noninvolved limbs

Patients also may present with claudication of the feet, legs, hands, or arms and often describe Raynaud phenomenon of sensitivity of the hands and fingers to cold.

Physical:

- The diseased hands and feet are usually cool and mildly edematous.
- Superficial thrombophlebitis is often migratory (in 50%). Paresthesias (numbness, tingling, burning, hypoesthesia) of the feet and hands.
- Impaired distal pulses in the presence of normal proximal pulses.

Imaging Studies:



Angiography/Arteriography:
This lower extremity arteriogram of the peroneal and tibial arteries of a patient with Buerger disease demonstrates the classic findings of multiple small and medium-sized arterial occlusions with formation of compensatory **"corkscrew collaterals."**

Other Tests:

- An abnormal Allen test indicating distal arterial disease and establishing involvement of the upper extremities in addition to the lower extremities helps to differentiate thromboangiitis obliterans from atherosclerotic disease.

TREATMENT: Absolute discontinuation of tobacco use.
Treatment with intravenous ***iloprost*** (a prostaglandin analogue), has been shown to improve symptoms, accelerating resolution of distal extremity trophic changes.
Surgical Care: Given the diffuse segmental nature and that the disease affects primarily small and medium-sized arteries; surgical revascularization is usually not feasible.
Autologous vein bypass of coexistent large-vessel atherosclerotic stenoses should be considered in patients with severe ischemia who have an acceptable distal target vessel.

- Other proposed surgical treatments for thromboangiitis obliterans are:
  - Omental transfer
  - Sympathectomy
  - Spinal cord stimulator implantation
- Distal limb amputation for nonhealing ulcers, gangrene, or intractable pain may be required.

Varicose veins

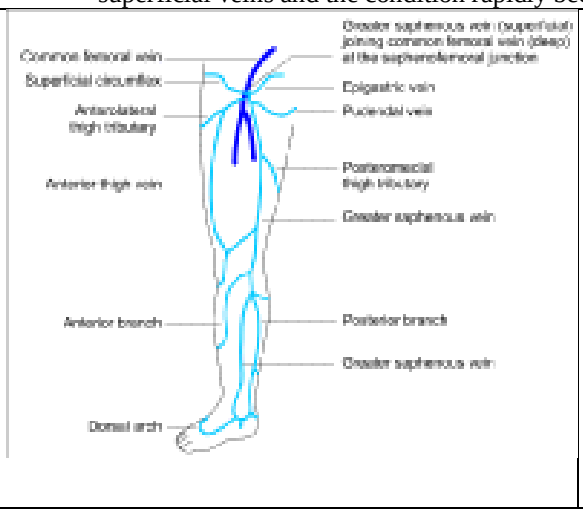
Varicose veins are veins that have dilated under the influence of increased venous pressure.

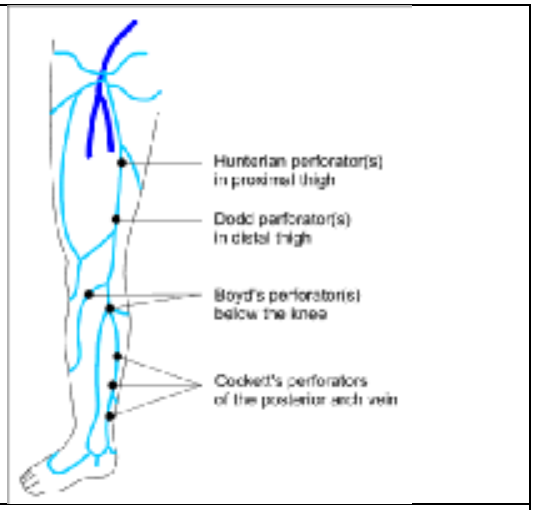
- Varicose veins affect: 20-25% of adult females.10-15% of adult males

Etiology:

- Intrinsic pathological conditions and extrinsic environmental factors combine to produce a wide spectrum of varicose disease.
- Most varicose disease is caused by elevated superficial venous pressures.
- Some people have an inborn weakness of vein walls.
- Reflux at the saphenofemoral junction (SFJ)
- Prolonged standing leads to increased hydrostatic pressures that can cause chronic venous distention and secondary valvular incompetence.

- If proximal junctional valves become incompetent, high pressure passes from the deep veins into superficial veins and the condition rapidly becomes irreversible.





Along its course, a variable number of perforating veins may connect the GSV to the deep system at the femoral, posterior tibial, gastrocnemius, and soleal veins. Between the ankle and the knee lie ***Cockett's perforators.*** Numerous superficial tributaries are there as it passes through the thigh like postero-medial and anterolateral thigh veins, and posterior accessory saphenous veins at the level of the canal of Hunter in the upper thigh. Just below the saphenofemoral junction, the GSV receives the lateral and medial femoral cutaneous branches, the external circumflex iliac vein, the superficial epigastric vein, and the internal pudendal vein The termination point of the GSV into the common femoral vein is called the saphenofemoral junction (SFJ).

History: Common symptoms include, leg heaviness, exercise intolerance, pain or tenderness along the course of a vein, pruritus, burning sensations, restless legs, night cramps, edema, skin changes, and paresthesias.

- ***Pain caused by venous insufficiency often is improved by walking in contrast to the pain of arterial insufficiency, which is worse with ambulation and elevation.***
- Acute varicose complications are variceal bleeding, dermatitis, thrombophlebitis, cellulitis, and ulceration.
- Poor correlation exists between symptoms and signs
- If history of DVT need preoperative investigation with duplex scanning

Examination

- Identify **distribution of varicose veins** - long saphenous vs short saphenous.
- Confirm with tourniquet testing and hand held-doppler probe (5 MHz)
- Indications for duplex scanning
    - Suspected short saphenous incompetence
    - Recurrent varicose veins
    - Complicated varicose veins (e.g. ulceration, lipodermatosclerosis)
    - History of deep venous thrombosis

Perthes maneuver: The Perthes maneuver is a traditional technique intended to distinguish antegrade flow from retrograde flow in superficial varices. Antegrade flow in a variceal system indicates that the system is a bypass pathway around a deep venous obstruction. This is critically important because if deep veins are not patent, superficial varices are an important pathway for venous return and must not be sclerosed or surgically removed.

If the Perthes maneuver is positive and the distal varices have become engorged, the patient is placed supine with the tourniquet in place and the leg is elevated (**Linton test**). If varices distal to the tourniquet fail to drain after a few seconds, deep venous obstruction must be suspected.
Trendelenburg test: The Trendelenburg test often can distinguish patients with superficial venous reflux from those with incompetent deep venous valves.

