Surgical Safety Checklist

World Health Organization | Patient Safety
A World Nation for safer Health Care

Before induction of anaesthesia

(with at least nurse and anaesthetist)

Has the patient confirmed his/her identity, site, procedure, and consent?
- ☐ Yes

Is the site marked?
- ☐ Yes
- ☐ Not applicable

Is the anaesthesia machine and medication check complete?
- ☐ Yes

Is the pulse oximeter on the patient and functioning?
- ☐ Yes

Does the patient have a:

Known allergy?
- ☐ No
- ☐ Yes

Difficult airway or aspiration risk?
- ☐ No
- ☐ Yes, and equipment/assistance available

Risk of >500 ml blood loss (7 ml/kg in children)?
- ☐ No
- ☐ Yes, and two IVs/central access and fluids planned

Before skin incision

(with nurse, anaesthetist and surgeon)

- ☐ **Confirm all team members have introduced themselves by name and role.**
- ☐ **Confirm the patient's name, procedure, and where the incision will be made.**

Has antibiotic prophylaxis been given within the last 60 minutes?
- ☐ Yes
- ☐ Not applicable

Anticipated Critical Events

To Surgeon:
- ☐ What are the critical or non-routine steps?
- ☐ How long will the case take?
- ☐ What is the anticipated blood loss?

To Anaesthetist:
- ☐ Are there any patient-specific concerns?

To Nursing Team:
- ☐ Has sterility (including indicator results) been confirmed?
- ☐ Are there equipment issues or any concerns?

Is essential imaging displayed?
- ☐ Yes
- ☐ Not applicable

Before patient leaves operating room

(with nurse, anaesthetist and surgeon)

Nurse Verbally Confirms:
- ☐ The name of the procedure
- ☐ Completion of instrument, sponge and needle counts
- ☐ Specimen labelling (read specimen labels aloud, including patient name)
- ☐ Whether there are any equipment problems to be addressed

To Surgeon, Anaesthetist and Nurse:
- ☐ What are the key concerns for recovery and management of this patient?

FIGURE 10-4 Surgical safety checklist published by the World Health Organization.

BOX 9-2 Elements of the Surgical Safety Checklist

Sign In

Before induction of anesthesia, members of the team (at least the nurse and an anesthesia professional) state that the following have been done:

- The patient has verified his or her identity, surgical site and procedure, and consent.
- The surgical site is marked or site marking is not applicable.
- The pulse oximeter is on the patient and functioning.
- All members of the team are aware of whether the patient has a known allergy.
- The patient's airway and risk of aspiration have been evaluated, and appropriate equipment and assistance are available.
- If there is a risk of blood loss of at least 500 mL (or 7 mL/kg body weight in children), appropriate access and fluids are available.

Time-Out

Before skin incision, the entire team (nurses, surgeons, anesthesia professionals, and any others participating in the care of the patient) or specific members state aloud the following:

- Team confirms that all team members have been introduced by name and role.
- Team confirms the patient's identity, surgical site, and procedure.
- Team reviews the anticipated critical events.
  - Surgeon reviews critical and unexpected steps, operative duration, and anticipated blood loss.
  - Anesthesia professionals review concerns specific to patient.
  - Nurses review confirmation of sterility, equipment availability, and other concerns.
- Team confirms that prophylactic antibiotics have been administered ≤60 minutes before incision is made or that antibiotics are not indicated.
- Team confirms that all essential imaging results for correct patient are displayed in operating room.

Sign Out

Before the patient leaves the operating room, the following are done:

- Nurse reviews the following aloud with the team:
  - Name of procedure, as recorded
  - That needle, sponge, and instrument counts are complete (or not applicable)
  - That specimen (if any) is correctly labeled, including patient's name
  - Whether there are any issues with equipment that need to be addressed
- The surgeon, nurse, and anesthesia professional review aloud the key concerns for the recovery and care of the patient.

Adapted from Haynes AB, Weiser TG, Berry WR, et al: A surgical safety checklist to reduce morbidity and mortality in a global population. *N Engl J Med* 360:491–499, 2009.

SURGICAL AUDIT

- Comparing aspects of surgical care (structure / process / outcome) against explicit criteria / difined standards and suggesting remedial measures at: (Donabedian)
  - individual level - training
  - team level - approach, definition of roles
  - institutional level - eg: antibiotic policy
  - regional level - eg: provision of tertiary / reference centres
  - National level - screening programmes
    Health education campaigns

AUDITS
- NATIONAL
- LOCAL / HOSPITAL
  - Eg: Mortality & Morbidity meetings

AUDIT CYCLE

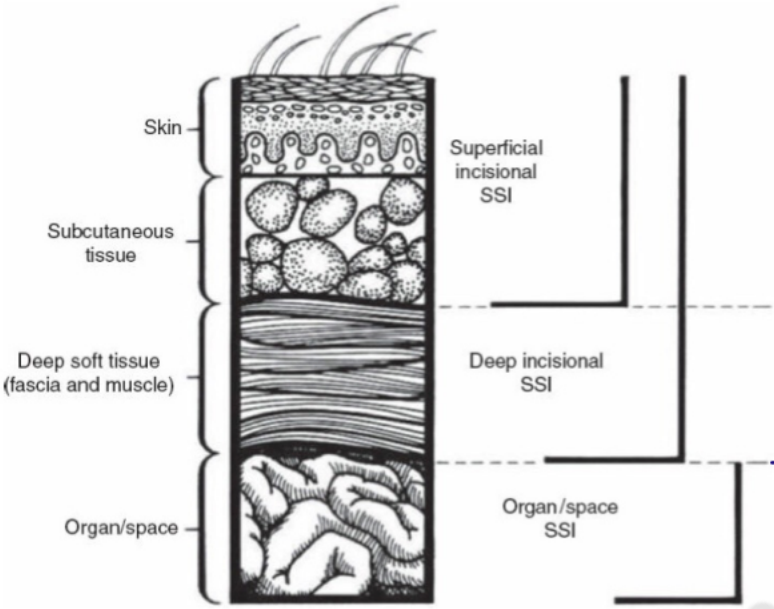
1) Define the audit question in a multidisciplinary team
2) Define the body of evidence & current standards
3) Design the audit
   - measure performance against agreed standards
4) Define the duration of the audit - measure performance over an agreed interval
5) Analyse results
6) Undertake gap analysis:
   - Standards are met → Plan for re-audit
   - Need for improvement → identify possible interventions
7) Reaudit

AUDIT	VS	RESEARCH	VS	SERVICE EVALUATION
'Does this service reach a predetermined standard?'		'Is this hypothesis correct?'		'What standard does this service achieve?'
Measures against some standard		Addresses clearly defined questions, aims & objectives		Measures current service without some def std
involves some intervention already in use		may involve evaluating or comparing interventions, esp new ones		involves some intervention already in use
No randomisation		May involve randomisation		No randomisation

Surgical Site Infections & Antibiotic Prophylaxis

SSI - an infection involving the surgical site within 30 d of Sx (no implant)
1y of Sx (if implant +)

NHS classification of SSI



Criteria

Purulent discharge
Organisms isolated from aseptically obtained sample culture
≥1 of: pain / tenderness
localized swelling
redness / warmth
Surgeon lets out sutures

- Purulent from depth but not organ/space
- Spontaneous dehiscence / Abscess / Surgeon opens

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involves parts opened / manipulated during procedure (excluding skin, subcuts, fascia, muscle layers)

- Purulent drainage from drain in organ/space
- Organisms isolated from aseptically obtained sample culture

Risk factors

Patient related

Age
Obesity
Malnutrition
T_2DM
Steroids
Immunosuppression
Colonization
Smoking
Remote infection

Procedure related

Issues i instrument cleaning, decontamination, sterilization
OR ventilation
Shaving
Skin prep
Scrub technique
Drain
tourniquet time
Duration

Management - Source control / focus elimination
Antibiotics
Supportive care

PRINCIPLES OF SURGICAL ANTIBIOTIC PROPHYLAXIS

- Goal - prevent HAI & SSI related mortality & morbidity in surgical pts
- Parenteral Antibiotics
  - Effective
    Active against the pathogens which are likely to contaminate the surgical site
  - Appropriate dosage
  - At the right time → i in 60-120 min before incision to ensure adequate tissue conc. during the period of potential contamination
  - Redosing if procedure duration exceeds 2 $t_{1/2}$ of the antibiotic
    → 4 hrs in case of cephazolin

Generally - Cefazolin 2g

- Duration - except for few cases, not need to extend post-op
  → upto 24h post op
- Indication

Clean
- ± Implants
- Cardiac surgery
- Breast surgery
- Hernia
- Extensive soft tissue procedures

Clean Contaminated
GI
Colorectal
Urological
cholecystectomy
Bariatric

MRSA nasal carriers - periop mupirocin 2% nasal cream

Contaminated
Dirty
} Need Abx treatment
NOT PROPHYLAXIS

Clean

An uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tracts are not entered. In addition, clean wounds are primarily closed and, if necessary, drained with closed drainage. Operative incisional wounds that follow nonpenetrating (blunt) trauma should be included in this category if they meet the criteria.

Clean-Contaminated

Operative wounds in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination. Specifically, operations involving the biliary tract, appendix, vagina, and oropharynx are included in this category, provided no evidence of infection or major break in technique is encountered.

Contaminated

Open, fresh, accidental wounds. In addition, operations with major breaks in sterile technique (e.g., open cardiac massage) or gross spillage from the gastrointestinal tract and incisions in which acute, nonpurulent inflammation is encountered are included in this category.

Dirty or Infected

Includes old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera. This definition suggests that the organisms causing postoperative infection were present in the operative field before the operation.

National Healthcare Safety Network. Patient safety component manual: key terms. www.cdc.gov/nhsn/PDFs/pscManual/16pscKeyTerms_current.pdf

SURGICAL COMPLICATIONS OF OBESITY

① Impaired wound healing

- ↓ Regional perfusion, ↓ O_2 tension
- Metabolic syndrome – hyperglycemia – ↑ risk of infections
  immune dysregulation
  redundant skin folds – colonization of bacteria
  maceration
  ulceration

↑ Seroma
↑ Hematoma
↑ Fat necrosis
↑ Anastomotic leakage

② Respiratory complications

Altered respiratory mechanics in obesity – OSA – Pulmonary HTN
– Decreased chest wall compliance ↓
worsened if GA

↑ Post op atelectasis, shunt physiology

③ Cardiovascular complications

Perioperative coronary events
venous thromboembolism

④ ↑ incidence of incisional hernia
↓
Fatty infiltration of muscle layers
↘ sarcopenia
↓
poor strength

⑤ ↑ Operative times
↘ Associated morbidity

STERILISATION & DISINFECTION

Sterilization: process that destroys / eliminates all forms of microorganisms

Disinfection: process that eliminates many / all pathogenic micro-organisms except spores

Antiseptics: Disinfectants that can be applied to living tissues safely to inhibit microbial growth

Cleaning: Removal of visible contamination from objects or surfaces done manually / mechanically using water / detergents / enzymatic products

Decontamination – removal of pathogenic organisms from objects so that they are safe to handle / use / discard

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CLEANING

- done before disinfection / sterilisation

Eg: Presoak, rinse surgical instruments to remove visible dirt like blood, secretions etc.

METHODS

Friction
↓
Rubbing
Scrubbing
Brushing

Fluidics
↓
Jet of liquid to remove dirt clinging to internal channels of instruments

Mechanical
Ultrasonic / automatic washers
↓
Agitation

Detergents
near neutral pH solutions
[↑/↓pH → corrosive; Spoils instruments]

Enzymatic
Proteases – to remove congealed blood

DISINFECTION

Chemical Disinfectants

1) Alcohol – ethyl alcohol
ISOPROPYL ALCOHOL } act by denaturation of proteins

Bactericidal
Tuberculocidal
Virucidal
NOT SPORICIDAL
CANNOT PENETRATE PROTEIN RICH MATERIAL
DAMAGE RUBBER TUBING, LENSED INSTRUMENTS
FLAMMABLE

Uses: Prepping surgical surfaces
Disinfecting scissors, oral & rectal thermometers, stethoscopes,
→ Not suitable for surgical instruments

2) Chlorine Compounds – HYPOCHLORITE → free radical damage
Sodium Hypochlorite – Household bleach
Broad spectrum antimicrobial activity
cheap
fast acting

used as spot disinfectant for decontaminating spills of blood/ infective secretions
Decontamination of discarded sharps & medical wastes
Disinfecting floors & surfaces

3) FORMALDEHYDE < gas / liquid } acts by alkylating amino & sulfhydryl groups of nucleic acids

↓ also has some sporicidal activity
↓ disadvantage – irritant

4) GLUTARALDEHYDE – MOA same as formalin
CIDEX
less irritant
lesser contact time
Non corrosive

Lap instruments
Endoscopes
Anaesthesia equipment
Dialysis equipment

most commonly used disinfectant solution for surgical instruments

STERILISATION

① HEAT

Dry heat

1) Direct Flaming
2) Incineration (for disposal)
3) Hot air oven
   - 2 hrs at 170°C
   - → Glassware

Moist heat

AUTOCLAVE

120° × 40 min

↓

Most surgical instruments

② GAS

→ ETO (Ethylene Oxide)

↓

for heat sensitive instruments

③ Plasma chamber

Hydrogen peroxide gas plasma

↓

- Plastics
- Electrical devices
- Corrosion susceptible alloys

GENERAL ANESTHESIA

TRIAD OF AMNESIA / UNAWARENESS / UNCONSCIOUSNESS
ANALGESIA
MUSCLE RELAXATION

Induction ⟶ IV induction agents - PROPOFOL, KETAMINE
THIOPENTAL, MIDAZOLAM, ETOMIDATE

Maintenance → Inhalational agents - N_2O, Halothane, Enflurane
Isoflurane, Sevoflurane
Desflurane

↓ Supplemented by

IV opioids
Fentanyl
Morphine
Hydromorphone
Meperidine
Remifentanil

muscle relaxants
NMBs

Depolarizing → Succinyl choline (non competitive)

Non-Depolarizing → Rocuronium
Vecuronium
Atracurium
Cisatracurium
Mivacurium

TIVA - Propofol + Newer opioids
Total intravenous anesthesia

Requires manual / mechanical ventilation

TABLE 14-3 Clinical Characteristics of Intravenous Induction Agents

IV INDUCTION AGENT	DOSE (MG/KG)	COMMENTS	SIDE EFFECTS	SITUATIONS REQUIRING CAUTION	RELATIVE INDICATIONS
Thiopental	2-5	Inexpensive; slow emergence after high doses	Hypotension	Hypovolemia; compromised cardiac function	Suitable for induction in many patients
Ketamine	1-2	Psychotropic side effects controllable with benzodiazepines; good bronchodilator; potent analgesic at subinduction doses	Hypertension; tachycardia	Coronary disease; severe hypovolemia	Rapid-sequence induction of asthmatics; patients in shock (reduced doses)
Propofol	1-2	Burns on injection; good bronchodilator; associated with low incidence of postoperative nausea and vomiting	Hypotension	CAD; hypovolemia	Induction of outpatients; induction of asthmatics
Etomidate	0.1-0.3	Cardiovascularly stable; burns on injection; spontaneous movement during induction	Adrenal suppression (with continuous infusion)	Hypovolemia	Induction of patients with cardiac contractile dysfunction; induction of patients in shock (reduced doses)
Midazolam	0.15-0.3	Relatively stable hemodynamics; potent amnesia	Synergistic ventilatory depression with opioids	Hypovolemia	Induction of patients with cardiac contractile dysfunction (usually in combination with opioids)

CI in Pneumothorax, SBO, Middle ear, retinal Sx, causes severe PONV

TABLE 14-2 Cardiopulmonary Effects of Inhalational Anesthetics

INHALATIONAL AGENT	BLOOD PRESSURE	HEART RATE	CARDIAC OUTPUT	SENSITIZATION TO CATECHOLAMINES	VENTILATORY DEPRESSION	BRONCHODILATION
Nitrous oxide	Little effect	Little effect	Little effect	No	Minimal	No
Halothane	Marked dose-dependent decrease	Moderate decrease	Marked dose-dependent decrease	Marked	Moderate dose-dependent effect	Moderate
Enflurane	Marked dose-dependent decrease	Moderate decrease	Moderate dose-dependent decrease	Moderate	Moderate dose-dependent effect	Minimal
Isoflurane	Moderate dose-dependent decrease	Variable increase	Minimal decrease	Minimal	Marked dose-dependent effect	Moderate
Sevoflurane	Moderate dose-dependent decrease	Little effect	Moderate dose-dependent decrease	Minimal	Moderate dose-dependent effect	Moderate
Desflurane	Minimal decrease	Variable; marked increase with rapid increase in concentration	Minimal decrease	Minimal	Marked dose-dependent effect	Moderate

BOX 14-1 Routine and Specialized Electronic Monitors Used in Anesthetic Practice and Their Indications

Routine Monitors

Pulse oximetry — Pulse ox
- Blood oxygen saturation
- Heart rate
- Tissue perfusion (via plethysmography)

Automated blood pressure cuff — NIBP
- Blood pressure

ECG — ECG
- Heart rhythm
- Heart rate
- Monitor of myocardial ischemia

Capnography — Capnography
- Adequacy of ventilation
- Intratracheal placement of endotracheal tube
- Pulmonary perfusion

Oxygen analyzer — O_2 analyser
- Monitoring of delivered oxygen concentration

Ventilator pressure monitor
- Ventilator disconnection during general anesthesia
- Monitoring of airway pressure

Temperature monitoring — temp

Specialized Monitors

Monitoring of urine output (Foley catheter) — U/O
- Gross indicator of intravascular volume status and renal perfusion

Arterial catheter — ABP
- Continuous measurement of arterial blood pressure
- Sampling of arterial blood

Central venous catheter — CVC
- Continuous measurement of central venous pressure
- Delivery of centrally acting drugs
- Rapid administration of fluids and blood

Pulmonary artery catheter — PAC, S-G
- Measurement of pulmonary artery pressure
- Measurement of left ventricular pressure
- Measurement of cardiac output
- Measurement of mixed venous oxygenation

Precordial Doppler — Echo
- Detection of air embolism

Transesophageal echocardiography
- Evaluation of myocardial performance
- Assessment of heart valve function
- Assessment of intravascular volume
- Detection of air embolism

Esophageal Doppler
- Assessment of descending aortic blood flow
- Assessment of cardiac preload

Transpulmonary indicator dilution
- Measurement of cardiac output
- Measurement of preload

Esophageal and precordial stethoscope
- Auscultation of breathing and heart sounds

EEG/BIS — EEG
- Depth of anesthesia

BIS, bispectral index; *ECG*, electrocardiography; *EEG*, electroencephalography.

HIV - Post Exposure Prophylaxis

Exposure	Risk of seroconversion
Blood transfusion	90-95%
Perinatal without any intervention	15-40%
Sexual intercourse	0.1-10%
IV drug use	0.7%
Needle stick exposure	0.3%
Mucous membrane splash to eye	0.09%

→ HCV - 1-1.8%.
HBV - 9-30%.