Indications for varicose vein surgery

- Most surgery is cosmetic or for minor symptoms
- Absolute indications for surgery :
    - Lipodermatosclerosis leading to venous ulceration
    - Recurrent superficial thrombophlebitis
    - Bleeding from ruptured varix

Contraindications: Venous outflow obstruction and during pregnancy.

LSV surgery

- Trendelenberg position with 20 - 30° head down
- Saphenofemoral junction (SFJ) found 2 cm below and lateral to pubic tubercle
- Essential to identify SFJ before performing flush ligation of the LSV
- Individually divide and ligate all tributaries of the LSV
    - ***Superficial circumflex iliac vein***
    - ***Superficial inferior epigastric vein***
    - ***Superficial and deep external pudendal vein***
- Check that femoral vein clear of direct branches for 1 cm above and below SFJ
- Stripping of LSV reduces risk of recurrence. Only strip to upper calf if needed.
- Stripping to ankle is associated with increased risk of saphenous neuralgia
- Post operative care: Elevate foot of bed for 12 hours. Varix stocking should be worn for at least 2 weeks

SSV surgery

- Patient prone with 20-30° head down
- Saphenopopliteal junction (SPJ) has very variable position
- Identify and preserve the sural nerve
- Need to identify the Sapheno-popliteal Junction
- Stripping associated with risk of sural nerve damage
- Subfascial ligation inadequate

Perforator surgery

- Perforator disease may be improved by superficial vein surgery
- Perforator surgery (e.g. Cockett's and Todd's procedure) associated with high morbidity
- Subfascial endoscopic perforator surgery (SEPS) recently described
- May have a role in addition to saphenous surgery in those with venous ulceration
- Sclerotherapy

Sclerotherapy "Varicose veins: sclerotherapy"

- Only suitable for below knee varicose veins
- Need to exclude SFJ or SPJ incompetence
- Main use is for persistent or recurrent varicose veins after adequate saphenous surgery
- Sclerosants
    - 5% Ethanolamine oleate/ 0.5% Sodium tetradecyl sulphate
- Needle placed in vein when full with patient standing
- Empty vein prior to injection
- Apply immediate compression and maintain for 4-6 weeks

Complications of sclerotherapy

- Extravasation causing pigmentation or ulceration
- Deep venous thrombosis

Other Modalities:

- **Endovenous laser:** Endovenous laser therapy is a thermal ablation technique that uses a laser fiber placed inside the vein to destroy the vascular endothelium.
- **Radiofrequency ablation:** Radiofrequency (RF) ablation is a thermal ablation technique. This tissue heating causes protein denaturation, collagenous contraction, and immediate closure of the vessel.
- **Ambulatory phlebectomy:** The stab-avulsion technique allows removal of short segments of varicose and reticular veins through tiny incisions.

Recurrent varicose veins "Varicose veins: recurrent"

- 15 - 25 % of varicose vein surgery is for recurrence

Reasons for recurrence

- Inaccurate clinical assessment
  - Confusion as to whether varicosities are in LSV or SSV distribution
- Inadequate primary surgery
  - 10% cases SFJ not correctly identified
  - 20% cases tributaries mistaken for LSV
  - Failure to strip LSV
- Injudicious use of sclerotherapy
  - 70% of SF incompetence treated with sclero-therapy will have recurrence
- Neovascularisation
  - With recurrent varicose vein need to image with duplex or varicography

COMPLICATIONS: ***Deep vein thrombosis and pulmonary embolism*** are the most serious complications. Other complications are dysesthesias from injury to the ***sural nerve or the saphenous nerve***, subcutaneous haematoma, infection and arterial injury.

THORACIC OUTLET SYNDROME

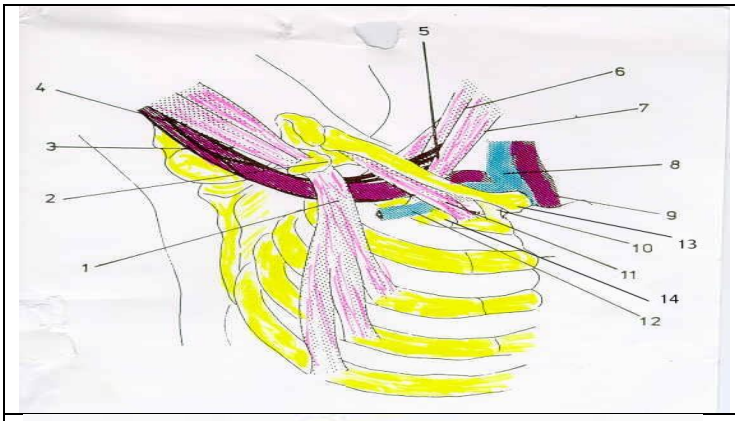
DEFINITIONS: Thoracic outlet syndrome is a disease of extrinsic compression of the artery, vein, or nerve at the thoracic outlet. The ***specific structures compressed are usually the nerves of the branchial plexus*** and occasionally the subclavian artery or subclavian vein. The compressing structures include the clavicle, the first rib, subclavian muscles, costoclavicular ligament and the anterior scalene.

Sir Astley Cooper first described axillary-subclavian artery symptoms due to compression from a cervical rib.

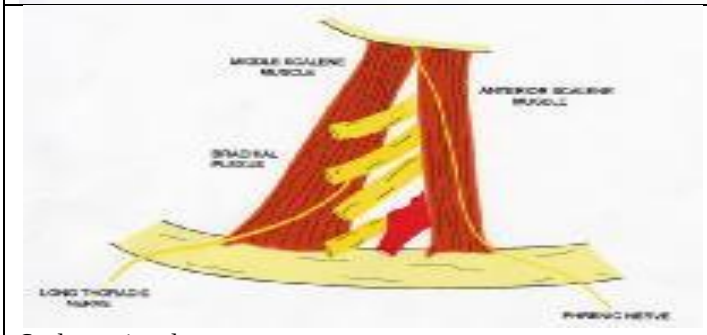
Thoracic outlet syndrome must be differentiated from symptomatic osteoarthritis of the cervical spine, tumors of the cervical spinal cord or nerve roots, periarthritis of the shoulder, and other cervicobrachial pain syndromes.

The predisposing factors are fibromuscular bands, bony protuberances and long or larger transverse processes, this together with the tendinous or cartilaginous muscular insertions are responsible for the compression of the neurovascular structures at the thoracic outlet.

Dynamic anatomical variations of tunnels have been postulated as possible etiologies for tunnel syndromes. This figure shows dynamic compression of the brachial plexus in the thoracic outlet.



1: Pectoralis minor muscle; 2: coracoid process; 3: median nerve; 4: subclavian artery; 5: brachial plexus; 6: medial scalene muscle; 7: anterior scalene muscle; 8: internal jugular vein; 9: common carotid artery; 10: costoclavicular ligament; 11: subclavious muscle; 12: subclavian vein; 13: Clavicle; 14: First Ribs.



Scalene triangle

SYMPTOMS

UPPER EXTEMITY	**ARTERIAL**	numbness of arms and hands
		tingling of arms and hands
		positional weakness of arms and hands
	VENOUS	swelling of fingers and hands
		heaviness of the upper extremity
	NERVES	upper extremity pain
		paresthesias of ulnar distribution
		weakness of the hands
		clumsiness of the hands
		coldness of the hands
		tiredness, heaviness and paresthesias on elevation of arms
SHOULDER AND NECK	~	pain - tightness
CHEST WALL	~	anginal chest pain
		inter-para scapular pain
HEAD	~	headaches
		funny feelings in face and ear
VERTEBRAL ARTERY	~	dizziness, lightheadness
		vertigo, syncope
		diplopia, dysarthria, dysphonia, dysphagia
		tinnitus, ear pain

Compression can be of different magnitude in each of these structures. For example, the subclavian vein can be the only compressed structure and this patient might have a thrombosis of the vein that was called in the past effort thrombosis, or a swelling of the fingers. The subclavian artery can also be compressed with symptoms of temporary, arterial, positional insufficiency of the upper extremity. When they are present for

a long time, aneurysm and thrombosis of the subclavian artery may develop with distal embolization. Nerve compression of the brachial plexus is very common and is or not associated with venous or arterial compression.

Paget Schroetter Syndrome: This is the name given to the subclavian vein thrombosis (beneath the clavicle) which results in pain, swelling, blue discoloration, and congestion of the arm. It is commonly caused by compression of the vein between the clavicle and the first rib, and is considered one of the venous manifestations of TOS.

PHYSICAL EXAMINATION:

- Posture
- The White Hand Sign
- C7-C8-T1 Testing
- Sweating, Swelling
- ***SELMONOSKY TRIAD***
    - Tenderness in the supra clavicular area.
    - Hand paleness and/or paresthesias on elevation.
    - Adduction and abduction weakness of fingers 4 & 5. (C8 - T1 testing)
- ***The Adson sign*** *is the loss of radial pulse by rotating the head to the ipsilateral side and inspiring.*

INVESTIGATIONS: Imaging Studies:

Chest x-ray: Cervical ribs or rudimentary first ribs often can be identified with a CXR.

CT scan:

- CT scans with 3-dimensional reconstruction have become popular for evaluating the thoracic outlet.
- CT scan angiography and venography.

Standard MRI*:* Dynamic MRI with gadolinium infusion also provides detail of the thoracic outlet and may be helpful when evaluating for compression.

Angiography with dynamic positioning.

Venography with dynamic positioning.

Other Tests:

Electromyography (EMG) and nerve conduction studies are useful in the workup of patients suspected of having neurogenic TOS. ***A reduction in nerve conduction velocity <85 m/s of either ulnar or median nerves across the thoracic outlet corroborates the diagnosis of neurogenic TOS***.

INDICATIONS: Failure of conservative treatment in a patient with severe disability.

TREATMENT

Physical therapy: Postural exercises, stretching, abdominal breathing, and medications used to relieve muscular tension and pain are beneficial.

No satisfactory medical treatment for arterial TOS exists.

Surgical therapy:

- Arterial TOS requires prompt surgical intervention to treat or prevent acute thromboembolic events.
- Treatment for venous TOS-related effort thrombosis relies on anticoagulation and arm elevation leaves.

Venous thoracic outlet obstruction: Surgical treatment of venous TOS consists of releasing the extrinsic compression and restoring luminal patency. ***After thrombolysis, surgeons wait one month before decompressive treatment surgery is undertaken***. Surgical decompression of veins within the scalene triangle is achieved by anterior rib resection, anterior scalene release and in some cases clavicular resection.

Neurogenic/arterial thoracic outlet obstruction

Thoracic outlet decompression can be performed through an ***axillary, supraclavicular, or posterior approach.*** Thoracic outlet decompression may entail ***anterior and middle scalenectomy, first rib resection, or scalenectomy plus first rib resection***.

Vascular trauma

- Vascular trauma can result from either blunt or penetrating injury

Types of vascular injury

- Contusion/ Puncture/ Laceration/ Transection

Pathophysiology

- Haemorrhage is the prime consequence of vascular injury.
- Bleeding may be obvious, with visible arterial haemorrhage, or it may be concealed.
- Ischaemia results from an acute interruption of flow of blood to a limb or organ.
- Peripheral nerves are more sensitive to ischaemia, and prolonged neurological deficit may result from relatively short periods of tissue ischaemia.
- If arterial supply is restored to ischaemia tissue, the sudden release of inflammatory mediators, lactic acid, potassium and other intracellular material into the circulation can cause profound myocardial depression, generalised vasodilatation and initiate a systemic inflammatory response.

Clinical features

- Depends on site, mechanism and extent of injury
- Signs classically divided into 'hard' and 'soft' sign

Hard signs of vascular injury

- Pulsatile bleeding
- Expanding haematoma
- Absent distal pulses, cold, pale limb- Distal ischaemia.
- Audible Bruit or palpable thrill
- Active haemorrhage

The presence of hard signs of vascular injury mandates immediate operative intervention without prior investigation.

Soft signs of vascular injury

- Haematoma
- History of haemorrhage at site of accident
- Unexplained hypotension
- Peripheral nerve deficit
- Decreased pulse compared to the contralateral extremity
- Bony injury or in proximity penetrating wound

Softer signs require close observation and monitoring. If the ABI is higher than 0.9, close observation is advocated, but if the ABI is lower than 0.9, further evaluation is warranted.

Investigation

- Arteriography should be considered:
    - To confirm extent of injury in stable patient with equivocal signs
    - To exclude injury in patient without hard signs but strong suspicion of vascular injury

Diagnostic Adjuncts

Pulse Oximetry: A reduction in oximeter readings from one limb, as compared to another is suggestive of significant vascular injury.