Prevention - Universal Precautions

Exposure management

① Rinse part with running water and soap
Do not scrub / use harsh products

② Categorise the exposure

Mild
Mucous membrane exposure
or
Non intact skin
or
small bore needle
&
small volume

Moderate
Mucous membrane exposure
or
Non intact skin
or
small bore needle
&
Large volume

Severe
Percutaneous exposure
& large volume
>18 G visibly contaminated by blood

③ Assess need for PEP

Intact skin - No PEP required
Source HIV negative - No PEP required

Source HIV positive
- Asymptomatic ↑ CD4 count
  - + ↓ titer exposure → No PEP
  - + ↑ titer exposure → PEP
- Advanced disease ↓CD4 count → PEP irrespective of exposure severity

PEP - initiate within 72hr
- within 2hr → ideal
- for 28 days

Seek Expert opinion i/e/o - Delayed reporting of exposure
Pregnancy
Source is on ART ∴ concern for drug resistance
Major toxicity

Regimen ① Tenofovir 300mg + Lamivudine 300mg OD
FDC → ×28d

② Lopinavir | Ritonavir → 28d
200mg 50mg BD

or

3 Drug - Tenofovir + Lamivudine + Efavirenz 600mg OD → 28d

Followup testing - HIV Ab 6 weeks
12 weeks
24 weeks

SURGERY IN HIV + PATIENTS

Current guidelines recommend ART irrespective of CD4 counts in HIV +ve patients

but especially if CD4+ count < 350/μL

Elective surgeries → postpone until ART is initiated

Surgical emergencies → operate if surgery is life-saving

MIS can be considered when appropriate to minimize exposure

Early HIV – perioperative risk ≈ Normal patient

↘ Asymptomatic / Mildly symptomatic & CD4+ >200

lower viral load, ↑ CD4+ count → beneficial for both surgeon & pt

SURGERIES FOR LEPROSY

TREATMENT OF DISABILITIES

1. Claw hand
   - Partial - Ulnar palsy
   - Total - Ulnar + Median Palsy

   Rx - Paul Brand's Multi tail tendon transfer

   ECRB is extended to all 4 digits using tendon graft

2. Weakness of Opponens pollicis

   FDS of ring finger re-routed through pulley of FCU and attached to thumb

   OPPONENSPLASTY

3. Wrist drop - Radial N palsy

   Jones transfer

4. Foot drop - Peroneal N Palsy

   Tibialis posterior to dorsum of foot

- Corneal ulcers - Corneal transplant
- Facial palsy
  - Static
  - Dynamic

Saddle nose - Rhinoplasty

TREATMENT OF TROPHIC ULCERS

- Surgical offloading
- Total Contact Casts
- Debridement
- Sequestrectomy
- Flaps
- Minor / Major amputations

PRINCIPLES OF BOWEL ANASTOMOSIS

1) Good blood supply

- Pulsatile flow after dividing a terminal arterial branch in the region where the bowel is to be transected
- No hematoma near the anastomosis
- Do not jeopardise the mesentery by excessive clamping & ligating

2) Avoid tension at suture line

3) Avoid tissue trauma - gentle handling

4) Only bowel of similar diameter should be brought together in an end-to-end anastomosis

Equal / Equivalent luminal caliber ✓

Minor discrepancy → Cheatle split along the antimesenteric border

Major discrepancy → side to side anastomosis ✓

5) Accurate seromuscular opposition. No extraneous intervening tissue

6) The submucosa must be included into the stitch while applying seromuscular stitches → max. collagen, tensile strength

7) Suture material - PDS generally preferred

Principle -

- Ideal suture material for intestinal anastomosis is the one that produces the smallest amount of tissue reaction while providing maximal strength during the lag / inflammatory phase (D_1-D_5) of wound healing

Inflammatory phase is fostered by - necrosis, debris, infection

Braided suture has 5-8x adherence of bacteria ← (PDS has lowest adherence of bacteria)

Easier - inner catgut, outer silk → Vicryl (Polyglactin) → PDS

8) Technique - Single vs Double layer / Continuous vs interrupted (matter of preference)

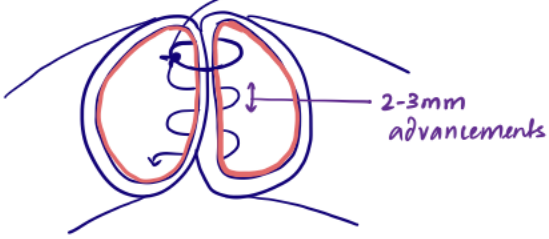
INVERSION > EVERSION → bad

STITCHES

CONNELL SUTURE

- Full thickness, usually continuous suture
- Causes MUCOSAL INVERSION
- usually serves as inner layer of 2-layer anastomosis

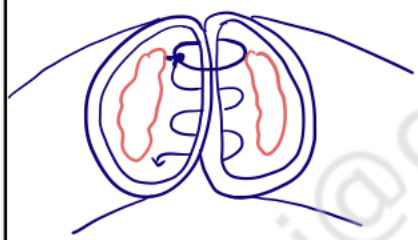
Inside-out- outside-in → Knot inside lumen



CUSHING SUTURE

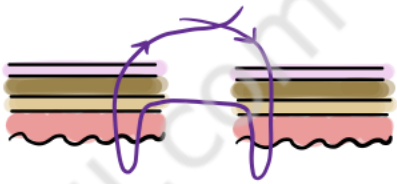
- similar to connell but the suture does not enter lumen, but exits through submucosa

(Excludes mucosa)



GAMBEE STITCH

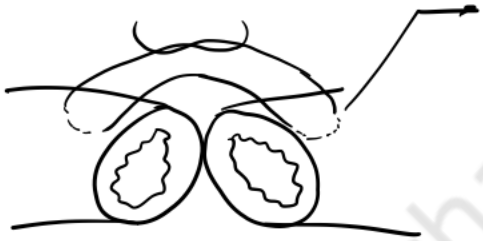
- interrupted suture that inverts mucosa into the lumen



tied extraluminally

- Used by some surgeons for pyloroplasty closure

LEMBERT SUTURE - started 3-4mm lateral to the ends of the bowel



only seromuscular layer

Done in an interrupted/continuous fashion

used as outer layer of 2-layer bowel anastomosis

HALSTED SUTURE

Horizontal mattress-like seromuscular apposition - interrupted

used when tissue is very friable & Lembert cuts through

DOUBLE LAYER BOWEL ANASTOMOSIS - Czerny Lembert suture

- Inner, full-thickness, continuous absorbable layer → catgut → Vicryl
- Outer, seromuscular, cont/interrupted, usually permanent layer → silk

Generally - posterior (1/2) seromuscular layer → stay suture
- inner continuous full-thickness layer → circumferential
Anterior (1/2) seromuscular layers → complete

FACTORS INFLUENCING HEALING OF INTESTINAL ANASTOMOSIS

1) Surgical factors

- Integerity of repair, secure knots
- Tension in the repair
- Vascularity of bowel ends
- Proper mucosal inversion
- Luminal equivalence
- Accuracy of seromuscular apposition

2) Tissue factors

- Edema
- Vascularity
- Infection, Inflammation, Malignancy
- Local infection
- Distal obstruction
- Irradiation
- Luminal contents

3) Patient factors

Immune status — Anemia, Steroids
Nutritional status — Uremia, T2DM
Systemic condition - Sepsis
Shock - hypotension

PHASES

- Inflammatory - D1-5
- Proliferative - 1-3 weeks
- Remodelling - >3 weeks upto 1y

CONFIGURATIONS OF BOWEL ANASTOMOSIS

END TO END

- Preferred when luminal calibers match
- Most physiological

Higher stricture rates ?

END TO SIDE

↓

done in bypass procedures

↓

the end of one loop is anastomosed to a defect of the same size created in the antimesenteric wall of another loop

Eg: Ileocolic after RHC

SIDE TO SIDE

Preferred when there is gross luminal discrepancy

↓

if there is a stump involved,

↓

risk of ↑ intraluminal bacterial proliferation & ↑ luminal pressure

↓

Blow-out

STAPLING DEVICES IN SURGERY

Staplers permit / facilitate surgical procedures like resection / transection and anastomosis in a rapid, accurate and reproducible fashion

1) Skin staplers
2) Laparoscopic hernia mesh tackers
3) Open hernia mesh staplers
4) Ligating clips / Clip applicators
5) Vascular staplers
6) GIA staplers

GIA - GASTRO INTESTINAL ANASTOMOSIS STAPLERS

- GI tissue is biphasic i both solid & liquid components in varying ratios
- GI stapling is based on the observation that proper compression of the tissue is necessary before application of staples in order to obtain good results (↓ leak, good hemostasis, ↓ contraction / stricture)
- Apply ⟶ Compress ⟶ Fire

TYPES OF GIA STAPLERS

1) LINEAR STAPLERS

Linear non cutting staplers

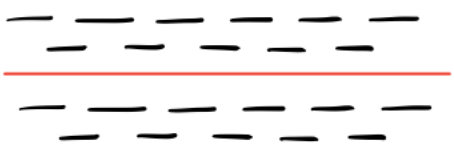
- Deliver a double staggered row of staples (triple in case of vascular staplers)

Used for
- closure of hollow viscus / free end of bowel
- ligation of large vessels

30, 55, 60, 90 mm - lengths
↳ Vascular

Linear cutting staplers

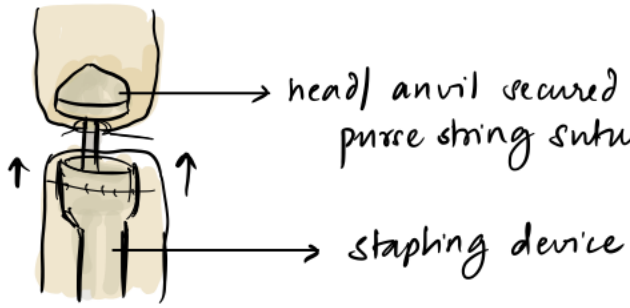
- Deliver (2) double staggered rows of staples and divides the tissue between the 2 rows

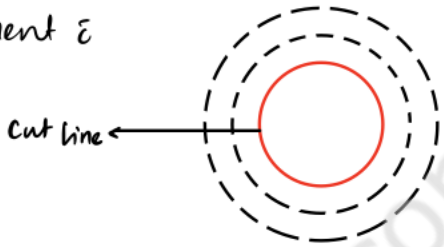


- transect & close tubular structures
- create side to side anastomosis
⟶ 55, 75, 100 mm lengths

	Closed staple height	Use
WHITE	1.0 mm	Mesentery, Vessels
BLUE	1.5 mm	Small intestine
GOLD	1.8 mm	thicker intestine
GREEN	2.0 mm	Stomach
BLACK	2.3 mm	very thick tissue

2) CIRCULAR STAPLERS - create end-to-end anastomosis (EEA) & INTRALUMINAL DEPLOYMENT





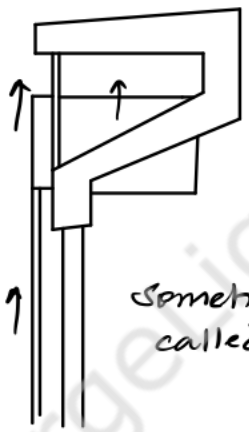
Anvil and stapler are engaged ⟶ stapler is deployed

A do-nut of tissue is resected - containing parts of both bowel segments and the 2 ends are anastomosed by a row of double-staggered staples

- Creates an inverted end to end anastomosis
- Esophagogastrostomy, Esophagoenterostomy, gastroenterostomy, Coloprochestomy
- Stapled hemorrhoidectomy → 25mm → 29-31mm

- CONTOUR - the stapler limb is curved to follow the sacral hollow
  - used for low anterior resection

3) TRANSVERSE ANASTOMOSIS (TA) staplers



Sometimes called thoracoabdominal stapler

- Provide 2 rows of staples for a single anastomosis
- Used for sealing enterotomies
  - creating gastric tubes
  - gastric partitioning

* Endo-GIA staplers are available for lap & robotic procedures

STAPLING PRINCIPLES

- check the instrument & familiarize yourself ε mechanism
  - load the stapler properly
- Following standard surgical principles,
  - determine viability of tissue to be stapled
  - rule out distal obstruction
- Avoid tension at the staple line
- Precise tissue dissection to avoid incorporating extra tissue in staple line
- Adequate compression to ensure hemostasis & prevent leakag
- Avoid excessive compression to avoid tissue damage
- After assembling staples ε tissue - allow ≥ 15s of compression before firing
- Ensure that no extra tissue in caught in the fire line
- Fire the stapler in a smooth movement
- check the staple line for integrity
- Reinfnce or bury the staple line by oversewing if necessary

ENERGY DEVICES IN SURGERY

- Produce tissue effects by
  - Thermal effects
  - Compression
    - Compression decreases tissue volume & water content
    - Apposition

- LIQUID GASES
  - N_2, N_2O, liq CO_2
- ELECTROMAGNETIC ENERGY
  - Electrosurgery
  - Laser
  - Microwave
  - RF
  - Argon beam coag
- MECHANICAL ENERGY
  - Ultrasonic devices
  - High velocity hydrodissection

THERMAL TISSUE EFFECTS

Tissue responds to heat in a REPRODUCIBLE MANNER

- ~40°C – irreversible tissue changes begin
- 50°-80°C – Protein denaturation
  Collagen breakdown
- 80°-100°C – Total dessication
  Shrinkage
- >100°C – Vaporisation
- >150°C – Carbonization – visible black eschar
- ~200°C – Fulguration

→ Electrosurgery (Monopolar & Bipolar) → can achieve upto 400°C
→ Laser – ~200°C
→ Ultrasonic devices – ~80°C

- Hypothermia ≤ -40°C → tissue freezing
  ↓ thawing
  - Vascular endothelial damage
  - Cell membrane dysfunction
- ≤ 195°C – intracellular & extracellular ice formation
  ↓
  Cell dehydration
  ↓
  Shrinkage
  ↓ thawing
  Osmotic damage

ELECTROSURGERY

- uses an ALTERNATING radiofrequency current ($F = 0.5 - 2\ MHz$)
- ionisation → heat

ELECTROCAUTERY
Electricity → heat a metal object
↓
Contact ⁻ tissue
↓
Effects

vs

ELECTROSURGERY
Electric current flows directly through tissue
↓
heats tissue via ionization
↓
Effects

→ Based on principle that current takes path of least resistance

ELECTRIC CURRENTS IN USE

- **DC / GALVANIC CURRENT** → for endothermy, Acupuncture
- **AC** → Electrosurgery
- **Pulsed current** → Electromyography, Nerve stimulation

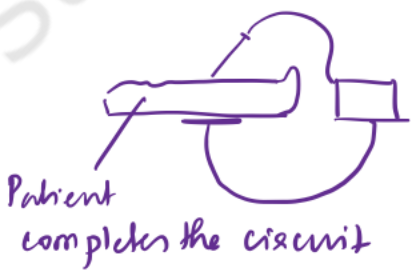
ELECTRICAL RESISTANCE IN TISSUE $\propto \frac{1}{(\text{Water content})}$ → ∴ Desiccated tissue is NON CONDUCTIVE

Most conductive - Blood → Nerve → Muscle → Adipose → Bone

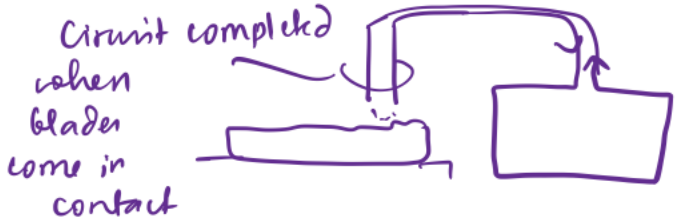
Density of current $\propto \frac{1}{\text{Area of contact}}$
↓
higher with point than spatula

Based on Circuits

MONOPOLAR



BIPOLAR



ACTIONS

- Cutting ← ↓ voltage
- Coagulation / Fulguration - short burst of high voltage
- Dessication

Blend current - intermediate between cutting & coagulation

COMPLICATIONS

- Grounding failures → d/t lack of uniform contact between ground pad & patient body
- Alternate site injuries → unpredictable pathways of current
- Demodulated currents - generally seen as muscle fasciculations
  Cardiac issues
- Tissue injury at a distal site - GB dissection → Duct injury
- Sparking - jumping of sparks - eschar at tip - esp in lap
- Direct Coupling - d/t insulation failure / inadvertant contact with conducting material
- Capacitive Coupling - between 2 conductive materials separated by insulation
- Explosions

BIPOLAR

Eliminates - grounding failure, alternative site injury, capacitative coupling, insulation failure

Direct coupling can occur only if metal is grasped between tips

lateral spread of current - ↓

issue - tissue sticking - needs irrigation

ADVANCED BIPOLAR - Ligasure, Enseal

Compression + Coagulation

can seal 4-7mm vessels / tissue bundles

Monopolar seals up to 2mm

ELECTROSURGERY - risky in pts ♂ metal implants, pacemaker

ULTRASONIC ENERGY

Electrical energy → Mechanical vibrations (>20,000 Hz) → tissue effects

Cutting
Coagulation
Back-scoring
drilling
Cavitation

Advantages

- Less heat generation
- ↓ tissue injury
- ↓ charring / Desiccation
- No risk of shock

↓ post op adhesions
Skin incisions superior

Blade-2mm
Shear 5mm
Can seal vessels up to 3mm

Disadvantages

- Aerosolized fatty droplets → interferes ↓ visualisation
- Slower coagulation
- Blade fatigue after prolonged use
- Not reliable for large vessels

→ **CUSA** - Cavitational Ultrasonic Aspirator - for liver surgery Neurosurgery

↳ low power ultrasonic dissector

High power dissection → frictional heating - Eg: HARMONIC SCALPEL

Cutting Coagulation

Used in open & lap surgeries

LASERS - CO_2
Nd : YAG
Argon pumped dye laser

Holmium YAG laser

Excimer laser
KTP/YAG laser

Potassium titanyl phosphate

NEGATIVE PRESSURE WOUND THERAPY

Application of subatmospheric pressures to wounds to facilitate wound healing

-75 to -125 mmHg pressures used

Mechanisms of benefit

1) Removal of edema fluid, wound exudate, but keeps the wound MOIST
2) ↑ local blood flow - 5× ↑, ↑ capillary calibre, angiogenesis
3) Stimulation of granulation tissue - at 'microstrain' & 'macrostrain'

(NPWT does not ↓ bacterial count)

PROCEDURE

Evacuation tube placed within → Black / White / Silver impregnated sterile polyurethane foam dressing tailored to the wound / defect

↓

Covered by air tight occlusive seal - film

Connected to vacuum pump via a canister to collect exudate

↓

INTERMITTENT VACUUM - 5 min on / 2 min off
(-125 mmHg) <upto

APPLICATIONS

1) To secure skin grafts in complex areas (like perineal wounds)
2) Sternotomy wound dehiscence
3) Burst abdomen
4) Wounds : small areas of bare bone
5) Venous ulcers - lower pressures ~ -50 mm Hg <continuous

Precautions

1) Should be preceded by sound surgical debridement
2) Residual tumor } CI to NPWT
3) Exposed large vessels }
4) Fistula }

Complications

- Pressure necrosis
- Maceration
- Pain
- Fluid imbalance

HYPERBARIC OXYGEN THERAPY

Hyperbaric Oxygen therapy (HBOT) involves the delivery of Oxygen at pressures higher than atmospheric pressure to achieve higher concentrations of oxygen in tissues

1.4 - 2.5 times atmospheric absolute
(ATA = sea level pressure)

Chronic wounds - ↓ O_2 supply - Ischemia - PO_2 < 30mmHg

O_2 - helps in wound healing by
- fulfilling metabolic demands
- production of ROS like superoxide
  - Bactericidal
  - stimulate angiogenesis
    - NO synthase
    - fibroblast & WBC function
    - normalises cutaneous microvascular reflexes

(can also be used for local treatment as O_2 dressings & oxygen therapy)

INDICATIONS

HBOT ↓ amputation rates

- Diabetic ulcers - Wagner ≥ 3
- Bacterial infections - Clostridial myonecrosis
- Decompression sickness
- to improve SSG take, flap survival & salvage
- acute thermal burns, crush injury
- Necrotising fasciitis
- Chronic wounds
- Hypoxic wounds
- Osteoradionecrosis
- Radiation injuries

CONTRAINDICATIONS

- Uncontrolled pneumothorax
- Current / recent Rx : Bleomycin / Doxorubicin (Worsens cardiopulmonary damage)
- Disulfiram (worsens O_2 toxicity)

- Involves inhaling 100% O_2 at 1.4 - 2.5 atm for 90-120 min in a hyperbaric chamber → TcO_2 rises 10x → sustained for 2-4 hrs post Rx
  - daily - 5-6 times a week
  - 15 - 20 treatments → Benefit

Target area revascularised if necessary before commencing Rx

Ischemia - TcO_2 - < 35mmHg ; post HBOT TcO_2 → > 200mmHg (in chamber) → Benefit

Complications - Barotrauma - middle ear hyperemia, TM perforation
Pneumothorax
Brain Oxygen toxicity - Seizures
Oxygen lung toxicity
transient myopia

LAPAROSCOPIC SURGERY

Advantages

- Reduced pain
- Improved post-op mobilisation → quicker resumption of activity
- Better cosmesis
- ↓ incisional hernia, SSI
- Reduced hospital stay

MODES OF PERITONEAL ACCESS

OPEN

↓

Hasson technique

- tiny skin incision
- directly incise layers of abdominal wall
- direct cut the peritoneum
- Insert Hasson cannula under vision & secure with sutures
- Then inflate

ADVANTAGES

↓ Visceral/Vascular injury
Prevents gas embolism
↓ risk of preperitoneal insufflation
Abdominal incision can be repaired meticulously

Drawbacks

time consuming
tough in obese patients

CLOSED

BLIND/ NON-VISUAL ENTRY

Insufflated

Veress needle

Needle inserted into peritoneal cavity
↓
Confirmed
↓
Insufflated
↓
Blind insertion of first trocar

Radially expanding trocar

↓

Central veress with sleeve trocar
↓
Remove needle after insufflation

Non insufflated

↓

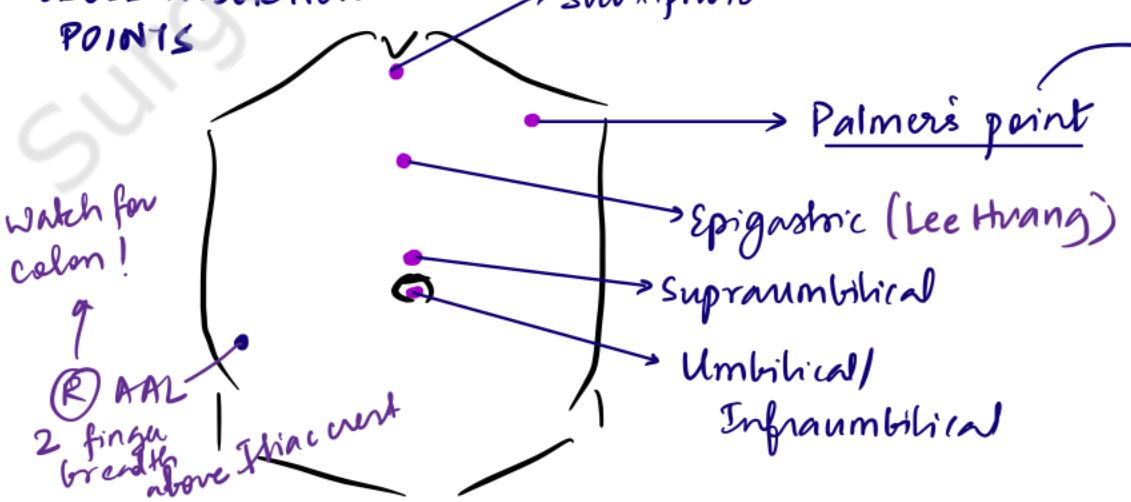
Direct sharp trocar entry
↓
Skin incision
↓
Lift abd wall
↓
Insert trocar blindly ± twisting movements

VISUAL ENTRY

↓

OPTIVIEW
↓
Optical trocar connected to camera
↓
Each layer visualised as trocar is advanced

VERESS INSERTION POINTS



LUQ - 3cm below costal margin in (L) MCL
Avoids major vessels
can be used in
- h/o laparotomy
- pregnancy
- umbilical adherions
- Verythmn pts
- avoid if h/o upper abd surgery & Portal HTN

Confirming Veress position – 2 pops < Fascia
Peritoneum

Hanging drop test
Aspiration test
Irrigation test
Drop of manometer reading
Uniform distension

Gas

CO_2 - ideal - non toxic, colorless, readily soluble in blood & expired through lungs, non inflammable, cheap

O_2, Air → inflammable → air embolism

N_2O → unpredictable absorption

Introduced at 21°C, '0' humidity
Rate - 1-6 L/min
Pressure - 12-14 mmHg
Flow - ~200-400mL/min to maintain intraop- pneumoperitoneum

Port placement

'Diamond of success'

The primary port must lie in an arc drawn at a distance [midway between 1/2 & 2/3rd of length of laparoscopic instrument] from the target

The same distance must be ensured between other ports. Angle between instruments - 60-90°

TRANSPLANTATION BASICS

TRANSPLANTATION: transferring an organ / tissue / cell from one place to another

ORGAN TRANSPLANT: surgical procedure in which a failing organ is replaced by a functional one.

ORTHOTOPIC
implanted in the same location (native site of the organ)
↓
Requires removal of the diseased organ

- heart
- lung
- liver
- intestine

HETEROTOPIC
implanted in another anatomic location
↓
Diseased organ is kept in place

- kidney
- pancreas

TYPES OF TRANSPLANTS based on the DEGREE OF IMMUNOLOGIC SIMILARITY between donor & recipient

1) **AUTOTRANSPLANT**: transfer of cells / tissue / organ from one site to another in the SAME INDIVIDUAL
   (No immunosuppression required)

   Eg: skin
   blood vessels
   bone
   cartilage
   Nerve
   Islet cell autotransplants

2) **ISOTRANSPLANT**: transfer of cells / tissue / organ between individuals who are GENETICALLY IDENTICAL
   (No immunosuppression required)

3) **ALLOTRANSPLANT**: between 2 individuals of the same species
   Immunosuppression is required

4) **XENOTRANSPLANT**: between individuals belonging to different species
   (Complex immunological & infectious issues – EXPERIMENTAL)

Transplantation Immunobiology

Transplants between genetically non-identical persons lead to recognition and rejection of the donor antigens by the recepients immune system

Rejection can be reduced by –
- matching the antigens
- immunosuppression

TRANSPLANT ANTIGENS

Allografts trigger a graft rejection response because of allelic differences at polymorphic genes that give rise to histocompatibility antigens.

Histocompatibility antigens of significance

ABO antigens

ABO antigens are expressed by several cells (in addition to RBCs)

ABO incompatibility causes **HYPERACUTE GRAFT REJECTION** due to preformed naturally occuring anti A / anti B antibodies

Permissible transplants

Donor ABO	Recipient ABO
O	A, B, AB, O
AB	AB
A	A, AB
B	B, AB

No need to consider Rh compatibility during transplantation

HLA antigens (Chromosome 6)

- Human leucocyte Antigens are a group of highly polymorphic cell surface molecules. (Codominant inheritance - haplotype)
- strong transplant antigens – act as antigen recognition units for **T lymphocytes**

TYPES

Class I	Class II
HLA-A, B, C	HLA-DP, DQ, DR
present in ALL NUCLEATED CELLS	present only on antigen presenting cells (dendritic cells, macrophage, B cells)
Heavy chain + β_2 microglobulin	α, β chains

Principal function of HLA → present fragments of proteins to T-cells (TCR – CD complex)

HLA-DR > B > A → matching - esp for kidney

Number of alleles (268) (258) (124)

HLA-A	HLA-B	HLA-DR
0	0	0

→ Complete match '000' mismatch

well matched renal allografts → ↓ immunosuppression requirement

CLINICAL GRAFT REJECTION: 2/t complex interaction of different components of immune system - T-cells, B-cells, APCs, Cytokines

↓

Graft damage 2/t inflammatory injury

based on onset & pathogenesis

HYPERACUTE REJECTION

within min - days

triggered by preformed antibodies against donor ABO / HLA antigens

'ESSENTIALLY UNTREATABLE BUT UNIVERSALLY PREVENTABLE'

↓

BY:
- ABO matching
- LYMPHOCYTOTOXICITY ASSAY (MHC class I)
- Cross matching (donor cells mixed i recepient serum + complement)
- FLOW CYTOMETRY
- BEAD-BASED SCREENING ASSAYS
- PRA - Panel Reactive Antibody assay

Preformed abs may arise from
- Previous blood transfusion
- Previous (failed) transplant
- Pregnancy

Once graft is revascularised, antibodies bind to vasculature

↓ Complement activation

- EXTENSIVE INTRAVASCULAR THROMBOSIS
- INTERSTITIAL HEMORRHAGE
- GRAFT DESTRUCTION WITHIN MINUTES

Kidney - vulnerable to Hyperacute rejection

Liver, Heart - Resistant

ACUTE REJECTION

within weeks - months (within 6m)

T-cell mediated rejection (CELLULAR)

also has components of antibody mediated rejection

REVERSED BY IMMUNOSUPPRESSION

Mononuclear cell infiltration in the graft
- Cytotoxic T cells
- NK cells
- macrophages
- B cells

All types of organs are susceptible to acute rejection

Most episodes of CELLULAR REJECTION can be reversed by additional IMMUNOSUPPRESSIVE ↑

Acute antibody-mediated rejection
- ↓ harder to treat
- May required
  - plasmapheresis
  - Immunoadsorption

ACUTE REJECTION occurs in 20-30% of all allografts

CHRONIC REJECTION

over months - years (after 6m)

Mechanisms are not well understood

↓

fibrosis

loss of graft function

BOTH IMMUNE & NON-IMMUNE mechanism

↓
- repeated / indolent T cell cytotoxicity / ab mediated injury

MOST COMMON CAUSE OF GRAFT FAILURE

Myointimal proliferation in graft arteries

↓

Ischemia, fibrosis

PREDICTORS OF CHRONIC REJECTION
- h/o acute rejection
- poor HLA match
- Long cold ischemia time
- CMV infection
- Hyperlipidemia
- Inadequate immunosuppression

Organ specific features

Kidneys: Glomerulosclerosis tubular atrophy

Pancreas: Acinar / Islet cell loss

Heart: Graft vasculopathy

Liver: Vanishing bile ducts

Lung: Obliterative bronchiolitis

IMMUNOSUPPRESSION

DRUGS

A. Immunophilin binders

Calcineurin inhibitors

CYCLOSPORINE, TACROLIMUS → (-) Calcineurin → IL-2 synthesis

Non-inhibitors of Calcineurin

EVEROLIMUS, SIROLIMUS (mTOR inhibitor) → (-) IL-2 receptor

B. Antimetabolites - inhibitors of de-novo purine synthesis

AZATHIOPRINE

MYCOPHENOLATE MOFETIL

C. Biologic Immunosuppression

Polyclonal abs

Atgam - rabbit antithymocyte Ig

Antithymocyte immunoglobulin

Monoclonal Abs

Rituximab (CD 20)

Basiliximab (CD 25)

Alemtuzumab (CD 52)

Eculizumab

Betalacept

D. Others - Corticosteroids - Prednisone

Commonly used regimen:

- Induction ē antibodies (1st month)
- Maintenance ē Calcineurin inhibitors + Antiprolif agents (MMF) + Corticosteroids → Dual therapy / Triple therapy

---

ADVERSE EFFECTS OF IMMUNOSUPPRESSIVE THERAPY

D/t immunosuppression

① Infections:

Early (1m): Bacterial - E. coli; Fungal - Candida

Late: Viral: HSV, CMV, EBV, VZV; Fungal: Histoplasma, Cryptococcus, Blastomyces; Others: PCP

② Malignancies: Kaposi Sarcoma, Non melanoma skin cancer, NHL - PTLD, Ca Anus, Lip, liver, vulva

Agent specific toxicities

Nephrotoxicity, Hypertension → Cyclosporine, Tacrolimus

Thrombocytopenia: Sirolimus, Azathioprine

Azathioprine, MMF - Leucopenia → liver failure

Betalacept - ↑ bacterial inf

ORGAN DONATION

Types of Donors

- Deceased donor (DD)
  - Donation after Brain Death (DBD)
  - Donation after Cardiac Death (DCD)
- Live donor (LD)

DBD

Brain death is defined as the IRREVERSIBLE CESSATION OF BRAIN FUNCTION, including brain stem

EXCLUDE MEDICAL CONDITIONS THAT MIMIC BRAIN DEATH, LIKE:
- severe hypothermia
- hypoglycemia
- drug overdose
- induced coma / persistent vegetative state → brain stem function ⊕

'irreversible brain damage while on life support, & no prospect of recovery'

STEPS IN CLINICAL DIAGNOSIS OF BRAIN DEATH

1. Estimation of Proximate cause of neurological insult
2. Clinical examination to determine Brain stem Death

ABSENCE OF CRANIAL NERVE REFLEXES

1) Pupillary reflex (CN II, CN III)
2) Corneal reflex (CN V, CN VII)
3) Pharyngeal gag & cough reflex (CN IX, X)
4) Oculovestibular reflex (CN VIII, III, IV, VI)

ABSENCE OF MOTOR RESPONSE

- Absent motor response to painful stimulus applied to head/face
- Absent motor response within CN distribution

(Spinal reflexes may be ⊕)

ABSENCE OF SPONTANEOUS RESPIRATION

Preventilate with 100% O_2 × 5min
↓
Disconnect from ventilator × 10min
& $PaCO_2$ > 60mm Hg (adequate stimulation)
↓
NO RESPIRATORY EFFORT

3. Ancillary testing: EEG, Cerebral angiography, nuclear scan
4. Appropriate Documentation

Testing on 2 separate occasions INDEPENDENTLY by 2 separate EXPERIENCED clinicians NOT connected with the transplant team

time interval between 2 occasions NOT FIXED

BOX 26-4 Confirmatory Testing for a Determination of Brain Death

Cerebral Angiography

The contrast medium should be injected under high pressure in both anterior and posterior circulation.

No intracerebral filling should be detected at the level of entry of the carotid or vertebral artery to the skull.

The external carotid circulation should be patent.

The filling of the superior longitudinal sinus may be delayed.

Electroencephalography

A minimum of eight scalp electrodes should be used.

Interelectrode impedance should be between 100 and 10,000 Ω.

The integrity of the entire recording system should be tested.

The distance between electrodes should be at least 10 cm.

The sensitivity should be increased to at least 2 μV for 30 minutes with inclusion of appropriate calibrations.

The high-frequency filter setting should not be set below 30 Hz, and the low-frequency setting should not be above 1 Hz.

Electroencephalography should demonstrate a lack of reactivity to intense somatosensory or audiovisual stimuli.

Transcranial Doppler Ultrasonography

There should be bilateral insonation. The probe should be placed at the temporal bone above the zygomatic arch or the vertebrobasilar arteries through the suboccipital transcranial window.

The abnormalities should include a lack of diastolic or reverberating flow and documentation of small systolic peaks in early systole. A finding of a complete absence of flow may not be reliable because of inadequate transtemporal windows for insonation.

Cerebral Scintigraphy (Technetium Tc 99m Hexametazime)

The isotope should be injected within 30 minutes after its reconstitution.

A static image of 500,000 counts should be obtained at several time points: immediately, between 30 and 60 minutes later, and at 2 hours.

A correct intravenous injection may be confirmed with additional images of the liver demonstrating uptake (optional).

DCD

Categories

1 : Dead on arrival at hospital

2 : Resuscitation attempted without success

3 : 'Awaiting Cardiac arrest' after withdrawal of life support

4 : Cardiac arrest while brain dead

5 : Cardiac arrest + unsuccessful resuse in hospital

1, 2, 5 → 'Uncontrolled' DCD donors
→ Longer, less predictable warm ischemic time

3, 4 → Controlled DCD donors

EVALUATION OF DONORS

DECEASED DONORS

Contraindications

Transmissible infections
- HIV → can be transplanted into HIV +
- Hep B
- Hep C
- Creutzfeldt Jacob disease
- Active systemic Sepsis
- IV drug abuse history

H/o Malignancy within past 5 years
exceptions - 1° CNS tumors
Non melanotic skin tumors
CIS of cervix

Chronological age no longer an absolute CI

Organs to be donated should be free from primary disease

Types of donors < Optimal / marginal

LIVE DONORS

Healthy, fully willing, free of coercion, no undue risk

Living Kidney donors

MR/CTA - for arterial anatomy
RFT > good renal reserve
MAG3 > DTPA

Compatibility

(L) Kidney - longer pedicle - prefer

Living liver donors

- less common
- usually adult donors for pediatric recepients

Other organs

Lungs - Lobectomy
Pancreas - distal pancreatectomy

ORGAN HARVEST PROCEDURES

Maintain Core temp - 36 - 37.5°C
SBP > 100 mmHg
MABP > 70 mmHg
Hb 7 - 10 g/dL
Correct arrhythmias & metabolic derangements

Long incision for good thorax + abdomen exposure

Cattell - Braasch ⟶ expose distal aorta

cannulate infrarenal aorta → flush organs with cold preservation solution

Order of retrieval → Heart → Lungs → SI → Pancreas → Liver → Kidneys

---

WARM ISCHEMIA TIME

Ischemia of cells & tissues under NORMOTHERMIC CONDITIONS

DONOR
From time of cross clamping (live DBD donor) or asystole (DCD donor) to time of COLD PERFUSION

RECIPIENT
From time of removal of organ from cold storage to time of reperfusion of graft

~40 mins - permissible

COLD ISCHEMIA TIME

Ischemia of cells & tissues under HYPOTHERMIC CONDITIONS (4°C)

COLD ISCHEMIA TIMES

Heart - 3-6 hours
Lungs - 3-8 hours
Small Intestine - 4-6 hours
Pancreas - 10-18 hours
Liver - 12-18 hours
Kidneys - 18-36 hours (max)

ORGAN PRESERVATION

Solutions - impermeants - to limit cell swelling
Buffers - to maintain electrolytes & acid/base balance
Composition reflects intracellular fluid

- UW - University of Wisconsin Solution

Potassium lactobionate	Adenosine	Raffinose	Dexamethasone
Sodium phosphate	Allopurinol	HES	
$MgSO_4$	Glutathione	Insulin	

- Euro-Collins Solution

HTK - Histidine, Tryptophan, Ketoglutarate Solution

RENAL TRANSPLANTATION

PATIENT SELECTION

INDICATIONS

ESRD d/t - eGFR < 15 ml/kg/m²
- Glomerulonephritis
- Diabetic Nephropathy
- Hypertensive Nephrosclerosis
- Renal Vascular Disease
- Pyelonephritis
- Analgesic nephropathy

Relative considerations:
- Recepient age < 65-70y
- Compliance ī immunosuppression
- No h/o / pre-existing malignancy ≤ 8y before transplant
- Active infection at time of transplant ✗
- Functional urinary tract - ? Need for corrective urological surgery

Donor Kidney

LD - Left Kidney chosen - longer pedicle - easier to harvest
other considerations