***Doppler* Ultrasound**: The diagnosis of a significant (ie. requiring intervention) vascular injury has been shown to be related to the presence or absence of a palpable pulse. Similarly, a reduction in the ankle-brachial pressure index (ABPI) in the presence of a palpable pulse does not indicate the presence of a vascular injury requiring intervention. Doppler ultrasound is therefore adds little to careful clinical examination.

Duplex Ultrasound: Duplex imaging is a non-invasive examination combining B-mode and Doppler ultrasound. Duplex can detect intimal tears, thrombosis, false aneurysms and arteriovenous fistulae.

Angiography: Angiography remains the gold-standard investigation for the further investigation and delineation of vascular injury. Proximal control may be possible with an angioplasty catheter prior to transfer to the operating room.

Management

- The priorities of vascular injury are arrest of haemorrhage and restoration of normal circulation.
- Airway control and respiratory assessment take priority over management of the circulation.

Immediate Haemorrhage Control: by direct pressure or where haemorrhage is welling up from a deep knife or gunshot track, control may be temporarily achieved by passing a urinary catheter into the track as far as possible, inflating the balloon. If angiography is performed prior to surgery, it may be possible to obtain proximal control by passing an angioplasty balloon catheter into the proximal vessel and inflating the balloon.

Volume resuscitation: Prior to haemorrhage control, minimal fluids should be administered. Raising the blood pressure will increase haemorrhage from the vessel injury. No inotropes should be given to the hypovolaemic patient as this will effectively deplete myocardial tissue oxygen and increase myocardial work. Once haemorrhage control is achieved, aggressive volume resuscitation is done.

Operative Strategy

- The basic principle of vascular repair is to gain proximal and distal control of the relevant vessel before investigating the site of injury.
- Proximal control is best achieved through a separate incision away from the site of injury.
- Distal control similarly is best achieved via a second incision.
- Once proximal and distal control is achieved, the site of injury can be explored and control made closer to the injury site.
- Once the vessel injury is identified, the first step is debridement of devitalized tissue and definition of the edges of the wound.
- Next an assessment of inflow and outflow is made. If it is inadequate, a balloon (Fogarty) catheter is passed proximally and distally to extract any thrombus.
- Following extraction, heparinized saline is instilled proximally and distally to locally antcoagulate the vessel.
- Small, clean, transverse wounds to vessels that involve only part of the circumference can be repaired with a direct suture technique.
- A vein or synthetic patch may be required where there is a larger defect in the vessel wall where direct suturing may lead to narrowing of the vessel lumen.
- While vein grafts probably have a longer patency, the graft infection rates are the same for both vein and synthetic grafts, regardless of wound contamination.

Compartment syndrome

- Prolonged interruprion of blood flow to a limb leads to cellular ischaemia, activation of cellular and humoral inflammatory responses and alterations in vascular permeability. Subsequent reperfusion of the limb leads to generalised tissue oedema.
- When this occurs in a limited, enclosed space - such as the fascial compartments of the lower limb, the pressure in the compartment may rise above capillary and venous pressure and cause vascular stasis, cellular ischaemia and death.
- The pressure in the compartments is rarely above arterial pressure and distal pulses are preserved.
- If the patient is awake, there is intense, disproportionate pain in the limb, worsened by passive flexion of the muscle groups.
- **In measurement of compartment pressures values over 30mmHg are diagnostic of compartment syndrome**.
- Fasciotomy is best performed at the time of initial surgery, rather than as a subsequent procedure for a second episode of limb ischaemia.

Aims of surgery are to:

- Control life-threatening haemorrhage
- Prevent limb ischaemia

- If surgery is delayed **more than 6 hours**, revascularisation is unlikely to be successful

Vascular repair

- Usually performed after gaining proximal control and wound debridement
- Options include :
  - Simple suture of puncture hole or laceration
  - Vein patch angioplasty
  - Resection and end-to-end anastomosis
  - Interpositional graft
- ***Contralateral saphenous vein is the ideal Interpositional graft***
- Prosthetic graft material may be used if poor vein or bilateral limb trauma

Complications of vascular injury

- ***Thrombosis of the graft remains the most common complication of vascular injury.***
- Narrowing of the vessel with primary repair or kinking of the graft, may require revision of the repair.

"False aneurysm"

- Most commonly occurs following catheterisation of femoral artery
- Often presents with pain, bruising and a pulsatile swelling
- Diagnosis can be confirmed by doppler ultrasound
- Suturing of puncture site/ Vein patching may be required

Arteriovenous fistula

- Often presents several weeks after the injury
- Patient complains of a swollen limb with dilated superficial veins
- **Machinery type bruit** (continuous) often present throughout cardiac cycle
- Diagnosis can be confirmed by angiography
- Fistula can be divided an both the vein and artery sutured
- Flap of fascia can be interposed between vessels to reduce risk of recurrence.

FLUID AND ELECTROLYTES

Distribution of body fluids

- ✓ Total Body Water (TBW) = 50 70% of body weight (BW)
- ✓ Depends upon
  - Lean body mass
  - Age

Fluid Compartments

Rapidly equilibrating with each other

1) Intracellular fluid (ICF) - 40% of Body Weight.
2) Extracellular fluid (ECF) - 20% of Body Weight
   a. Interstitial fluid (IF) - 14-15%BW
   b. Intravascular fluid (IVF)-5%-6% BW
3) Third space fluid & transcellular fluid - fluid outside the first two compartments.

- New born - 75%
- 1 Year - 65% (Constant throughout childhood)
- Adult Male-60%

Adult Female 55% (more s/c fat & small muscle mass)
(Blood volume= roughly 7-8% body wt)

Electrolyte	Intracellular fluid	Plasma	Intestinal fluid
Sodium	10	142	144
Potassium	150	5	4
Magnesium	40	3	2
Calcium	-	5	3
Total	200	155	153
Chlorides	-	103	114
Phosphates	120	2	2
Sulfates	30	1	1
Bicarbonaies	10	27	30
Protein	40	16	1
Organic acids	-	6	5
Total anions	200	155	153

	ICF	ECF
Principal cation	K^+ 97% intracellular (Mg^{2+} is second)	Na*(represents 90% of all ECF cations)
Principal anion	Phosphate	CI (although an accurate index of ECF volume, but total plasma chloride can change as a consequence of changes in acid base status)

Osmolarity (Osmotic pressure)

- Depends upon actual number of osmotically active particles in the solution and not their size
- ECF osmolality (mosm/Kg) = 2 (Na^+) mEq/1 + Glucose/18 rag/dl + BUN/2.8 mg/dl Normal serum osmolality is 285-290 mosm/1

Colloid Osmotic pressure (COP) [oncotic pressure)

It is the osmotic pressure generated by the presence of colloid on one side of a membrane which is impermeable to them. It is primarily responsible for effective osmotic pressure between the plasma and the interstitial fluid compartment. It is normally about 25 mmHg and tends to draw fluid into the intravascular compartment.