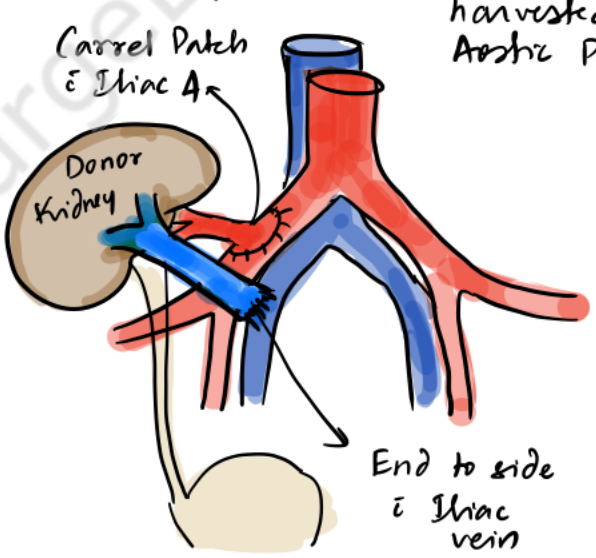
RECEPIENT SURGERY

- Heterotopic transplantation - (R) Iliac fossa

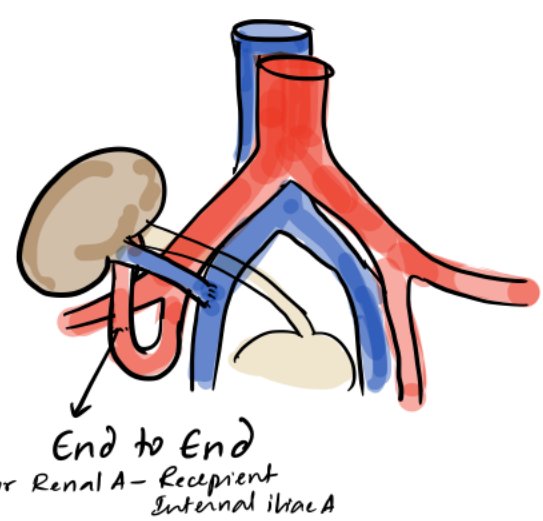
retroperitoneal position

Native Kidney generally left in situ

DBD / DCD - Kidney can be harvested ī Aortic Patch



LD Kidney



NUTRITIONAL ASSESSMENT IN SURGICAL PATIENTS

MEASURES OF NUTRITIONAL STATUS

i) ANTHROPOMETRY

i) Body weight

→ Day to day changes

Reflects fluid balance & nutritional status → over weeks to months

ii) Ideal Body Weight

Weight for height: Men: 48kg for first 152cm + 2.7kg / every 2.54cm

Women: 45kg for first 152cm + 2.3kg / every 2.54cm

iii) Lean body mass

- non adipose tissue mass
- excludes mass from acute shifts in water content

helps identify sarcopenic obesity

iv) Body mass index

$$Wt\,(kg) / [height\,(m)]^2$$

< 5th percentile → underweight

≥ 95th percentile → obese

v) Skin fold thickness - using skin calipers

Index of distribution of body fat (subcutaneous)

Subscapular (truncal) skin fold vs Triceps (limb)

vi) Mid arm circumference

in children

2) CLINICAL IMAGING

i) Dual Energy X-ray Absorptimetry (DEXA)

for monitoring long term nutritional progress
- measures changes in body tissue composition
  - lean body mass
  - fat mass
  - Bone density

ii) CT/USG

3) LABORATORY TESTS

i) Biochemistry:

Albumin : ≥ 50% of total body protein
$t_{1/2}$ - ~20d
helps detect / quantify chronic malnutrition
<3g/dL pre-op level → ↑ risk of 30d morbidity
Negative acute phase reactant : not reliable for assessing nutrition in stress of illness injury infection
→ added capillary leakage

Transferrin

Prealbumin

Nitrogen balance

ii) Immunological tests:

Lymphocyte count - ↓ lymphocyte count

Delayed hypersensitivity : abnormal reaction to intradermal test

Based on the observation that immune system is deficient in patients ∴ malnutrition

EVALUATION OF METABOLISM AND ENERGY REQUIREMENTS

1) RESTING ENERGY EXPENDITURE / BASAL ENERGY EXPENDITURE

a) Harris Benedict Equation

$REE \approx BMR_{♂} = 66.5 + (13.75 \times Wt\ in\ kg) + (5 \times ht\ in\ cm) - (6.775 \times age\ in\ y)$

$♀ = 665 + (9.6 \times wt\ in\ kg) + (1.7 \times ht\ in\ cm) - (4.7 \times age\ in\ y)$

Calorie requirement = REE × Activity factor (1.2) × Injury factor (0.3–0.6)

b) Indirect Calorimetry - using oxygen consumption (VO_2) & expired CO_2 (VCO_2) measured via tight-fitting face mask / adapter in mechanical ventilator circuit

$REE\ (kCal/d) = 1.44\ (3.9 \times VO_2) + 1.1\ (VCO_2)$

used in - Severe burns
Ventilator dependent patients
Spinal cord injury / coma
Morbidly obese

Indirect Calorimetry can also measure RQ

2) NITROGEN BALANCE - to monitor adequacy of protein intake

Nitrogen Balance = Total nitrogen intake − Total nitrogen loss

Nitrogen loss = Total (Urine Urea nitrogen) + 2 g/d (Stool + Skin)

$24\text{hr Urine Urea nitrogen} = \frac{(\text{Urine Urea nitrogen}\ mg/dL) \times (\text{Urine output}\ mL/day)\ (g/d)}{1000\ mg \times 100\ mL}$

ENTERAL NUTRITION (EN)
(SYN: TROPHIC FEEDS)

- a means of nutritional support in a patient i functional GIT who cannot take enough nutrition ORALLY to meet caloric requirements
  ↓ impossible / inadequate / unsafe

In a patient taking oral feeds, EN maybe initiated if ≥60% of requirements cannot be met by oral route alone for >10d

EN may be supplemented if caloric requirements >60% cant be met by EN alone

Advantages

1) Lower cost
2) ↓ risk of IV route complications
3) Prevents / reduces consequences of prolonged GI tract disuse

CONSEQUENCES OF PROLONGED GI DISUSE
- ↓ production of soluble IgA
- ↓ production of cytokines
- Bacterial overgrowth
- alteration in mucosal barrier & defenses
- Altered Gut microbiota

Gut bacteria → Bacterial fermentation of polysaccharides (Dietary fibre)

- Supports (N) gut flora
- Produces shortchain fatty acids (acetoacetate, Butyrate)
  ↓ preferred fuel for colonic mucosal cells
  ↓ IMPORTANT FOR MUCOSAL INTEGRITY

∴ ENTERAL NUTRITION IS RECOMMENDED as the FIRST CHOICE of NUTRITIONAL SUPPORT in patients who can tolerate it.

CONTRAINDICATIONS FOR ENTERAL SUPPORT

1) Intractable vomiting / diarrhea refractory to medical management
2) Paralytic ileus
3) High output intestinal fistulas - too distal to bypass with feeding tube
4) GI obstruction / ischemia
5) Diffuse peritonitis
6) Severe shock / hemodynamic instability
7) Severe GI hemorrhage
8) Severe short bowel syndrome (< 100cm small bowel remaining)
9) Severe GI malabsorption

STRATEGIES IN ENTERAL FEEDING

- Early vs late feeding in critically ill patients
  - → Current recommendation - start early enteral nutrition (within 48 h)

EARLY 'FULL' NUTRITION
- ↳ avoided → can ↑ infection
- ~80% of caloric needs → gradually stepped up over 3-4 days
- ↳ Preserves gut microbiota, enteral epithelial barrier

PERMISSIVE UNDERFEEDING / Hypocaloric nutrition – recommended
- ↳ ~1500 kcal/d + 40mg/d protein
- ↳ ~1500 kcal/d + 140g/d protein

Recovery period
- ↳ ↑ Calorie + Protein inputs

- Recommended in obese critically ill
- (N) wt pt in early acute period of critical illness

Intermittent vs Continuous
- ↳ preferred - lower complication rate
- ↳ promotes protein anabolism

CHOICE OF ROUTES OF ENTERAL FEEDING

< 4 weeks
- Nasogastric
- Nasoduodenal
- Nasojejunal

> 4 weeks

1) - Gastrostomy
- PEG
- Fluoroscopic
- Surgical

2) - Jejunostomy
- PEG assisted
- Direct Percutaneous endoscopic jejunostomy
- Fluoroscopic
- Surgical
  - Lap
  - Open

NASOENTERIC ROUTES

NASOGASTRIC TUBE

Advantages

- Simple access
  Easy to insert
  replace
  can monitor gastric pH
  & residual volume
  Bolus feeding possible
- Suitable for short term use

Complications

rhinosinusitis
epistaxis
Nasal necrosis
Esophageal strictures
Erosive esophagitis
frequent
dislodgement

Risk of aspiration +
↓
Try to reserve NG use
for pts i intact
mentation and protective
laryngeal reflexes

Cannot be used in patients
i significant gastroparesis
or gastric outlet obstruction

NASODUODENAL / NASOJEJUNAL TUBE

The feeding tube is advanced beyond the pyloric mechanism

useful in patients with a functional GIT but i
- poor gastric emptying
- reflux
- aspiration risk

Placement

→ Blind bedside - not reliable
→ Fluoroscopic assistance - Fluoroscopy guided intubation past the pylorus
  -> 90% success rate ; >50% reach jejunum
→ Endoscopy guided placement

Advantages

- ↓ aspiration risk
- some NJ tubes allow simultaneous gastric decompression + NJ feeding

Disadvantages

- Rhinosinusitis, epistaxis, nasal necrosis
- Esophagitis / stricture

→ Requires continuous infusion
→ cannot check gastric residuals except i specialized port
→ Clogging / kinking / displacement

- Small bowel feeding more reliable for delivering nutrition than NG feeding
- Risk of aspiration lower i small bowel feeding

GASTROSTOMY

Indications

- Impaired swallowing mechanisms
- Oropharyngeal / Esophageal obstruction
- Major facial trauma

Advantages

Bolus feeding possible
Large bore tube

Contraindications

- Ascites (especially for PEG)
- Coagulopathy
- Gastric varices
- Gastric neoplasm
- Lack of suitable abdominal site

Complications

Aspiration
Bleeding, perforation
Dislodgement → Peritonitis
Surgical site infection, necrosis

Most tubes - 18-24F → can be used for 12 to 24 m → ↓ clogging risk

PERCUTANEOUS ENDOSCOPIC GASTROSTOMY

Insufflation (distension) of the stomach + endoscopic transillumination of the anterior stomach wall against the anterior abdominal wall

↓

Catheter passed across the anterior abdominal wall - Guidewire threaded into catheter

↓

Guidewire pulled out via mouth - PEG tube threaded - brought out through abdominal wall & fixed

↓

Passive decompression ×24h

↓

Use

FLUOROSCOPIC GASTROSTOMY

Blind placement using needle & T prongs to anchor to stomach after insufflating stomach against anterior abdominal wall

SURGICAL GASTROSTOMY

Requires GA

↓

Laparotomy

STAMM METHOD - Malecot / catheter c balloon tip

↓

Secured c purse string

Gastrostomy can be used to decompress stomach in
- Gastroparesis
- GOO

- Gastrostomy PEG tube can be converted into transpyloric feeding tube

↓

PEG-Jejunostomy

JEJUNOSTOMY

- For long term feeding esp in pts ↓ Gastroparesis / GOO, reflux, aspiration risk
- Generally performed as an adjunct in complex abdominal surgery

CONTRAINDICATIONS

Absolute - Distal intestinal obstruction
Relative - severe edema of bowel wall
Radiation enteritis
Inflammatory bowel disease
Ascites
Severe immunodeficiency
Bowel ischemia

Disadvantages
Migration / Displacement - peritonitis
fistula
Requires continuous infusion

Complications

- Pneumatosis intestinalis & small bowel necrosis - contributing factors - hyperosmolarity of solution, bacterial overgrowth → Perforation
  BOWEL DISTENSION ⟶ ↓ BOWEL PERFUSION
  ↑ Shock, Vasopressors | Critical illness
- Abdominal distension, cramps

ENDOSCOPIC JEJUNOSTOMY

PEG-J
↓
advanced via gastrostomy access beyond ligament of Treitz

Direct percutaneous Endoscopic Jejunostomy
↓
uses enteroscope or colonoscope to reach jejunum
↓
Requires complex endoscopic skills
Variable success

Needle jejunostomy

SURGICAL JEJUNOSTOMY

WITZEL - 15-20cm distal to Ligament of Treitz - loop of jejunum ↓ good mobility & tension free apposition to anterior abdominal wall
- tube introduced - fixed via purse string - serosal tunnel - 6-8cm (Lembert) - fix to parietal peritoneum, fix to skin. (Pg 670 - Shackelford)

STAMM - similar to gastrostomy
- no seromuscular tunnel

ENTERAL FORMULAS

Considerations while choosing enteral formulas
- Functional GI status
- Organ dysfunction
- Nutritional status of patients

• STANDARD POLYMERIC FORMULAS

→ Ⓝ GIT, stable pts

1-2 KCal/ml
Daily req - ~1500-1800ml

Baseline carbs, protein, fat, electrolytes, water, fat soluble vitamins

No fibre → min residue

• CALORIE DENSE FORMULAS

↑ KCal/ml - 1.5-2.5 kcal/mL

Suitable for pt requiring fluid restriction

higher osmolarity - suitable for intragastric feeds

• IMMUNE ENHANCING FORMULAS

Contain glutamine, arginine, omega-3 fatty acids, nucleotides

↓

Anti inflammatory, antioxidant

• FIBER CONTAINING FORMULAS

- delay transit time → ↓ diarrhea
- Gut microbiome friendly - prebiotic
- Colonocyte metabolism

• HIGH-PROTEIN/ BARIATRIC FORMULAS

Part of high protein hypocaloric feeding regimens in critically ill obese patients

~1 Kcal/ml ~ 37% Protein

• ELEMENTAL FORMULAS

Predigested nutrients - small peptides

used in malabsorption
Gut impairment
Pancreatitis

• RENAL FAILURE FORMULAS

↓ Fluid volume

↓ K^+, Mg^{2+}, PO_4^{3-}

essential aas

• HEPATIC FAILURE FORMULAS

↑ Branched chain amino acids
- Leucine, Isoleucine, Valine

↓ Aromatic aas

- helpful in hepatic encephalopathy

COMPLICATIONS OF ENTERAL NUTRITION

1) Diarrhea - d/t
- infection / antibiotics
- ↑ osmolarity of feeds
- acquired lactase deficiency
- Medications

℞ - R/o infection - antibiotics
Fibre supplement
↓ Osmolarity, ↓ Infusion rate | antimotility
Loperamide
Codeine

2) Nausea & Vomiting

d/t delayed gastric emptying, constipation

℞ Gastroprokinetics

3) Constipation - d/t dehydration
↓ fibre

℞ - Fluid, fibre

4) Aspiration d/t delayed gastric emptying, reflux
prolonged supine, altered mental status

℞ - head up, stop EN in gastroparesis, ℞ of pneumonia

5) Electrolyte disturbances

Dehydration - Hypernatremia | Overhydration - ↓ Na+

Hyperkalemia

6) Hyperglycemia - ↑ Carb, insulin resistance

7) Refeeding Syndrome - refractory hypokalemia, hypomagnesemia
hypophosphatemia

Cause: Transition from body fat metabolism to carbohydrate metabolism
↓
Abrupt ↑ in insulin
↓
Electrolyte disturbances → arrhythmias, neurological disturbance,
renal & hepatic failure

℞ - start low, go slow

PARENTERAL NUTRITION

Parenteral nutrition involves IV infusion of nutrients in an elemental form, bypassing the usual processes of digestion

Indications

→ ± malnutrition / sepsis / surgical / traumatic injury

Pts ± partial / complete GI dysfunction who are unable to digest and absorb sufficient nutrients

- Intestinal obstruction
- Enteritis
- Fistulas
- Short Bowel Syndrome
- Chemotherapy toxicity

For critically ill / injured patients in whom EN is not feasible

PN

Total Parenteral Nutrition
or
CENTRAL PARENTERAL NUTRITION

delivery of entire nutritional requirements of the individual

Hyperosmolar solution (>850mOsm/L)
↑ Dextrose - 15-25%.
macro & micronutrients

central venous access
Longer duration >1-2wks

Peripheral Parenteral Nutrition

administered via peripheral veins
Lower osmolarity
↓ Dextrose - 5-10%.
↓ Protein - 3%.

Some nutrients cannot be administered as they can not be concentrated into smaller volumes

- used when PN is required for <2 wks
- not suitable for severe malnutrition

ROUTES OF ACCESS

Requires central venous access

Temporary / short-term
- 16 G percutaneous subclavian / IJV line threaded into SVC

For long term / home parenteral nutrition

- PICC line
- Tunneled central line ± subcutaneous port

COMPOSITION

TOTAL CALORIE REQUIREMENTS - 25-35 kCal/kg/day
(~30 kCal/kg/d)

70 kg man → 30×70

= 2100 kCal/d

PROTEIN REQUIREMENT: 1.5g/kg/d

70Kg man → 1.5×70 — 105 g/d

Protein Calories: 105g × 4 kcal/g = 420 kCal

20% of total Caloric requirements given as lipid

2100 × 20% = 420 kCal

9 kCal — 1g
420 kCal — ?

$\frac{420}{9} \simeq 47g$

Remaining as carb: 2100 − 420 − 420 = 1260 kCal

3-4 kCal — 1g
1260 kCal — ?

$= \frac{1260}{4} \simeq 370g$

CARBOHYDRATES

D-glucose / Dextrose

Available as 70% stock solution.