Composition of GI fluid loss

SOURCE	**DAILY LOSS (ML)**	**[NA*]**	*an*	[CL1	[$HC0_3$]
Saliva	1000	30-80	20	70	30
Gastric	1000-2000	60-80	15	100	0
Pancreas	1000	140	5-10	60-90	40-100
Bile	1000	140	5-10	100	40
Small bowel	2000 - 5000	140	20	100	25-50
Large bowel	200- 1500	75	30	30	0
Sweat	200-1000	20-70	5-10	40-60	0
Total secretions = 8-10 litres. Almost all reabsorbed in intestines (jejunum 6000, ileum 2000-3000).					

Daily electrolyte requirements & commonly use I/V fluids

	Daily requirement
Sodium	1 - 2 meq/kg
Potassium	0.5 -1.0 meq/kg
Calcium	0.2 - 3.0 meq/kg
Magnesium	0.35 - 0.45 meq/kg

Solution	**PH**	**Na+**	**CI-**	**K+**	**Ca+2**	**Bicarbonates**
Plasma mEq/1	**7.4**	**135-145**	**90-110**	**3.5-4.5**	**3-5**	**22-27**
D5%	5		-	-	-	-
Normal saline (NS) 0.9%	4.5	154	154	0	0	-
Lactated Ringer's (LR)	6.5	130	109	4	3	28 meq/L (Lactates)
Darrows	6.5	124	104	36		56 meq/L (Lactates)
3% saline	-	513	513	-		-
5% saline	-	855	855	-	-	-

	Prerenal Oliguria	**Renal Oliguria**
1. Urine Osmolality (mosm/1)	>500	~ 300
2. BUN / S.cretinine	> 10	< 10
3. Urine sodium mEq/L	<20	>40
4. U/P creatinine	>40	<20
6. Renal failure Index (RFI) UNaxPCr/UCrxlOO	< 1	> 1
7. Fractional excretion of sodium UNa/PNax PCr/UCrxlOO	<1	>1
8. Urine specific gravity	>1.020	~ 1.010
9. Urinary Sediment	Hyaline casts	Granular cast
Examples	Prerenal azotemia, acute GN, hepatorenal syndrome, early sepsis	ATN, severe obstructive uropathy, preexisting CRF, diuretic use

Electrolytes Imbalance

Sodium balance
Normal range - 135 - 145 mEq/L
Hyponatremia

Types:

1. Hypovolemic hyponatremia [TBS i]
   - Severe isotonic dehydration (ECF volume loss).
2. Hypervolemic hyponatremia [Edematous states TBS t]
   - Occurs in conditions of
     a. Cirrhosis, CHF, nephrotic syndrome - 'Effective' volume decreases because of low cardiac output (CHF) or sequestration of fluid outside the central circulation e.g.-↓ plasma oncotic pressure resulting in reduced renal perfusion
     b. Acute stress, trauma, hypovolemia - endocrine response to injury
3. Isovolemic hyponatremia [TBS normal]
   a. SIADH is the most prevalent etiology of euvolemic hyponatremia.
      i. Specific diagnostic criteria that define SIADH include the following:
         a. Hyponatremia
         b. Hypotonicity
         c. Inappropriately concentrated urine
         d. Elevated urine sodium concentration
         e. Clinical euvolemia
         f. Normal renal, adrenal, and thyroid function
         g. No edema
      ii. Excess ADH may emerge from the pituitary gland or an ectopic source:
         a. CNS disorders: Head trauma. Stroke, Neonatal hypoxia, Brain tumor, Hydrocephalus, Cerebral abscess. Meningitis, Encephalitis, Subarachnoid hemorrhage e.t.c.
         b. Malignancies: neoplasms with a potential to synthesize, store, and secrete ADH (eg, increased levels of ADH found in -60% of patients suffering from small cell carcinoma of the lung). Others: Brain, Pancreas, Prostate, Ovary, Lymphoma, Leukemia, Thymoma.
         c. Pulmonary disease: Pneumonia. Tuberculosis, Empyema, Abscess, Asthma, COPD
         d. Endocrine disorders: Hypothyroidism / myxedema, deficiency
         e. Drugs
            - Analgesics (eg, narcotics, NSAIDS)
            - Antidepressants (eg, MAO inhibitors, tricyclic antidepressants, selective serotonin reuptake inhibitors)
            - Barbiturates
            - Carbarn azepine
            - Cyclophosphamide Clofibrate
            - Diuretics (especially thiazides)
            - Neuroleptics (eg, phenothiazines)
            - Oral hypoglycemics (eg, chlorpropamide, tolbutamide)
      - Treatment: For asymptomatic or mildly symptomatic hyponatremia, water restriction.
      - Demeclocycline- Interferes with action of ADH at renal collecting duct.

C/F of hyponatremia:

- Neurological dysfunction

- Intracellular movement of water -brain cell edema ↓→ flCT→HT, lethargy, confusion, coma. Later tissue signs of excessive intracellular water e.g. - "Finger printing sign"
- If Hyponatremia develops rapidly, signs of hyper excitability - irritability, muscular twitches & hyperactive deep tendon reflexes

Treatment

Asymptomatic hyponatremia are managed with free water restriction.
Severe, Symptomatic hyponatremia should be treated with hypertonic saline.
Rapid correction of hyponatremia can pontine myelinolysis
Once S. Sodium levels reach 130mEq/L, the further correction is carried out more slowly by water restriction.

Hypernatremia

Causes:

Solely due to water loss

- Extrarenal- insensible loss- skin/lungs.
- Renal-Diabetes insipidus

Water loss with sodium loss

- Extrarenal- sweat
- Renal- osmotic diuresis-glycosuria, urea.

Due to sodium gain

- Iatrogenic
- Adrenal hyperfunction- hyperaldosteronism, Cushing's.