100ml — 70g
? — 370

$\frac{370 \times 100}{70} \simeq 528$ ml

PROTEINS

Generally available as 10% stock solution

100ml — 10g
? — 105

$\frac{105 \times 100}{10} = 1050$ml

LIPIDS

Generally available as 20% stock solution (emulsion)

100ml - 20g
? - 47

$\frac{47 \times 100}{20} = 235$ mL

Total volume = 1813 mL/d

FLUID & ELECTROLYTES

30-40mL/kg fluid, 1-2mEq/kg Na^+ & K^+
10-15mEq Ca, & 8-20mEq Mg^{2+}, 20-40mmol-PO_4^{3-}

Add vitamins

Initiation of Parenteral Nutrition

First week of PN in critically ill → give ~ 80 % of total caloric requirements

Hypocaloric

Reduces hyperglycemia & insulin resistance

↓ Infection risk

Step up

Insulin may be added to titrate Glucose level to 140-180 mg/dL

Replace extra on-going fluid losses

COMPLICATIONS OF PARENTERAL NUTRITION

TECHNICAL

Central line - related

- Blood stream infections
  - Highest in Femoral line
  - lowest in subclavian line

indwelling time 3-7 d → > 3-5 % risk

Indwelling time > 7 d → 5-10 % risk

Central line insertion complications

- Pneumothorax
- Hemothorax
- Subclavian artery injury → Bleeding
- Thoracic duct injury
- Arrhythmia
- Air embolism
- Thrombosis

METABOLIC

1) Hyperglycemia

hyperosmolar solutions

Diabetes / insulin resistance

Stress

Rx - volume replacement, electrolyte correction, Insulin

2) Respiratory disturbances

↑ Calorie infusion → ↑ CO_2 → Respiratory insufficiency

3) REFEEDING SYNDROME

↓ starvation, alcoholics

happens when metabolism shifts from lipid / protein to Carbohydrate after feeding

↓

Abrupt ↑ in insulin

- ↓ K^+, ↓ Mg^{2+}, ↓ PO_4^{3-}
- Cardiac & respiratory dysfunction
- Liver & Renal failure

INTESTINAL ATROPHY

Lack of intestinal stimulation

↓

- Mucosal atrophy
- ↓ villous height
- Bacterial overgrowth
- ↓ lymphoid tissue
- ↓ Ig A production

↓

Bacterial translocation

Rx

- small trophic feeds if possible

DIABETIC FOOT ULCER

PATHOMECHANISMS

Neuropathy ← Sensory, Motor, Autonomic
Ischemia
Impaired wound healing

→ minor trauma → DFU

Foot deformity → - Altered foot biomechanics

- tendons & ligaments - glycosylation → become less elastic

Charcot's foot

- claw / hammer toes
- 1st MTJ dislocation
- Bunion

Neuropathy

SENSORY

- Distal symmetrical Sensory neuropathy
- Loss of protective sensation

- Semmes Weinstein monofilament testing (10g) (Pg 1819 Ruthenford)
- Testing for vibration sense

MOTOR

- wasting of intrinsic muscles of foot - upsets the balance between flexors & extensors

MALLET TOE

MTPJ } Normal
PIPJ }
DIPJ - flexion
- hyperflexion of DIPJ
- contracture/spasm of FDL
- Rupture of EDL at DIPJ

℞
FDL tenotomy — Percutaneous / open
FDL transfer to dorsum of phalanx
DIPJ - Excisional arthroplasty

HAMMER TOE

MTPJ - N/ slight extension
PIPJ - Flexion

DIPJ - Normal

- imbalance of intrinsic
- overpull of EDL
- a/c painful corns over dorsal PIPJ

m/c deformity of lesser toes

℞ - FDL → EDL tendon transfer
EDL lengthening

CLAW TOE

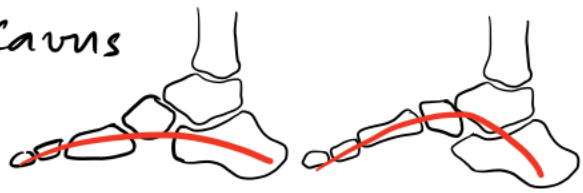
MTPJ - hyperextension
PIPJ } Flexion
DIPJ }

MTPJ hyperextension is the primary pathology
↓
chronic MTPJ hyperextension
↓
unopposed flexion of PIPJ & DIPJ by FDL

℞ EDL tenotomy / lengthening arthroplasty

Hallux valgus

Pes Cavus



AUTONOMIC NEUROPATHY: Dry skin, ↓ sweat & oil gland function

CLASSIFICATION OF DIABETIC FOOT ULCERS

Neuropathic Foot

Neuropathy → fissures, bullae, callosities
Charcot arthropathy
Neuropathic edema

Neuro-ischemic foot

Vascular disease predominates - rest pain, ulceration over foot margins, digital necrosis, gangrene

WAGNER CLASSIFICATION

0 - No open foot lesion

1 - Superficial ulcer
- Partial thickness
- Full thickness

2 - Ulcer extends to ligaments, tendons, joint capsule or deep fascia without abscess / osteomyelitis

3 - Deep ulcer ± abscess / OM / jt sepsis

4 - Gangrene localized to forefoot / heel

5 - Extensive gangrene

UNIVERSITY OF TEXAS CLASSIFICATION

0 - Pre-ulcer / Post ulcer epithelisation

1 - Superficial ulcer

2 - Ulcer extends to tendon / JC

3 - Ulcer penetrates to bone / jt

A - Non infected, non ischemic

B - Infected

C - Ischemic

D - Infected + Ischemic

Others: PEDIS classification
SINBAD classification
SAD classification
IDSA classification

Evaluation

- C & S → Antibiotics
- Routine blood work - Glycemic status, comorbid conditions
- Vascular evaluation → Doppler → if revasc planned - CTA
- Radiology - X-Ray, MRI - osteomyelitis

MANAGEMENT - General- Glycemic control, Neuropathy Rx, Hygiene

- Debridement → Mechanical
  → Autolytic
  → Enzymatic
  → Surgical
  → Biological

- Dressing - Moist wound therapy
- Negative pressure wound therapy
- Non surgical pressure offloading — offloading shoe inserts

Gold std- Total contact casts, Special footwear, orthotic devices

- Surgical offloading

Ulcer resection + Tendon lengthening / transfer
Exostectomy
Arthroplasty

* Tendon Lengthening & transfer →
  Achilles tendon lengthening → Reduces forefoot pressure } in equinus deformity

if there is additional varus deformity →
Tibialis anterior tendon transfer - from medial cuneiform → lateral cuneiform/cuboid

* Percutaneous / open tenotomies for toe deformities
* Toe arthroplasties
* Metatarsal head resections - for plantar metatarsal head ulcers which penetrate bone
* Digital & mid foot amputations toe / transmetatarsal

- Reconstructions: V-Y advancement / toe island / Medial plantar A flap
  Free tissue transfer
- Revascularisation procedures for PAD
- Major amputations if tissue not viable / spreading inf

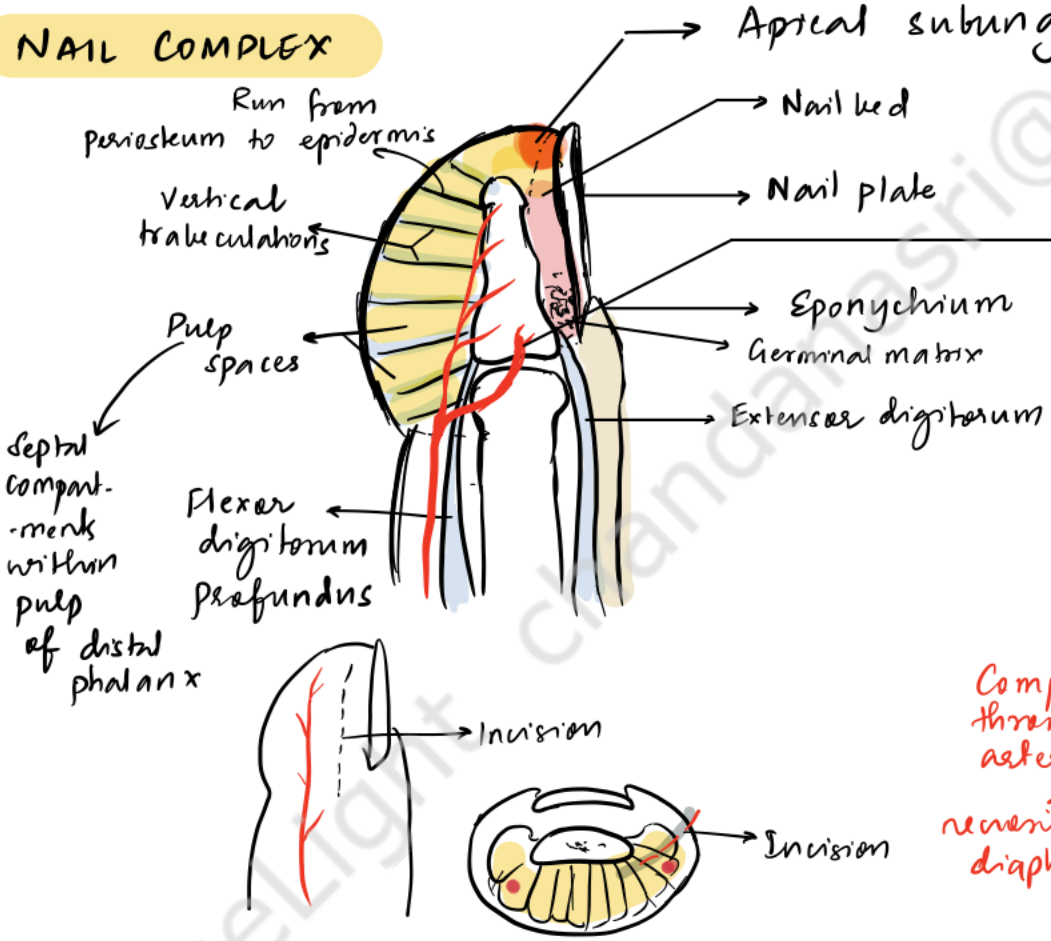
HAND INFECTIONS

SURGICAL ANATOMY

SPACES OF THE HAND

1) Nail complex and pulp space
2) Synovial spaces
   - Flexor and extensor tendon sheaths
   - Radial and ulnar bursae
3) Volar and dorsal spaces

NAIL COMPLEX



Digital artery gives off epiphyseal branch before entering pulp space
↓
Volar nutrient arteries to diaphysis
↓
Compression and thrombosis of these arteries
- necrosis of diaphysis
- Sparing of epiphysis

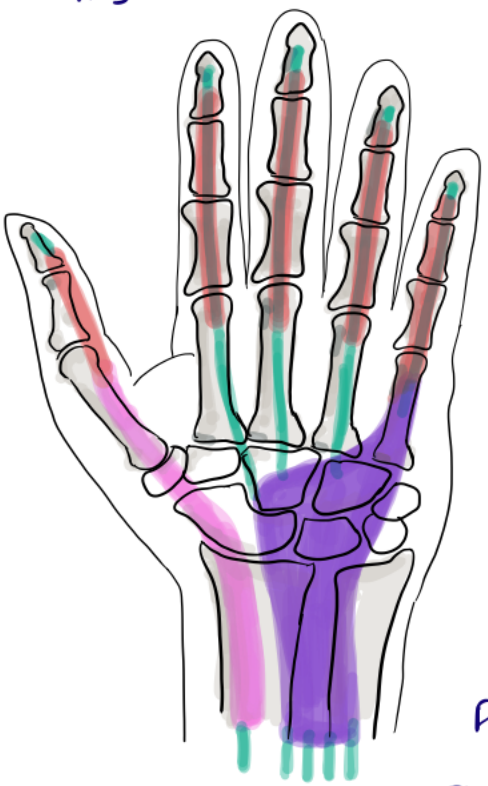
- **Felon** = Pulp space infection
- drained by longitudinal incision over point of max fluctuation
- **Paronychia** - infection of soft tissue fold surrounding the nail plate
  - **Acute**
    - I & D – tip directed away from nail bed
    - Nail excision
  - **Chronic**
    - Eponychial marsupialization
    - Partial/total nail excision
- **Herpetic Whitlow** - herpetic infection of fingertip - HSV 1&2
  Rx - <48h - Antivirals, superadded bact inf - abx | **No I&D**

FLEXOR AND EXTENSOR TENDON SHEATHS

Flexor tendon sheaths → 2 layers
- Visceral - forms epitenon
- Parietal - abuts pulley mechanism

Extend from the level of metacarpal neck upto DIPJ

Form a closed system by connecting proximally & distally → sheath



Flexor tendons derive nutrition from vincular arteries which enter the tendon sheaths

↑ Pressure in flexor tendon sheath
↓
- Obstruction to arterial supply
↓
Tendon necrosis & rupture

Flexor sheath of thumb → communicates with radial bursa

Flexor sheath of little finger → communicates with ulnar bursa

Synovial sheaths for each of the 6 extensor compartments are present beneath dorsal carpal ligament & extend a short distant & proximal to dorsal carpal ligament

RADIAL AND ULNAR BURSAE

Continuation of Flexor tendon sheath of flexor pollicis longus from I-MCPJ to 1-2cm proximal to proximal edge of Flexor retinaculum

Continuation of flexor tendon sheath proximal to V MCPJ to 1-2cm proximal to flexor retinaculum

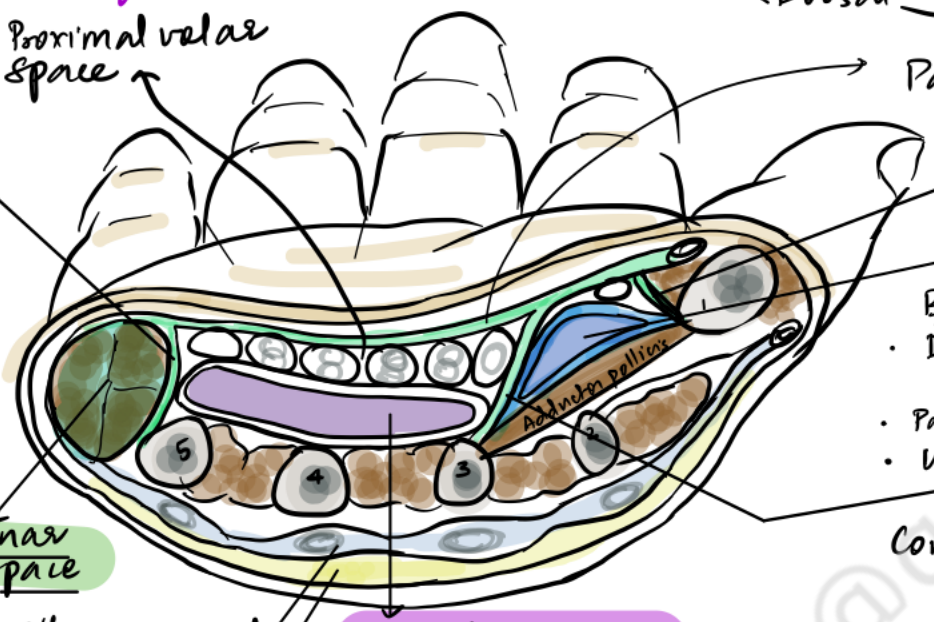
(Tendons invaginate the bursa - they aren't enveloped in it)

Radial & ulnar bursae can intercommunicate

VOLAR AND DORSAL SPACES

- Volar
  - Palm
    - Thenar
    - Midpalmar
    - Hypothenar
  - Forearm
    - Space of Parona
- Dorsal
  - s/c
  - s/a

Web space inf - 'Collar stud abscess'



Thenar space

Boundaries
- Dorsal - Adductor pollicis
- Palmar - Palmar aponeurosis
- Ulnar - Intermediate oblique septum

Flexor retinaculum
Distal palmar crease

Contents: FPL, I lumbrical
Palmar neurovasc to thumb
Flexor to index finger

Hypothenar space

Dorsal - 5th metacarpal
Palmar - Hypothenar fascia
Radial - Hypothenar septum

Midpalmar space

Dorsal - Metacarpals & interossei (3rd, 4th, 5th)
Palmar - Palmar aponeurosis
Radial - Midpalmar / oblique septum
Ulnar - Hypothenar septum
Contains - 3rd, 4th, 5th Flexor tendons
2nd, 3rd, 4th lumbricals
Sup. palmar arch, digital Ns & vessels

infection can point in 3rd & 4th web space
Can extend to Parona space

Dorsal subcutaneous space

Between skin & fascia
Contains - Dorsal digital branch of radial & ulnar N

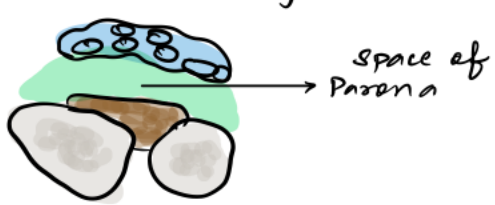
→ easily spread into s/c space of forearm

Dorsal Subaponeurotic space

Between aponeurosis / fascia and dorsal surface of metacarpal bones & interossei
Contains - Extensor tendons
Dorsal carpal arch

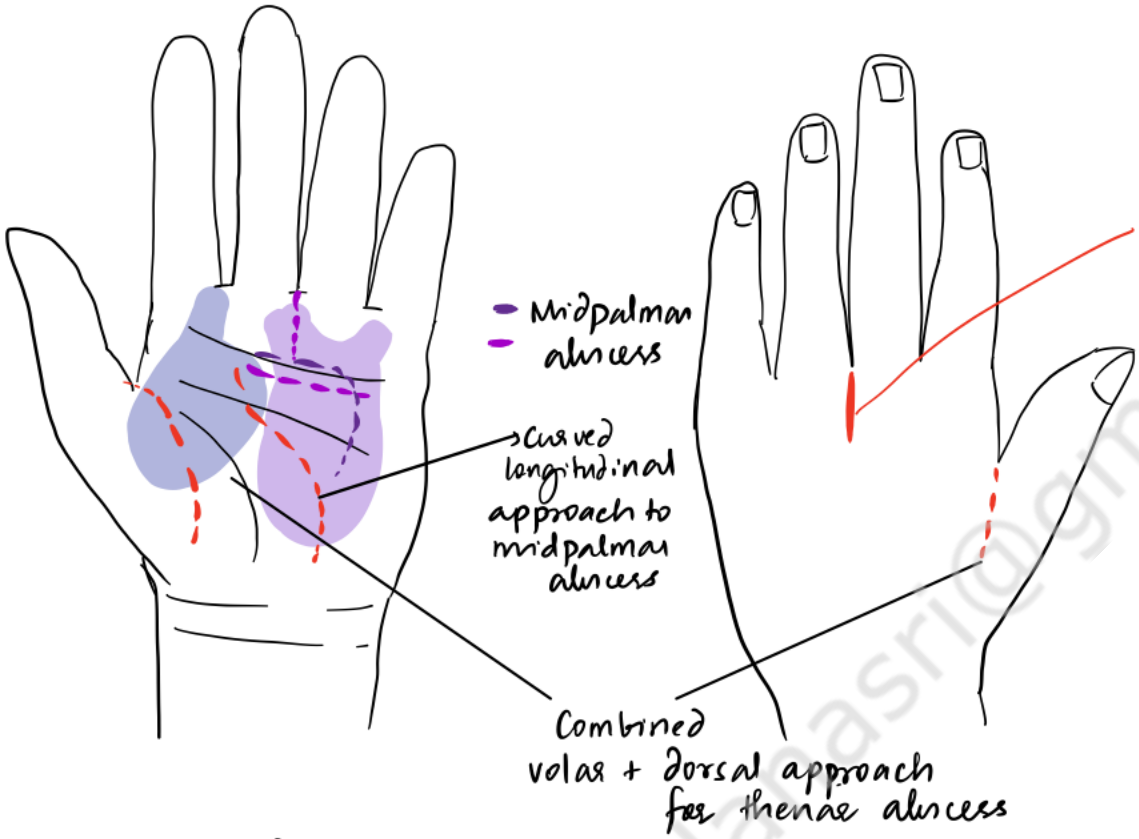
Space of Parona - Potential space in the distal forearm between fascia of pronator quadratus muscle and flexor digitorum profundus tendon sheath

→ Communicates underneath flexor retinaculum & midpalmar space

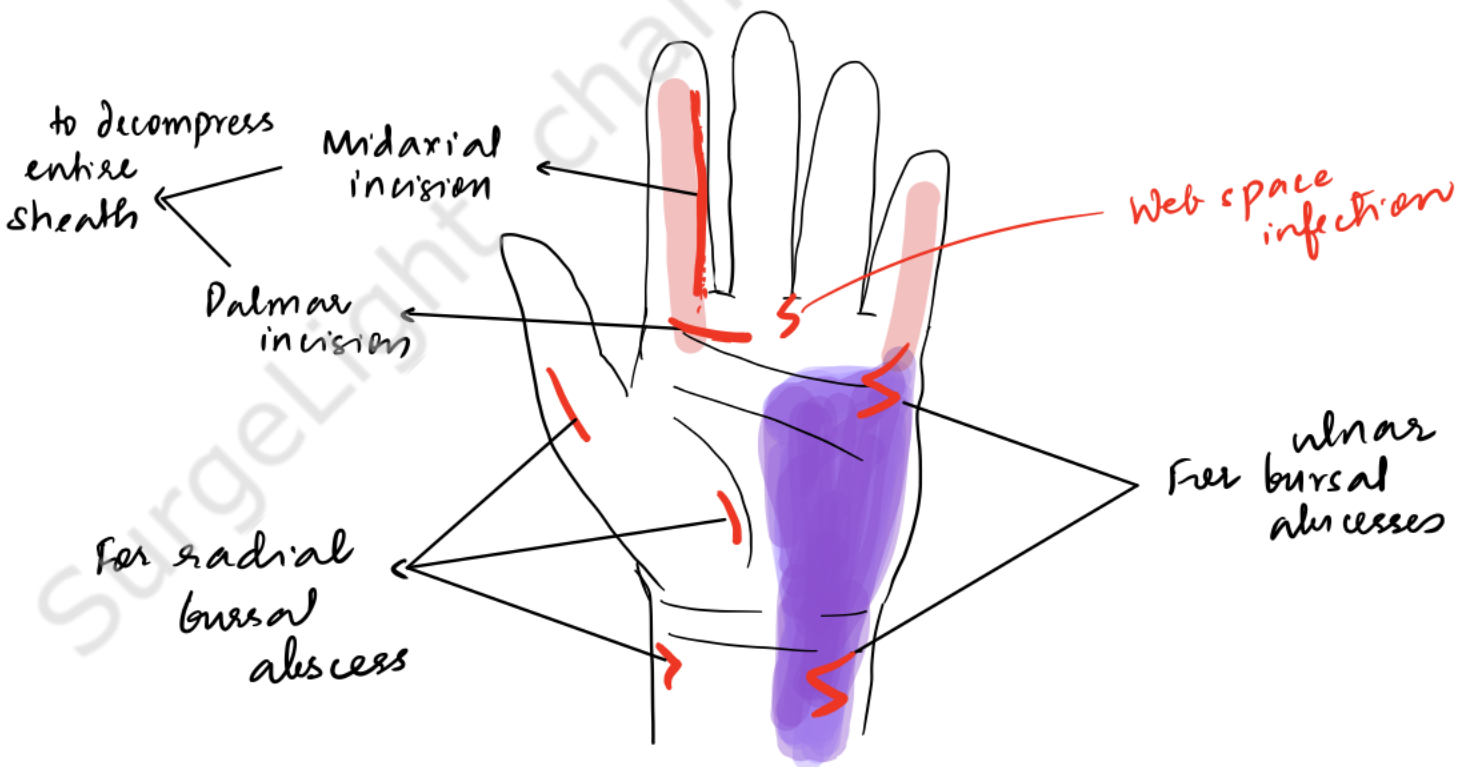


INCISIONS TO DRAIN HAND INFECTIONS

THENAR & MIDPALMAR ABSCESS



SUPPURATIVE TENOSYNOVITIS



HAND INFECTIONS

Common organisms – Staph aureus → abscess (non-smelly)
Strep pyogenes → cellulitis, lymphangitis
Gram-negatives → smelly abscess
Gram-negatives → Cellulitis

↓

Abx cover

Penicillins
I/II Gen Cephalosporin

General modes of infection

Direct implantation – penetrating trauma
- pricks
- bites
- abrasions

Hematogenous – Septic arthritis → extension
Osteomyelitis

FLEXOR SHEATH INFECTION

↓

Kanavel's sign – 4 Cardinal signs

- Pain ± passive extension
- fusiform digital swelling
- Stiffness in semiflexed position
- Tenderness along flexor sheath into the palm

Point of maximal tenderness in ulnar bursitis is on the ulnar side of the area between proximal & distal palmar creases

---

General management

Rest, antibiotics, elevation → I & D / debridement

Splinting, physiotherapy

PRESSURE SORES

A pressure sore is a tissue injury caused by sustained physical pressure applied to the tissues from an external source at a magnitude that exceeds the capillary perfusion pressure (~32 mmHg)

External pressure > Capillary perfusion pressure

↓

↓ Capillary perfusion

↓

Prolonged tissue ischemia

↓

Local tissue necrosis

Sites of occurence - bony prominences

- SACRUM
- CALCANEUM
- ISCHIUM
- GREATER TROCHANTER

RISK FACTORS

EXTRINSIC

Sustained pressure
- Loss of protective sensation
  Neuropathy, Spinal cord pathology
- Loss of mobility
  Paralysis
  Bedridden - chronic illness

INTRINSIC

Poor wound healing
- diabetes, smoking, PVD
- immunosuppression / steroids
- advanced age
- malnutrition
- edema, shock

Aggravating factors

- Moisture in perineal area
- Incontinence - soiling / contamination
- shearing forces while repositioning the patient

RISK ASSESSMENT SCORES

BRADEN SCALE : Sensory perception, Moisture, Activity, Mobility, Nutrition, Friction, shear

WATERLOW SCORE: BMI, Continence, mobility, Nutrition, Skin, Age, Sex, Adverse wound healing factors, neurological deficit, trauma/surgery, drugs

NORTON SCALE

Prevention : 3 'R's - Redistribute surfaces
Remobilise
Reposition

GRADING OF PRESSURE SORES

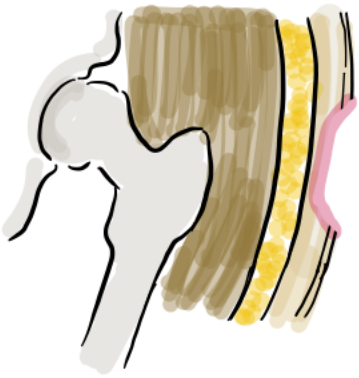
STAGE - I

Intact skin ± non-blanching erythema

altered skin
temperature
consistency
color

STAGE - II

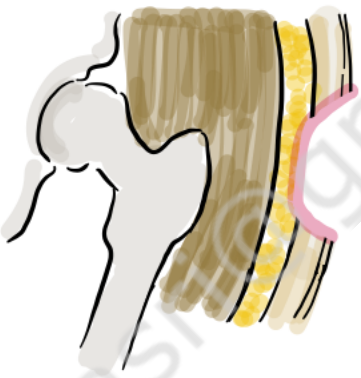
Partial thickness loss of dermis - shallow ulcer



Superficial ulcer
blister
shallow
crater

STAGE - III

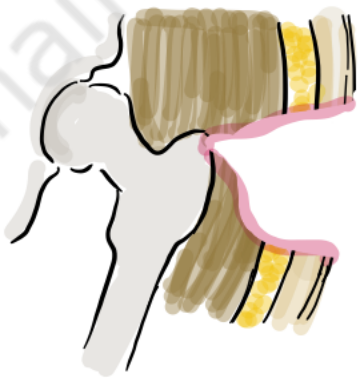
Full thickness loss exposing subcutaneous tissue



Deep crater exposing subcutaneous tissue ± undermining of adjacent tissue

STAGE - IV

Full thickness loss exposing tendon/ muscle / bone



Exposes bone / tendon/ joint capsule / muscle
± osteomyelitis

SUSPECTED DEEP INJURY

Purple / maroon localized area of discolored intact skin
-OR-
BLOOD FILLED BLISTER
↓
usually has deeper damage

UNSTAGEABLE

Full thickness tissue loss in which the base of the ulcer is covered by
SLOUGH / ESCHAR
True depth & stage cannot be determined without removing slough / eschar

EVALUATION

- Culture & Sensitivity
- X-Ray, MRI to detect osteomyelitis
- Routine

MANAGEMENT OF PRESSURE SORES

1) Pressure relief
   - Frequent position change
   - Foam mattresses
   - Dynamic support surface - Air bed / Water bed

2) Correction of other causative factors like spasticity
   joint contractures
   incontinence
   malnutrition

3) Debridement
   - Drain collections
   - Excise dead tissues
   - Excise sinus tracks
   - Ostechomy of involved bone, bony prominences

4) DRESSING
   - Moist wound healing
   - NEGATIVE PRESSURE WOUND THERAPY

5) SURGICAL PROCEDURES

Primary closure & skin grafts are poor solutions

∴ FLAPS → procedure of choice

SACRAL PRESSURE SORES: Gluteal flaps based on superior / inferior pedicle

- Rotational flap
- V-Y advancement flap

ISCHIAL SORES: Gluteus maximus rotational flap
V-Y hamstring advancement flap
Tensor fascia lata rotational flap

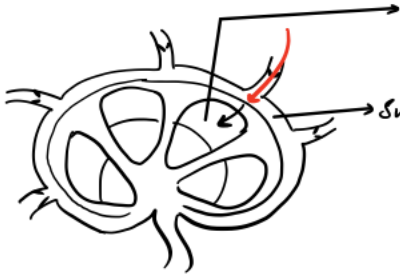
TROCHANTER SORES: trochanter resection, bursectomy
Local rotational / advancement flaps

FOOT & HEEL → Small - conservative
Large - local fasciocutaneous flaps

TB LYMPHADENITIS

'Scrofula'

- m/c site - neck nodes
  - Jugulodigastric (Level II) > Posterior △ (Level V)
  - 20 % bilateral
- Mode of infection:
  - m/c - tonsils
  - lungs → hematogenous



CORTEX — ① ADENITIS → Enlarged discrete nodes

Subcapsular sinus → ② PERIADENITIS → MATTING → fixed to each other

Caseation

③ COLD ABSCESS → Deep fascia

④ COLLAR STUD ABSCESS

⑤ SINUS

℞

Zig-zag aspiration in non-dependent position to prevent sinus formation

Soft Tissue Sarcoma

Soft-tissue sarcomas arise predominantly from embryonic mesoderm but can also arise from the ectoderm. Mesodermal cells give rise to the connective tissues distributed throughout the body; therefore, soft-tissue sarcomas can occur anywhere in the body. The majority of primary lesions originate in an extremity (45%), with the next most frequent anatomic site of origin being intra-abdominal/retroperitoneal (40%), followed by trunk (10%) and head/neck region (5%) (Fig. 5.1). Sarcoma is a heterogeneous disease group that encompasses >60 histologic subtypes. Each subtype has its own unique behavior, different recurrence pattern, and distinct survival. Excluding gastrointestinal stromal tumors (GISTs), the most common histologic types of soft-tissue sarcoma in adults are undifferentiated/unclassified sarcoma (with pleomorphic, round cell, and spindle cell variants), leiomyosarcoma, liposarcoma, synovial sarcoma, and malignant peripheral nerve sheath tumor (MPNST) (Fig. 5.2). Rhabdomyosarcoma is the most common soft-tissue sarcoma of childhood.

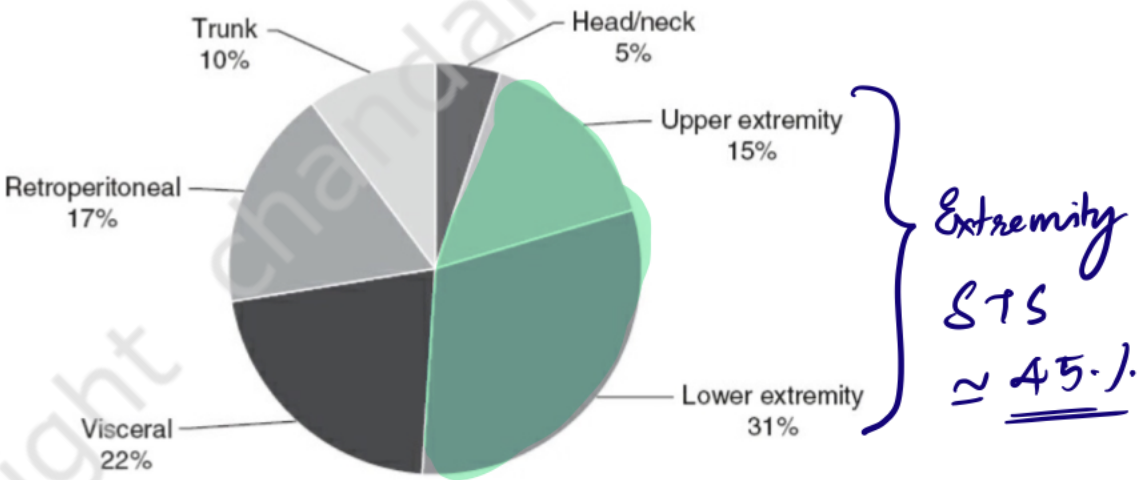


Figure 5.1 Distribution by location for adult patients with soft-tissue sarcoma. (Data from DeVita VT Jr., Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 10th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2015:1253–1291.)

Extremity > Visceral > RP > Trunk > HgN

Males – m/c in extremeties

Females – m/c in trunk

Etiology

The vast majority of sarcomas are sporadic with unknown etiology, but a number of factors have been associated with increased risk of soft-tissue sarcoma, including previous radiation exposure, chronic lymphedema, genetic predisposition, trauma, and occupational chemicals such as phenoxyacetic acids and wood preservatives containing chlorophenols.

1) *Previous Radiation Exposure*

External-beam radiation therapy is a rare but well-established cause of soft-tissue sarcoma. An 8- to 50-fold increase in the incidence of sarcomas has been noted for patients treated with radiation therapy for cancers of the breast, cervix, ovary, testes, and lymphatic system. In addition, the risk of developing a sarcoma after radiation therapy increases with higher dosage. The median latency between irradiation and the development of a sarcoma is approximately 10 years, but can range from 1 to 40 years. The most common histologic types of radiation-associated sarcomas are osteogenic sarcoma, undifferentiated/unclassified sarcoma, angiosarcoma, and lymphangiosarcoma. Radiation-associated sarcomas are associated with a worse prognosis compared with non–radiation-associated sarcomas, even when matched for stage.

2) Chronic Lymphedema - Stewart Treves SO
- following axillary dissection
- lymphangiosarcoma

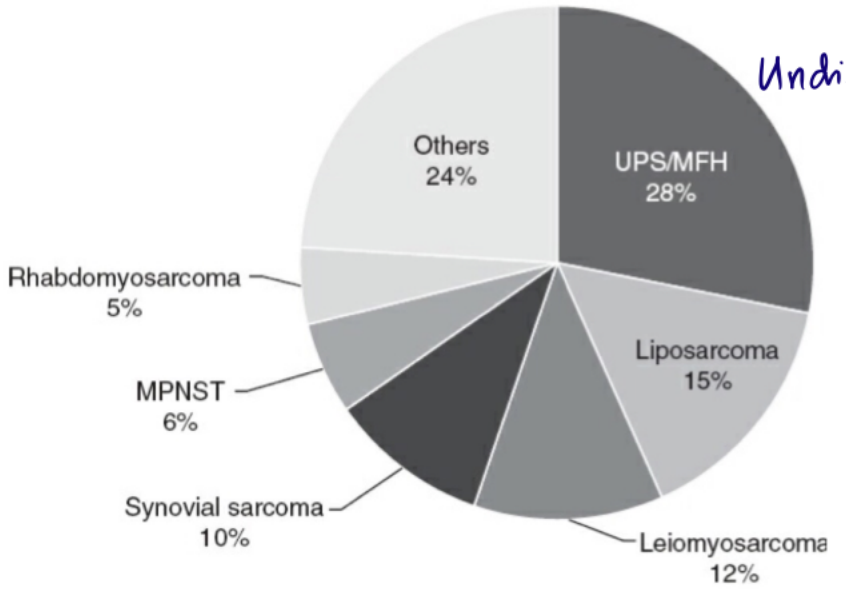
→ can also be seen i filariasis a/i chronic lymphedema

3) Genetic Predisposition

Gardner S°- Desmoid tumors
NF-1 - MPNST
Li fraumeni - Sarcomas
Retinoblastoma - STS may be 2nd malignancy
MDM-2
CDK-4
c-erbB-2
RAS
Chromosomal translocations - 11 & 22

Sarcomas usually do not arise from benign precursors
Exception - MPNST (20-50-1 from NF in NF-1)

Histological Subtypes



Undifferentiated Pleomorphic Sarcoma / Malignant Fibrous Histiocytoma

Figure 5.2 Common histologies of soft-tissue sarcoma. (Data from Coindre JM, Terrier P, Guillou L, et al. Predictive value of grade for metastasis development in the main histologic types of adult soft tissue sarcomas a study of 1240 patients from the French Federation of Cancer Centers Sarcoma Group. *Cancer* 2001;91:1914–1926.)

Sarcomas : Lymphatic Spread

'RACE for MS'

- **R**habdomyosarcoma (alveolar type)
- **A**ngiosarcoma
- **C**lear cell sarcoma
- **E**pithelial sarcoma, Goring's
- **M**alignant fibrous histiocytoma
- **S**ynovial Sarcoma

Low Metastatic Potential

Desmoid tumor
Atypical lipomatous tumor/Well-differentiated liposarcoma
Dermatofibrosarcoma protuberans
Hemangiopericytoma

Intermediate Metastatic Potential

Myxoid liposarcoma
Myxofibrosarcoma (previous myxoid malignant fibrous histiocytoma)
Extraskeletal chondrosarcoma

High Metastatic Potential

Undifferentiated pleomorphic sarcoma (previously pleomorphic malignant fibrous histiocytoma)
Liposarcoma (dedifferentiated and pleomorphic)
Leiomyosarcoma
Angiosarcoma
Alveolar soft-part sarcoma
Clear-cell sarcoma
Epithelioid sarcoma
Extraskeletal Ewing sarcoma
Extraskeletal osteosarcoma
Neurogenic sarcoma (malignant schwannoma)
Rhabdomyosarcoma
Synovial sarcoma

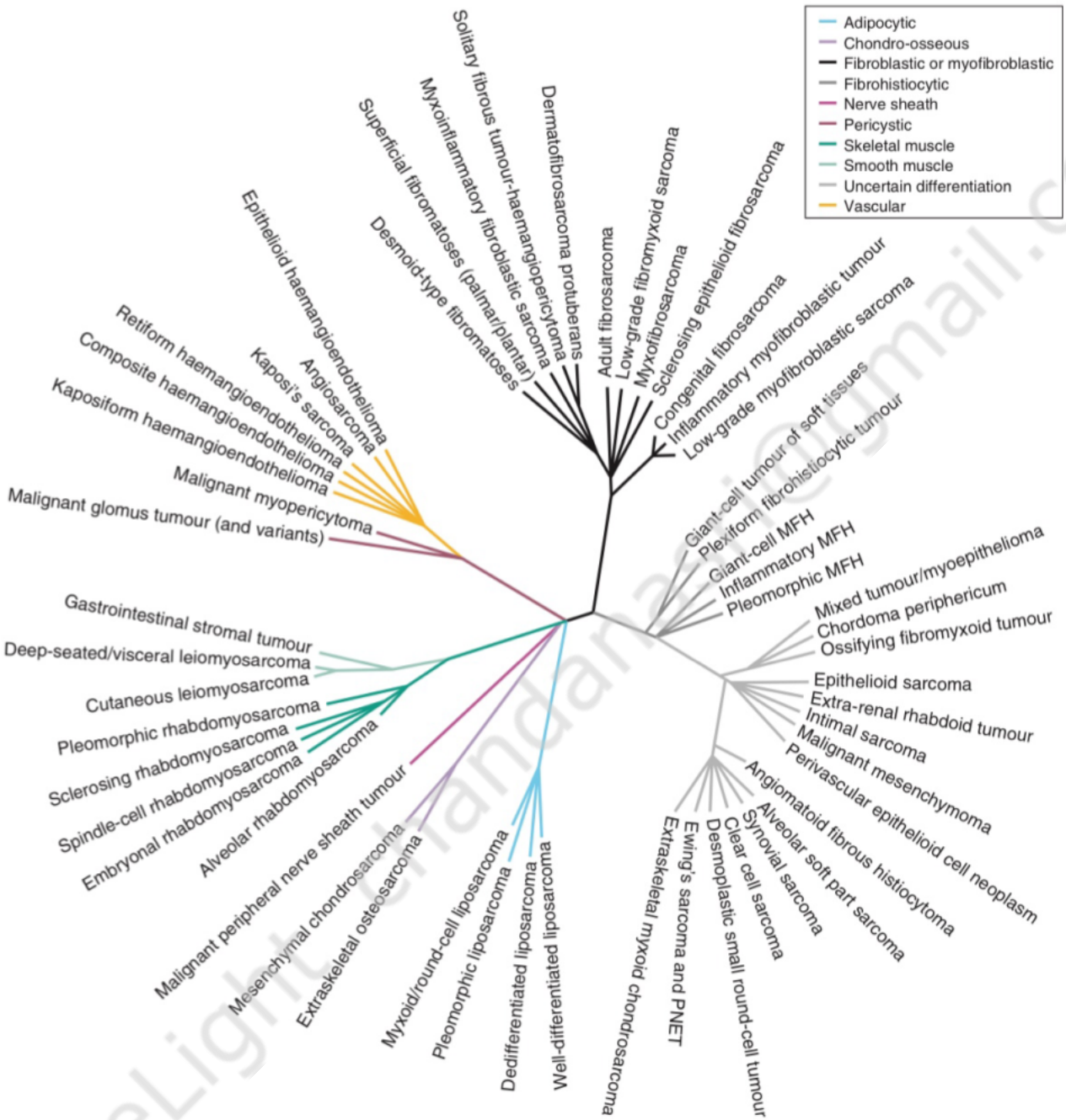


FIGURE 31-1 Taxonomy of Soft Tissue Sarcoma. This unrooted phylogeny shows about 60 sarcoma subtypes, as originally defined by the World Health Organization International Agency for Research on Cancer, amended and updated on the basis of current knowledge. The classification reflects relationships among lineage, prognosis (malignant, intermediate or locally aggressive, intermediate or rarely metastasizing), driver alterations, and additional parameters. Branch lengths are determined by nearest neighbor joining of a discretized distance matrix based on the aforementioned variables. Initial branching reflects differences in lineage, with associated lineages appearing closer in distance (such as skeletal and smooth muscle). Subsequent branching denotes similarity in prognosis, whether they are translocation associated, and if so, the genes shared among distinct fusions (in this order). Although incomplete, as many subtypes lack sufficient global molecular profiling data on which to base a phylogeny, this initial formulation minimally reflects the relationships among lineage and major molecular lesions in the subtypes. The illustration excludes 52 benign types of tumor. *MFH,* undifferentiated pleomorphic sarcoma; *PNET,* primitive neuroectodermal tumor. (From Taylor BS, Barretina J, Maki RG, et al: Advances in sarcoma genomics and new therapeutic targets. *Nat Rev Cancer* 11:541–557, 2011.)