Principal C/F

CNS system
Due to dehydration of brain cells
↑ neuromuscular excitability, twitching, seizures, stupor & coma
Tissue signs - "dry sticky mucous membranes" are characteristic of this condition

Treatment

I/V infusion of free water (5% dextrose)
Correction advised slowly over days.
Rapid correction may lead to cerebral edema

Potassium balance: hyperkalemia & Hypokalemia

98% of potassium is intracellular, with the concentration gradient maintained by the sodium- and potassium-activated adenosine triphosphatase (Na^+/ K^+-ATPase) pump that is controlled by insulin and p-2 receptors
Cellular concentration is approx 40 times the ECF.
The normal potassium level is 3.5-5.0 mEq/L.

Potassium balance:

Minute-to-minute levels of potassium are controlled by intracellular to extracellular exchange. A balance of GI intake and renal potassium excretion achieves long-term potassium balance. *All regulation of K+ excretion occurs at distal nephrons.* The excess K^+ is excreted prompdy. The filtered K^+ is nearly completely reabsorbed in the proximal segments and the K^+ in urine is derived almost entirely from K^+ secreted in the distal convoluted tubules. K^+ secretion is influenced by:

- Aldosterone
- Distal tubular fluid flow rate
  - ❑ Increased distal delivery of fluids, e.g. loop diuretics, favors K^+ excretion,

- Acid base balance
  - Alkalosis enhances and acidosis depresses renal potassium secretion, probably by inducing corresponding changes in tubular cell potassium.

Hyperkalemia:

Defined as a potassium level greater than 5.5 mEq/L

Causes:

- Pseudohyperkalemia
  - Sample hemolysis
- Redistribution
  - Acidosis
  - Insulin deficiency
  - Drugs
    - Beta-blockers
    - Acute digoxin intoxication or overdose
    - Succinylcholine (releases K* from muscles by depolarizing cell membranes)
    - Arginine hydrochloride - used to treat metabolic acidosis (drives K^+ out of cells)
  - Hyperkalemic familial periodic paralysis -1 [K^+] is associated with repeated attacks of muscle paralysis. Mechanism obscure.
- Excessive endogenous potassium load
  - Trauma
  - Burns
  - Hemolysis
- Excessive exogenous potassium load
- Diminished renal potassium excretion (principal cause)
- Potassium-sparing diuretics (spironolactone, triamterene, amiloride)
- ↓ Effective circulating volume.
- Laboratory error

History:

- Patients may be asymptomatic or report the following:
  - Generalized fatigue & weakness
  - Paresthesias
  - Paralysis
  - Palpitations

ECG changes:

- Peaked (tented) T waves (earliest)
- PR interval prolongation
- QRS widening
- Loss of P wave
- Sine wave
- Ventricular fibrillation or cardiac arrest in asystole.

Treatment:

1. Calcium: Calcium chloride or calcium gluconate
2. Alkalinizine agents: Sodium bicarbonate
3. Beta-agonists: Albuterol
4. Loop diuretics: Purosemide (Lasix)
5. Binding resins: Sodium polystyrene sulfonate (Kavexalate)
6. Dialysis

Hypokalemia

Hypokalemia is defined as a plasma potassium level of less than 3.5 mEq/L.

Causes:

- Gasrointestinal losses
  - o Gastrointestinal losses from vomiting, diarrhea, NG suction e.t.c.
- Renal
  - o Metabolic alkalosis (excess bicarbonate delivery to the distal nephron)
  - o Diuretics (MC cause of |[K*]
    - Thiazides
    - Loop diuretics
    - CA inhibitors
  - o Excessive mineralocorticoid effects
  - o Renal tubular disease
- Hypokalemia due to shifts into the cells (no depletion)
  - o Hypokalemic periodic paralysis - sudden movement of potassium into the cells
  - o Insulin effects o Alkalosis
  - o Increased β- adrenergic activity (or ↓ α - adrenergic activity).
- Drugs
  - o P-agonists and a-blockers.
  - o Theophylline
  - o Verapamil (with overdose)
  - o High-dose penicillin
  - o Ampicillin
    - Carbenicillin

Signs of ↓ **K*:**

- Absent tendon reflexes & paralaytic ileus

A) Complications

- Cardiac arrhythmias and acute respiratory failure from muscle paralysis.
- TT sensitivity to digitalis → arrhythmias

Lab Studies:

- Serum electrolytes

> Unlike hyponatremia, serum potassium may not accurately reflect total body stores.

- Blood gas analysis
  - o Assess acid-base status.
  - o Alkalosis may induce hypokalemia

Other Tests:

- ECG
  - o T-wave flattening
  - o Appearance of U waves
  - o ST-segment depression
  - o Prolongation of PR interval
  - o QT prolongation.
  - o Cardiac arrest in systole

• Symptomatic or severe hypokalemia should be corrected with a solution of intravenous potassium.

- Potassium chloride -- First choice for IV therapy. 10-40 mEq IV infused over 2-3 h; not to exceed 10 mEq/h (40 mEqA with monitoring)

Calcium regulation; Hypercalcemia & Hypocalcemia

• Approximately 99% of calcium is found in bone, and 1% is found in extracellular fluid. Of this 1 %, 50% is in the free (active) ionized form (1-1.15 mmol/L), 40% is bound to protein (predominantly albumin), and 10% circulates bound to anions (phosphate, carbonate, citrate, lactate, sulfate).

- Normal S. calcium levels - 8 to 10 mg / dL (2.0 to 2.5 mmol/ L or 4 to 5 mEq/L).
- Normal ionized calcium levels - 4 to 5.6 mg / dL (1 to 1.4 mmol / L).
  - Clinical signs and symptoms are observed only with decreases in ionized calcium concentration. Alkalemia increases binding, thereby decreasing the ionized calcium. Plasma [Ca^{2+}] is maintained within the reference range by a complex interplay of 3 major hormones, PTH, 1,25-dihydroxyvitamin D (i.e. calcitriol), and calcitonin.