STAGING

- STS staging depends on site & grade
- Available site-specific stagings (AJCC)
  1) Abdomen & Thoracic Visceral organs
  2) Head & Neck
  3) Retroperitoneum
  4) Trunk & extremeties
  5) STS - Unusual histologies & Sites
     → Here, grading for differentiation is assigned a score based on histological appearance

[Refer ONCO-ASSIST APP]

STS of Extremities & Trunk

T

- T_0 – No tumor
- T_x – cannot be assessed
- T_1 – < 5 cm
- T_2 – 5–10 cm
- T_3 – 10–15 cm
- T_4 – > 15 cm

N

- N_0 – no nodes
- N_1 – Nodal mets (+)

M

- M_0 – no mets
- M_1 – distant mets (+)

Grading < Differentiation (D)
Mitosis (M)
Necrosis (N)

Differentiation Score	Definition
1	Sarcomas closely resembling normal adult mesenchymal tissue (e.g., low-grade leiomyosarcoma)
2	Sarcomas for which histologic typing is certain (e.g., myxoid/round cell liposarcoma)
3	Embryonal and undifferentiated sarcomas, sarcomas of doubtful type, synovial sarcomas, soft tissue osteosarcoma, Ewing sarcoma /primitive neuroectodermal tumor (PNET) of soft tissue

In the most mitotically active area of the sarcoma, 10 successive high-power fields (HPF; one HPF at 400× magnification = 0.1734 mm^2) are assessed using a 40× objective.

Mitotic Count Score	Definition
1	0–9 mitoses per 10 HPF
2	10–19 mitoses per 10 HPF
3	Greater than 20 mitoses per 10 HPF

Evaluated on gross examination and validated with histologic sections.

Necrosis Score	Definition
0	No necrosis
1	Less than 50% tumor necrosis
2	Greater than or equal to 50% tumor necrosis

GRADES

G_x – cannot be assessed

G_1 – D+M+N = 2-3

G_2 – D+M+N = 4-5

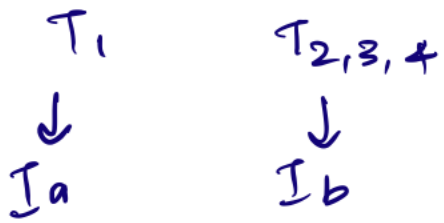
G_3 – D+M+N = 6-8

STAGE - GROUPING

When T is…	And N is…	And M is…		Then the stage group is…
T1	N0	M0	G1, GX	IA
T2, T3, T4	N0	M0	G1, GX	IB
T1	N0	M0	G2, G3	II
T2	N0	M0	G2, G3	IIIA
T3, T4	N0	M0	G2, G3	IIIB
Any T	N1	M0	Any G	IV
Any T	Any N	M1	Any G	IV

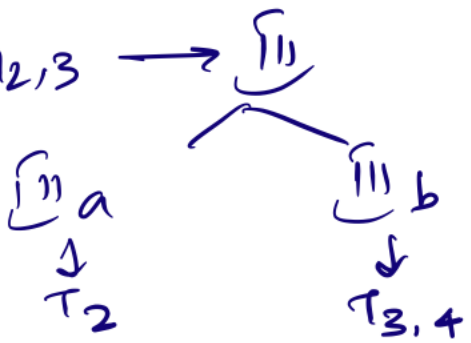
$N_1, M_1 \rightarrow$ Stage 4

Any T N_0 M_0 & G_1 / G_X $\rightarrow$ I



T_1, N_0, M_0 + $G_{2,3}$ $\rightarrow$ II

$T_{2,3,4}, N_0, M_0$ + $G_{2,3}$ $\rightarrow$ III



NCCN Guidelines for Workup of STS

EXTREMITY/SUPERIFICIAL TRUNK, HEAD/NECK

→ IOC

Workup

- Primary tumor imaging using MRI with and without contrast ± CT with contrast is recommended. Other imaging studies such as angiogram and plain radiograph may be warranted in certain circumstances.
- Chest imaging
  - X-ray or CT without contrast (preferred)
- Additional imaging studies as indicated:
  - PET/CT scan may be useful in staging, prognostication, and grading.
  - Consider abdominal/pelvic CT for myxoid/round cell liposarcoma, epithelioid sarcoma, angiosarcoma, and leiomyosarcoma.
  - Consider MRI of total spine for myxoid/round cell liposarcoma.
  - Consider CNS imaging with MRI (or CT if MRI is contraindicated) for alveolar soft part sarcoma and angiosarcoma.
  - Consider pelvic CT imaging for lower-extremity well-differentiated liposarcoma.

MRI ≥ CECT for primary + CT Plain chest } usually mandatory

Abd/Pelvis CT / Head & Spine CT/MRI → In specific situations

Biopsy

- A pretreatment biopsy to diagnose and grade a sarcoma is highly preferred. Biopsy should be carried out by an experienced surgeon (or radiologist) and may be accomplished by open incisional or needle technique. Core needle biopsy is preferred; however, an open incisional biopsy may be considered by an experienced surgeon. Image-guided needle biopsy may be indicated for extremity/truncal sarcomas.

Although fine-needle aspiration (FNA) is a convenient technique, it can be difficult to make an accurate primary diagnosis with FNA alone due to small specimen size and is thus discouraged.[33] FNA may be acceptable in select institutions with clinical and pathologic expertise. Endoscopic or needle biopsy may be indicated for deep thoracic, abdominal, or pelvic STS.

} FNAC not recommended - अपवाद !

MANAGEMENT OF EXTREMITY STS

Sabiston 20 Ed

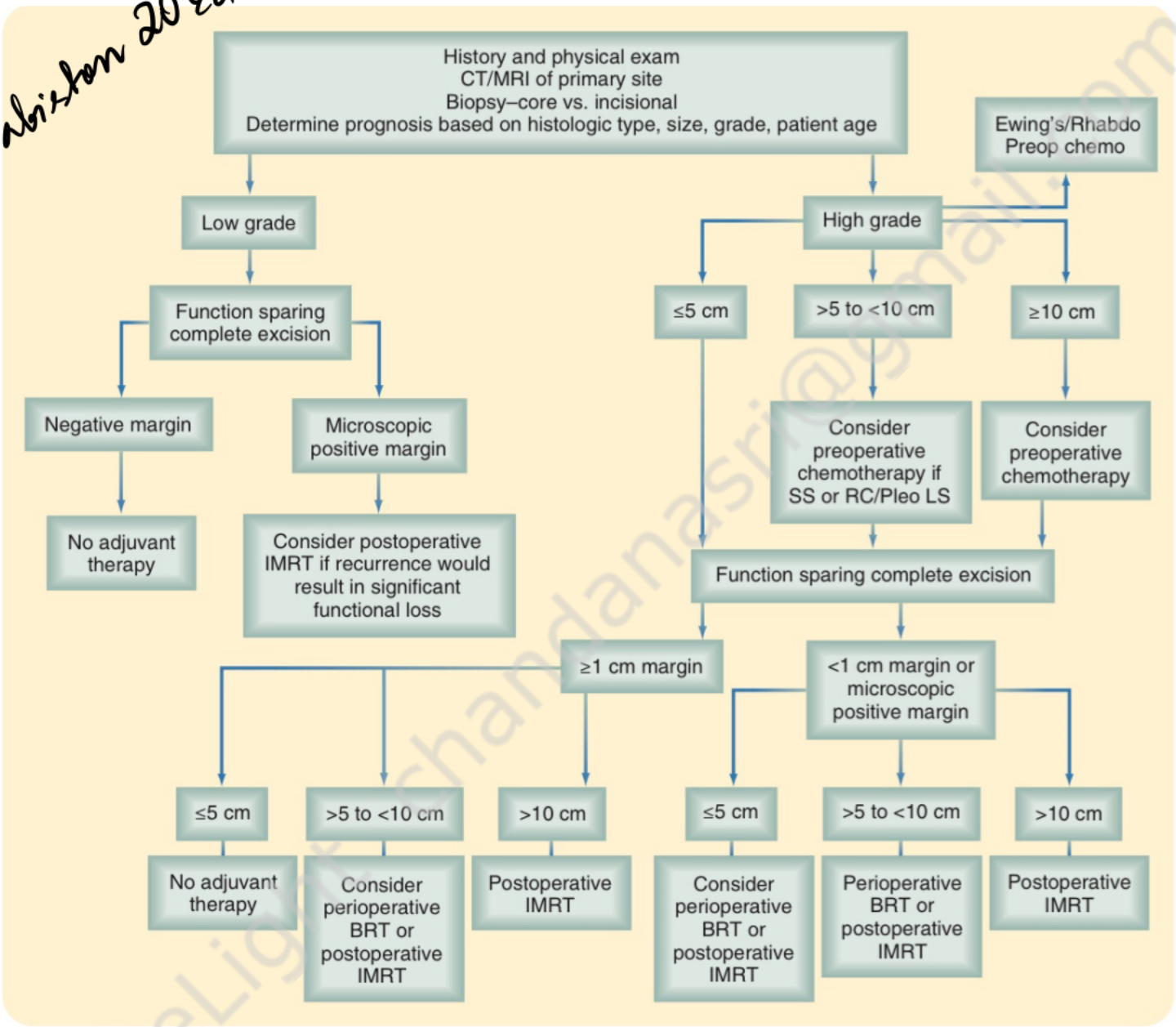


FIGURE 31-4 Algorithm for the management of primary (with no metastases) extremity or trunk soft tissue sarcoma, using a biologic rationale (i.e., size and grade of tumor). *BRT,* brachytherapy; *EBRT,* external beam radiation therapy; *IMRT,* intensity-modulated radiation therapy; *RC/Pleo LS,* round cell–pleomorphic liposarcoma; *SS,* synovial sarcoma.

1 cm Margin

(MDAnderson Manual has said even 2cm margin)

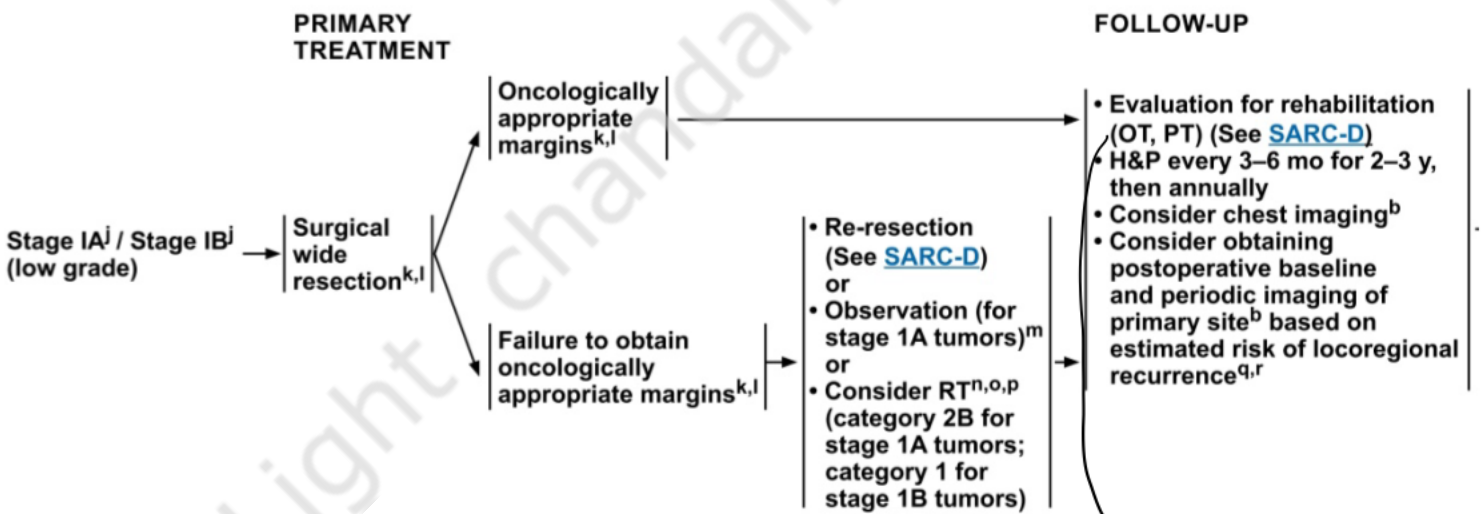
Stage Specific Management of Extremity / Trunk STS } Acc to NCCN

① Stage 1 - WLE ± ≥1 cm margin

This will be curative if
- tumors are low grade / favorable histology
- Fascial planes are intact

If margins are less than 1cm / Positive / Fascial planes are not intact
→ Re-excision should be considered
vs
"observation" → decide after MDT discussion

Post op RT
→ close margins
→ Large tumors
→ Some trials have shown improvement in DFS
- no improvement in OS

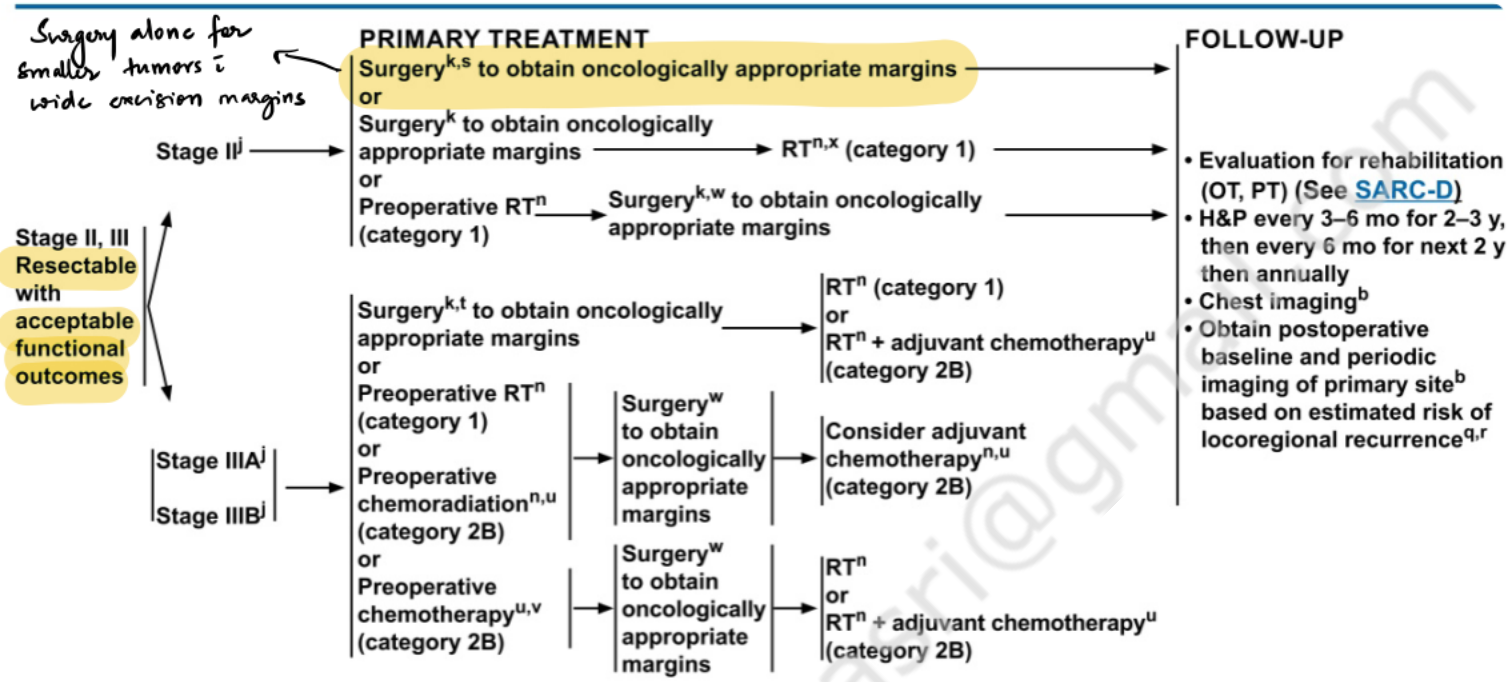


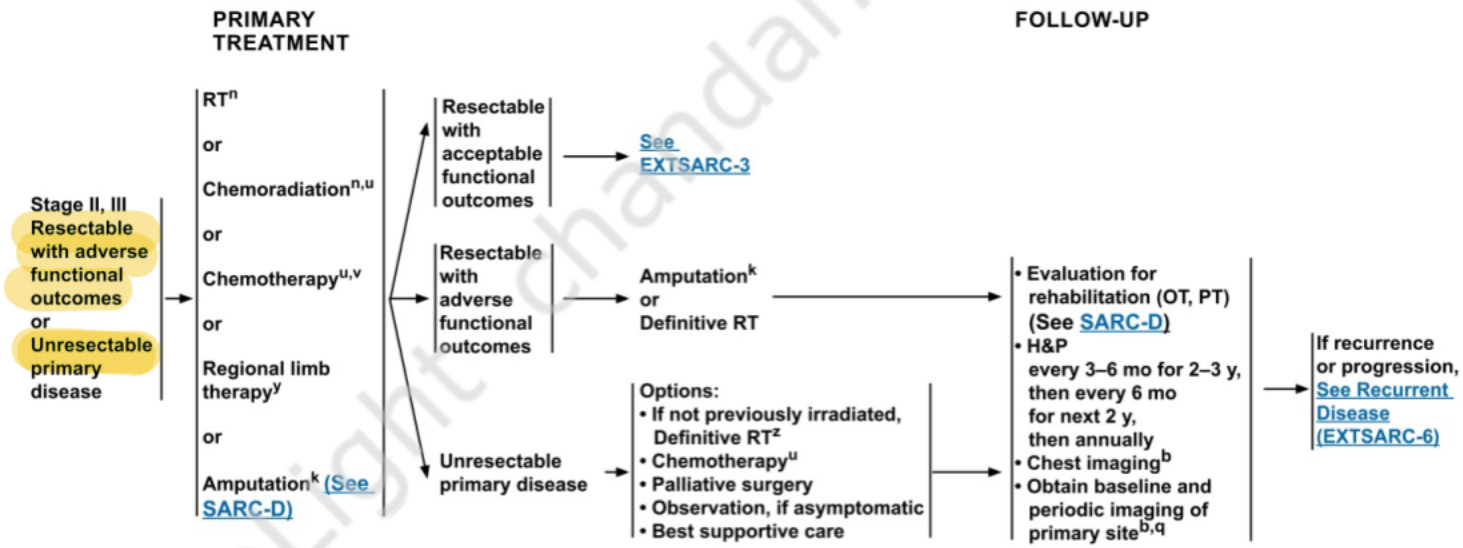
- OT - Occupational Therapy

PT - Physical Therapy

- H&P - History & Physical exam

Stage II-III





[b] See Principles of Imaging (SARC-A).