Actions of the Hormones Involved in Calcium Homeostasis

Hormone	Effect on bones	Effect on gut	Effect on kidneys
Parathyroid hormone ↑Ca^{++}, 4'$P0_4$ levels in blood	Supports osteoclast resorption	Indirect effects via ↑ calcitriol from 1-hydroxylation	Supports Ca^{++} resorption and $P0_4$ excretion, activates 1-hydroxylation
Calcitriol (vitamin D) ↑Ca^{++}, ↑$P0_4$ levels in blood	Indirect effects. Supports osteoblasts	↑Ca^{++} and $P0_4$ absorption	No direct effects
Calcitonin causes ↑Ca^{++}, ↓$P0_4$ levels in blood when hypercalcemia is present	Inhibits osteoclast resorption	No direct effects	Promotes Ca^{++} and $P0_4$ excretion

Hypercalcemia

- Hypercalcemia is defined as a serum calcium level greater than 10.5 mg/dL.

Causes:

- ✓ Hyperparathyroidism is overall the most common cause of hypercalcemia. Malignancy is the second most common cause.
- ✓ Hyperparathyroidism is the most common cause of hypercalcemia on routine screening.
- ✓ Malignancy is the commonest cause of hypercalcemia in hospitalized patients.

PTH-mediated hypercalcemia (Primary hyperparathyroidism)

- It is overall the commonest cause of hypercalcemia. Usually in 3-5 decades.
- The incidence of primary hyperparathyroidism is considerably higher in women.

Non-PTH-mediated hypercalcemia

Malignancies:

- Hypercalcemia is the most common life-threatening metabolic disorder associated with neoplastic diseases.
- Bronchogenic carcinoma (MC), followed by CA Breast, RCC, and hematological disorders e.g. multiple myelomas, leukemias or lymphomas (specially theT cell variant).

✓ The remaining 10% of cases of hypercalcemia are caused by many different conditions, including vitamin D-related problems, disorders associated with rapid bone turnover, thiazides or renal failure, and, in rare cases, familial causes.

Causes related to vitamin D:

- Vitamin D toxicity
  → Excessive ingestion of vitamin D t intestinal calcium absorption
- Granulomatous disease (especially sarcoidosis)
  → Abnormal metabolism of vitamin D.
- Idiopathic infantile hypercalcemia (Williams syndrome)

Causes related to high bone turnover:

- Hyperthyroidism
- Immobilization
- Thiazides
- Vitamin A intoxication

Causes related to renal failure:

- Severe secondary hyperparathyroidism due to progressive renal damage,
- Milk-alkali syndrome
- Aluminum intoxication as occurs in patients with chronic dialysis

Other causes related to particular mechanisms:

- Decreased renal calcium excretion (or increase renal calcium reabsorption)
  - Familial hypocalciuric hypercalcemia
  - Thiazide diuretics
  - Hypophosphatasia

Signs and symptoms

- Symptoms relate to CNS, renal, GI, and cardiac. CNS **symptoms are the most common and the earliest symptom usually is lethargy or feeling tired.**
- Central nervous system:
  - Irritability
  - Memory loss
  - Apathy
  - Depression
  - Dementia
  - Lethargy
  - Confusion
  - Coma
- Renal effects:
  - Polyuria
  - Nocturia
  - Volume contraction
  - Thirst .
- Gastrointestinal effects:
  - Anorexia
  - Pain
  - Nausea
  - Vomitings
  - Constipation (due to dehydration) & Fecal impaction

ECG Changes:

- QT interval shortening.
- PR interval prolongation.
- QRS interval lengthening (at very high levels)
- T waves flattening or inversion(at very high levels)
- A variable degree of heart block.(at very high levels)
- Digoxin effects are amplified.
- **Treatment**

- Volume expansion with NS followed by Loop Diuretics
- Inhibition of bone resorption
  - Calcitonin
  - Bisphosphonates
  - Mithramycin (Plicamycin)
  - Gallium nitrate
- Mobilization
- Reduction of gastrointestinal calcium absorption
  - Reduction of dietary calcium
  - Oral phosphate - forms insoluble calcium phosphate in the gut.
- Dialysis

Surgical Care:

- Parathyroidectomy is the definitive treatment for hyperparathyroidism.
- Hypercalcemia due to malignancy may require surgical resection of the tumor.

Hypocalcemia:

- A serum calcium level less than 8.5 mg/dL

Causes:

- PTH deficiency
- Vitamin D deficiency
- Miscellaneous disorders
  - Acute pancreatitis
  - Toxic shock syndrome.
  - Hypoalbuminemia.
  - Infiltrative disease: Sarcoidosis, tuberculosis may infiltrate & dysfunction parathyroids,
- Drugs
  - Calcitonin and bisphosphonates.
  - Diuretics - Furosemide.
  - Estrogen inhibits bone resorption.

Clinical features:

- Numbness and tingling sensations in the perioral area (earliest sign).
- Muscle cramps; may progress to carpopedal spasm (i.e. tetany).
- Neurological symptoms, including irritability, confusion, depression, and personality changes, hallucinations, dementia, extrapyramidal manifestations, and seizures.
- Respiratory - laryngospasm and bronchospasm.
- Subclinical tetany
  1. Chvostek sign
  2. Trousseau sign
- ECG changes:
  1. ↑ Q T interval-used to monitor serum calcium

Medical Care:

10 ml of 10% calcium gluconate.
Vit D supplement & Calcium
PTH if required

Magnesium

- Magnesium (Mg) is the second-most abundant intracellular cation and, overall, the fourth-most abundant cation.
- The intracellular concentration is 40 mEq/L, while the normal serum concentration is 1.5-2.0 mEq/L. Serum levels do not necessarily reflect the status of total body stores.
- Approx. 60% of total body magnesium is located in bone, 38% in the soft tissues (intracellular) and only less than 2% is present in the ECF compartment. Of this serum component, 30% is protein bound, 20 % is complexed, and the remaining 50% is ionized. Analogous to plasma calcium, the free (ie.ionized) fraction of magnesium is the active component.
- Almost all enzymatic processes using phosphorus as an energy source (eg, adenosine triphosphatase [ATPase]) require magnesium for activation. It is involved in nearly every aspect of biochemical metabolism (eg, deoxyribonucleic acid [DNA] and protein synthesis, glycolysis, oxidative phosphorylation).
- Magnesium is a component of chlorophyll and is present in high concentrations in all green plants. Seed grains, nuts, peas and beans are rich source. Less than 40% of dietary magnesium is absorbed, predominantly in the jejunum and ileum, and excreted in stool and urine.
- Elimination is predominantly renal. The kidney is the main regulator of magnesium concentrations. Normally, only 3% of filtered magnesium appears in urine; thus, 97% is reabsorbed by the renal tubules. When serum levels rise above 2.5 mEq/L, magnesium excretion increases dramatically. Conversely, the magnesium retention by the kidneys is very efficient i.e. the kidney retains a strong capacity to resorb magnesium, and the main site for reabsorption is the thick ascending loop of Henle (THAL). Several factors may impair renal reabsorption, such as volume expansion, ethanol ingestion, hypercalcemia, and diuretic administration (eg, osmotic, thiazide, loop). Of these 3 types of diuretics, loop diuretics have the greatest effect on renal magnesium wasting because of their site of action.

Hypermagnesemia:

Hypermagnesemia is a rare electrolyte abnormality because the kidney is very effective in eliminating excess magnesium by rapidly reducing its tubular reabsorption to almost negligible amounts.

Causes:

MC cause: Renal insufficiency

II MC Cause: Iatrogenic, especially errors in calculating appropriate infusions.

Additional causes include the following:

- Acidosis
- Ingestion of magnesium-containing substances such as vitamins, antacids, or cathartics by patients with chronic renal failure
- Acute renal failure (oliguric phase)
- Neonates bom to eclamptic mothers treated with magnesium, which passes through the placental circulation.
- Decreased GI elimination and increased GI absorption of magnesium due to intestinal hypomotility.
- Tumor lysis syndrome, by releasing massive amounts of intracellular magnesium.
- Adrenal insufficiency (secondary hypermagnesemia).
- Rhabdomyolysis, like tumor lysis syndrome, by releasing significant amounts of intracellular magnesium
- Milk-alkali syndrome
- Hypothyroidism
- Hypoparathyroidism

- Neoplasm with skeletal muscle involvement
- Lithium intoxication by supposedly decreasing urinary excretion, although the mechanism for this is not completely clear.
- Extracellular volume contraction, as in diabetic ketoacidosis (DKA)
- Familial hypocalciuric hypercalcemia- This autosomal dominant disorder is characterized by very low excretion of calcium and magnesium, and the increase in magnesium reabsorption appears to occur from an abnormal sensitivity of the loop of Henle to magnesium ions.

Signs an,d symptoms;

- ✓ Hypermagnesemia affects the neuromuscular, CNS and cardiac organ systems.
- ✓ Symptoms of hypermagnesemia usually are not apparent unless the serum magnesium level is greater
- ✓ than 2 mmol/L.
- ✓ Concomitant hypocalcemia, hyperkalemia, or uremia exaggerates the symptoms of hypermagnesemia at any given level
  - **Nonspecific symptoms (earliest, at** 2-4 **mmol**/1)
  - These symptoms include nausea (earliest), vomiting, and cutaneous flushing.

Neuromuscular symptoms

These are the most common presenting problems.

Hypermagnesemia causes blockage of neuromuscular transmission by preventing presynaptic acetylcholine release. **One of the earliest symptoms is loss of deep-tendon reflex.**

- Facial paresthesias also may occur at moderate serum levels.
- Muscle weakness is a more severe manifestation, occurring at levels greater than 5 mmol/L. This manifestation can proceed to flaccid paralysis, then to depressed respiration, and, eventually, to apnea.

• **CNS system**

- Lightheadedness
- Depressed levels of consciousness.
- Stupor or coma

• **Conduction system symptoms**

- Hypermagnesemia depresses the conduction system of the heart and sympathetic ganglia.
  - Hypotension
  - Bradycardia
  - Intraventricular conduction delay
  - Arrhythmia, including atrial fibrillation
  - Complete heart block and cardiac arrest may occur at levels greater than 7 mmol/L

• **Hypocalcemia**

- Discussed already

Lab Studies:

- Electrolytes, including potassium, magnesium, and calcium levels
  - o Elevation in magnesium level is usually not found as an isolated electrolyte abnormality,
  - o Hyperkalemia and hypercalcemia are often present concurrently.
- BUN and creatinine levels
- Arterial blood gases (ABG) may reveal a respiratory acidosis.

Other Tests:

- An ECG and cardiac monitor may show prolongation of the PR interval or intraventricular conduction delay, which are nonspecific findings.
- The ECG findings may reflect other electrolyte abnormalities such as hyperkalemia.

Treatment:

- In patients with mildly increased levels, simply stop the source of magnesium.
- In patients with higher concentrations or severe symptoms, other treatments are necessary as follows:
    - **Intravenous fluids with diuretics:**
        - Intravenous fluids e.g. NS, cause the dilution of the extracellular magnesium. These are used with diuretics to promote increased excretion of magnesium by the kidney. Furosemide (Lasix) is the diuretic of choice. It acts at loop of Henle to promote magnesium diuresis.
    - **Calcium gluconate:**
        - Calcium directly antagonizes the neuromuscular and cardiovascular effects effects of magnesium. Reserved for patients with severe or symptomatic hypermagnesemia. 10% IV solution
    - **Dialysis:**
        - Best used when levels exceed 8 mEq/L, when life-threatening symptoms are present, or in patients with poor renal function.

Hypomagnesemia

Causes: Most causes are related to renal and GI losses.

- **GI losses or low intake**
    - Malabsorption.
    - GI secretions in large amounts, e.g. chronic diarrhea, laxative abuse, inflammatory boweldisease, or neoplasm,
    - Prolonged TPN.
- **Renal losses**
    - Primary renal disorders - by decreased tubular reabsorption of magnesium.

Clinical effects:

- Neuromuscular irritability (Earliest, at serum magnesium levels less than 1.0 mEq/L)
    - Hyperactive deep tendon reflexes
    - Muscle cramps
    - Trousseau and Chvostek signs
- CNS hyperexcitability
    - Irritability
    - Psychosis

Treatment:

- Magnesium is administered PO (oxide or gluconate form) for patients with mild depletion,
- IV replacement, as a sulfate salt is indicated for severe clinical effects.

Miscellaneous Facts:

Pyloric Stenosis

- K, *I* CL\ metabolic alkalosis with paradoxical acidosis
- Rx = replace ECF with Isotonic NaCl & K^+

Anion gap

Anion gap = $(Na^+ + K^+) - (CI + HC0_3)$

= 10-15 meq/1

Metabolic acidosis

↑ Anion Gap.	(N) Anion Gap.
-Commonest = shock	- Diarrhea
-Diabetic ketoacidosis	- Small bowel fistula
-Alcohol intoxication	-Uretrosigmoidostomy
-Uraemia	-Proximal RTA
-Salicylate toxicity	- Distal RTA
-Oxaloisis	- Dilutional acidosis