Pre-op RT - non-significant trend towards reduced late toxicities if RT is given pre-op (fibrosis, edema, joint stiffness). Also, post-op RT fields are typically larger than pre-op RT fields

→ Pre-op generally preferred by NCCN panel

LIMB SALVAGE
(REGIONAL LIMB THERAPY)

Isolated limb perfusion (ILP) or

Isolated limb infusion (ILI)

- done in cases of locally advanced STS

- ILP : Melphalan + TNF-α
- To be combined : post-op RT

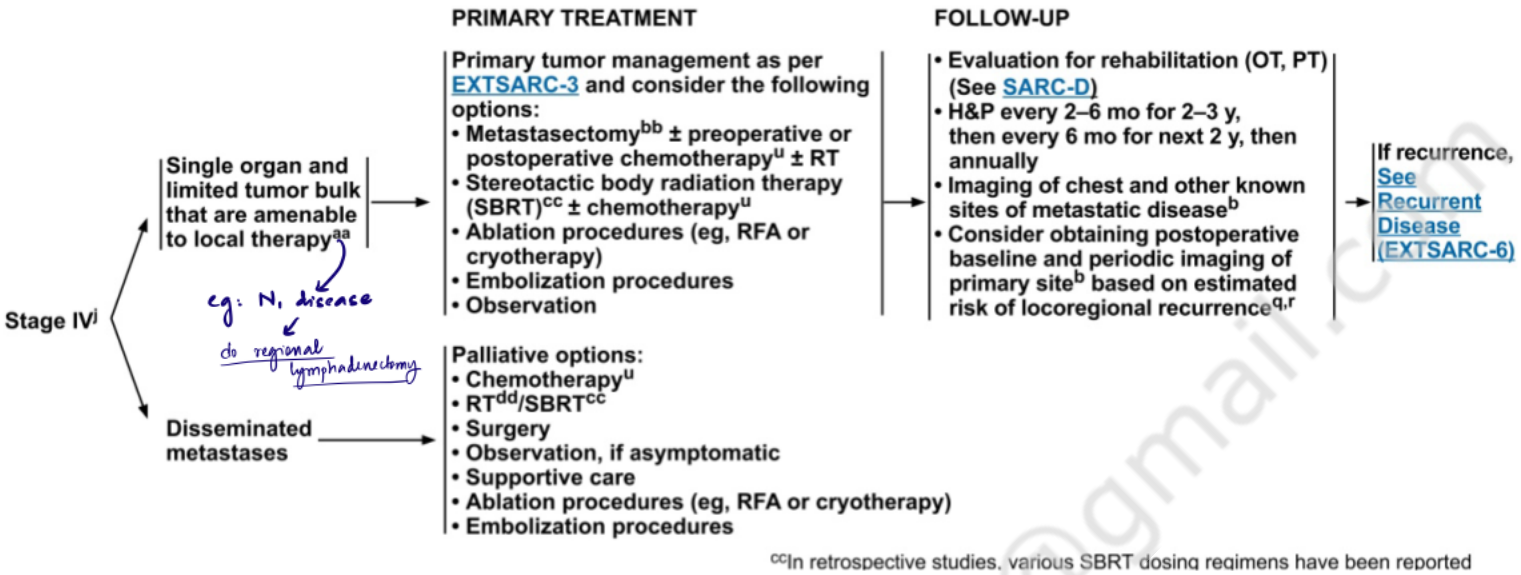
(No difference in survival benefit compared to amputation)

If tumor is grossly unresectable : satisfactory margins

↓

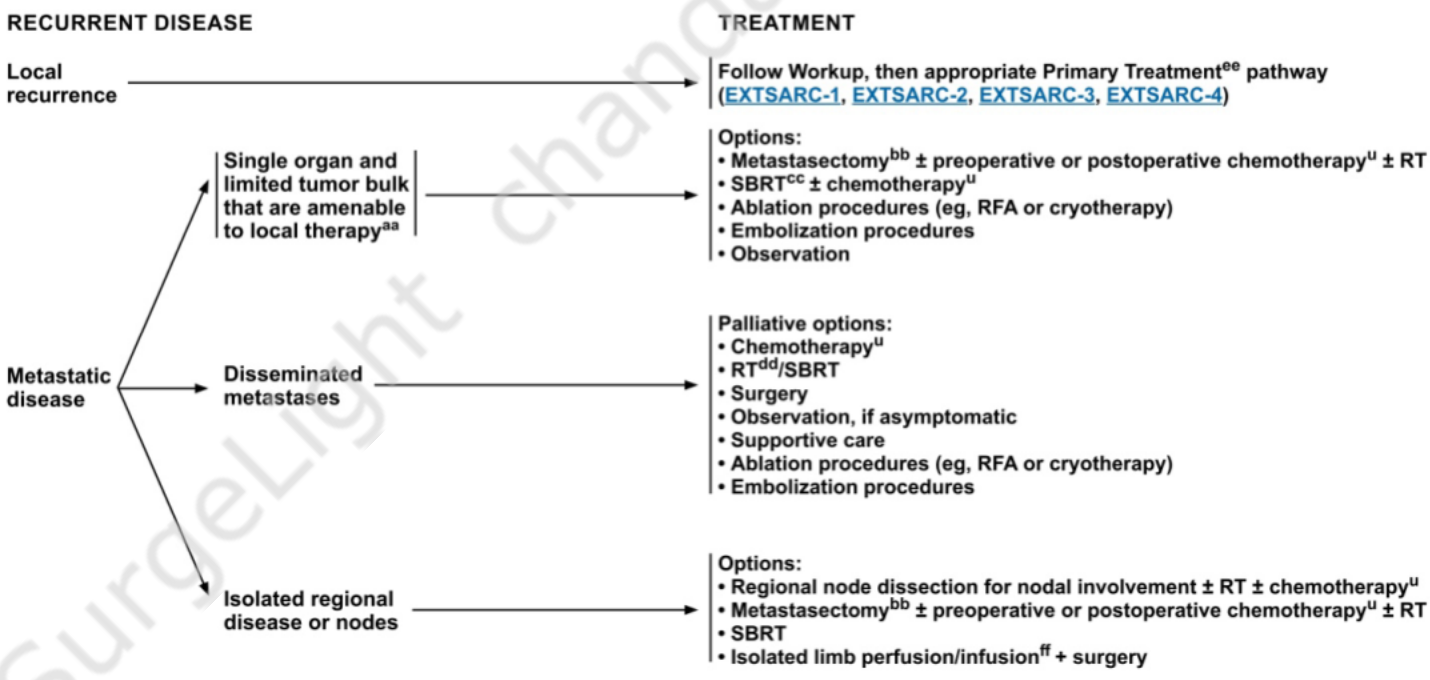
AMPUTATION

STAGE IV (N1, M1 disease)



[cc]In retrospective studies, various SBRT dosing regimens have been reported

RECURRENT DISEASE



[ee]If local recurrence can be excised, a decision will need to be made on a case-by-case basis whether re-irradiation is possible. Some case series suggest benefit with re-irradiation [Catton C, Davis A, Bell R, et al. Soft tissue sarcoma of the extremity. Limb sparing after failure of combined conservative therapy. Radiother Oncol 1996;41:209-214. while others do not [Torres MA, Ballo MT, Butler CE, et al. Management of locally recurrent soft-tissue sarcoma after prior surgery and radiation therapy. Int J Radiat Oncol Biol Phys 67:1124, 2007], likely reflecting differences in selection of patients for treatment with surgery and radiotherapy or surgery alone. Traditionally, the re-irradiation has been done with postoperative adjuvant brachytherapy but may now be able to be done as a combination of brachytherapy and IMRT to reduce the risks of morbidity with re-irradiation.

Surgery Principles

Enneking classification of surgical procedures

- *Intralesional excision*—done inside pseudocapsule very high recurrence 100%—not used.
- *Marginal excision*—en bloc resections through the reactive zone—high recurrence rate 70%
- *Wide excision* means en bloc resection done through normal tissues beyond the reactive zone; it means if the margin is less than 5 cm; tumour is never visualised during surgery; it has local recurrence rate of 30%. Wide margin is classified as adequate if margin is at least beyond 1cm outside the reactive zone or inadequate if margin is within 1 cm.
- *Radical excision*—if the margin is more than 5 cm outside the reactive zone. It is like compartment excision with very low recurrence rate.

Other procedures

- Compartmental excision; function/limb sparing.
- Vascular resections with vascular reconstruction.
- Amputation.

Note:

Limb sparing; function preserving; margin free wide excision—is the new trend.

A thin barrier is considered to be a 2 cm thickness of normal tissue; a thick barrier is 3 cm thickness; and joint cartilage is said to be equivalent to a 5 cm thickness margin. A surgical margin that is outside a barrier, with normal tissue between the barrier and the reactive zone of the tumour, is considered to be curative.

- **Wide local excision** with clearance of 2 cm (minimum need is 1 cm) or more with preservation of function is needed. Depth clearance is also important. 3–5 cm clearance even though was practiced in olden days, is not necessary (Figs 1.583A to E).
- **Compartment resection** is a radical limb saving procedure. Here muscle group of one compartment (anterior, posterior or medial) is resected entirely from its origin to insertion with the tumour. It is done only when tumour is intracompartmental. It is not suitable when tumour is extracompartmental or many compartments are involved or encased to major neurovascular bundle.

  Basis for compartmental excision is—STS rarely penetrate anatomical barriers unless it is very advanced.
- Amputation is done in large tumours of upper or lower limbs.
  - *Radical amputation* is done as disease has not spread systemically which should be confirmed by CT chest, abdomen and pelvis. In metastatic disease there is no need to do amputation as long-term survival is not possible except if primary is fungating and distressing.

SYSTEMIC THERAPY AGENTS

SYSTEMIC THERAPY AGENTS AND REGIMENS WITH ACTIVITY IN SOFT TISSUE SARCOMA SUBTYPES (NON-SPECIFIC)[a,b,c]

Soft Tissue Sarcoma Subtypes with Non-Specific Histologies[d,e]		GIST	Desmoid Tumors (Aggressive fibromatosis)
Combination regimens • AD (doxorubicin, dacarbazine)[1-4] • AIM (doxorubicin, ifosfamide, mesna)[3-6] • MAID (mesna, doxorubicin, ifosfamide, dacarbazine)[3,4,7,8] • Ifosfamide, epirubicin, mesna[9] • Gemcitabine and docetaxel[10,11] • Gemcitabine and vinorelbine[f,12] • Gemcitabine and dacarbazine[13]	Single agents • Doxorubicin[3,4,14] • Ifosfamide[9,15] • Epirubicin[16] • Gemcitabine • Dacarbazine • Liposomal doxorubicin[17] • Temozolomide[f,18] • Vinorelbine[f,19] • Eribulin[f,g,20] • Trabectedin[f,h,21,22,23] • Pazopanib[f,24] • Regorafenib[i,25] • Larotrectinib[j,26] (for *NTRK* gene fusion-positive sarcomas) • Entrectinib[k,27] (for *NTRK* gene fusion-positive sarcomas)	• Imatinib[l,28,29] • Sunitinib[l,30] • Regorafenib[l,31] • Avapritinib[l,m,32] Disease progression after imatinib, sunitinib, and regorafenib • Sorafenib[33-35] • Nilotinib[36,37] • Dasatinib[38] (for patients with D842V mutation) • Pazopanib[39] • Everolimus + TKI[n,40] • Avapritinib[32]	• Sulindac[41] or other nonsteroidal anti-inflammatory drugs (NSAIDs), including celecoxib • Tamoxifen ± sulindac[42,43] • Toremifene[44] • Methotrexate and vinblastine[45] • Low-dose interferon[46] • Doxorubicin-based regimens[47-49] • Imatinib[50,51] • Sorafenib[52] • Methotrexate and vinorelbine[53] • Liposomal doxorubicin[54]

Non-Pleomorphic Rhabdomyosarcoma		
Combination regimens • Vincristine, dactinomycin, cyclophosphamide[55] • Vincristine, doxorubicin, cyclophosphamide[56] • Vincristine, doxorubicin, and cyclophosphamide alternating with ifosfamide and etoposide[57] • Vincristine, doxorubicin, ifosfamide[58] • Cyclophosphamide and topotecan[59,60] • Ifosfamide and doxorubicin[61]	• Ifosfamide and etoposide[62] • Irinotecan and vincristine[63,64] • Vincristine and dactinomycin[65] • Carboplatin and etoposide[66] • Vinorelbine and low-dose cyclophosphamide[f,67] • Vincristine, irinotecan, temozolomide[68]	Single agents • Doxorubicin[69] • Irinotecan[60,70] • Topotecan[71] • Vinorelbine[f,72] • High-dose methotrexate[o,73] • Trabectedin[f,21,22,23]

SYSTEMIC THERAPY AGENTS AND REGIMENS WITH ACTIVITY IN SOFT TISSUE SARCOMA[a,c]

Tenosynovial Giant Cell Tumor/Pigmented Villonodular Synovitis • Pexidartinib[74] (category 1) • Imatinib[75]	
Angiosarcoma • Paclitaxel[76,77] • Docetaxel[78] • Vinorelbine[f] • Sorafenib[79] • Sunitinib[80] • Bevacizumab[81] • All other systemic therapy options as per Soft Tissue Sarcoma Subtypes with Non-Specific Histologies (SARC-F 1 of 7)	Solitary Fibrous Tumor/Hemangiopericytoma • Bevacizumab and temozolomide[82] • Sunitinib[80,83] • Sorafenib[84] • Pazopanib[85]
Alveolar Soft Part Sarcoma (ASPS) • Sunitinib[86,87] (category 2B) • Pazopanib[88] • Pembrolizumab[89] (category 2B)	PEComa, Recurrent Angiomyolipoma, Lymphangioleiomyomatosis • Sirolimus[90-93] • Everolimus[94] • Temsirolimus[95,96]
Inflammatory Myofibroblastic Tumor (IMT) with Anaplastic Lymphoma Kinase (ALK) Translocation • Crizotinib[97] • Ceritinib[98]	
Well-Differentiated/Dedifferentiated Liposarcoma (WD-DDLS) for Retroperitoneal Sarcomas[p] • Palbociclib[99,100]	
UPS[q] • Pembrolizumab (category 2B)[101]	

Radiotherapy for STS

Modalities – EBRT
Brachytherapy < LDR (Low dose rate)
HDR (High dose rate)
IORT (Intra-op)

- **Preoperative RT**
  - 50 Gy external-beam RT (EBRT)[4] (surgery with clips to follow)
  - Following preoperative 50 Gy EBRT and surgery, for positive margins, consider observation or RT boost
  - If using RT boost, consider:[6,7]
    - ◊ EBRT:
      - – 16–18 Gy for microscopic residual disease[5,8]
      - – 20–26 Gy for gross residual disease[5]
    - ◊ Brachytherapy (low-dose rate):
      - – 16–18 Gy for microscopic residual disease
      - – 20–26 Gy for gross disease
    - ◊ Brachytherapy (high-dose rate):
      - – 14–16 Gy at approximately 3–4 Gy BID for microscopic residual disease
      - – 18–24 Gy for gross residual disease
    - ◊ IORT:
      - – 10–12.5 Gy for microscopic residual disease
      - – 15 Gy for gross residual disease

- Postoperative RT following surgery[5] with clips
  - EBRT (50 Gy) + EBRT boost[4,6]
    - ◊ Boost Dose
      - – Negative margins: 10–16 Gy
      - – Microscopically positive margins: 16–18 Gy[5,8]
      - – Gross residual disease: 20–26 Gy[5]
  - IORT (10–16 Gy) + EBRT (50 Gy)[4,6]
  - Brachytherapy ± EBRT
    - ◊ Positive margins:[5]
      - – Low-dose-rate (16–20 Gy) or high-dose-rate equivalent (14–16 Gy) brachytherapy + 50 Gy EBRT[6]
    - ◊ Negative margins:[5]
      - – 45 Gy low-dose-rate or high-dose-rate equivalent (ie, 36 Gy in 3.6 Gy BID over 10 fractions in 5 days)[6] brachytherapy

- Potential benefits of preoperative radiation therapy:
  - Lower total radiation dose
  - Shorter course of treatment
  - Treatment field size is frequently smaller
    - ◊ Associated with less late radiation toxicity and improved extremity function
  - The primary sarcoma is a defined target for radiation treatment planning
  - Treatment delivery not impacted by postoperative wound healing issues
  - Potential downstaging of borderline resectable extremity sarcomas for possible limb salvage
  - Ability to restage patients after preoperative radiation but before wide resection
    - ◊ Distant metastases would prevent a noncurative surgery

Dermatofibrosarcoma Protuberans

- Low grade sarcoma arising in DERMIS
- Local recurrence ↑↑
- Metastasis VERY rare
- M/c site - Trunk (40%) > Extremities > H&N
- Large lesions are a/i satellite nodules
- CD 34 ⊕
- Nodular cutaneous mass
- Rx - WLE ± special attention to radial margins

  Imatinib ?

DESMOIDS

- Low grade locally aggressive tumors
- Do not metastasize
- Extremeties > Trunk > RP
- Abd wall desmoids - Pregnancy - Hormonal
- FAP + Desmoids - Gardner
- Sporadic CTNNB-1 - β catenin
- WLE, RT (50-54Gy)
- ? Tamoxifen
- MTx + Vinblastin / Peg Liposomal doxorubicin
- Sorafenib
- ? Imatinib
- Recurrence seems to be independent of quality of surgical margins

HODGKIN'S LYMPHOMA

Hodgkin Disease is a hematological malignancy arising from mature B cells.

EPIDEMIOLOGY:

- Bimodal age distribution — 1st peak - 20s → Nodular sclerosis type
  2nd peak - 50s → Mixed cellularity, lymphocyte depleted
- M > F : Nodular sclerosis type - slight female preponderance
  ↳ 85%
- EBV association
- HIV infection - Risk factor
  ↳ constitutional symptoms, advanced stage
  unusual sites - marrow, skin, leptomeninges

TYPES:

2017 WHO classification of lymphoid tumors

HODGKIN'S LYMPHOMA (HL)

CLASSICAL HL (95%)

1) Nodular Sclerosis
2) Mixed Cellularity
3) Lymphocyte rich
4) Lymphocyte depleted

Reed-Sternberg cell

↓

Pattern is diffuse, interfollicular, nodular

Fibrosis common

EBV infection ⊕ (variable)

CD 15 ⊕	CD 20 ⊖
CD 30 ⊕	CD 45 ⊖
PAX-5 ⊕	

Background cells: (Non neoplastic)
Lymphocytes
Eosinophils
Plasma cells
Polymorphonuclear cells

NODULAR LYMPHOCYTE PREDOMINANT HL (5%) (NLPHL)

Pattern A: Typical, B-cell rich, nodular
B: Serpiginous nodular
C: Nodular & predominant extranodular LP cells
D: T-cell rich nodular
E: T-cell, Histiocyte rich - Large B cell lymphoma like
F: Diffuse B cell rich

RS-LP (Lymphocyte predominant) cell / POPCORN CELL
↓ ↓
Pattern is nodular L&H cells (Lymphocyte, Histiocyte)

Fibrosis Rare

EBV infection ⊖

CD 15 ⊖	CD 20 ⊕
CD 30 ⊖	CD 45 ⊕

of the RS cells

Background cells - lymphocytes only

BEST PROGNOSIS

CLASSICAL HODGKIN'S LYMPHOMA

NODULAR SCLEROSIS	MIXED CELLULARITY	LYMPHOCYTE RICH	LYMPHOCYTE DEPLETED
Most common (70%)	2nd m/c (20-25%) m/c in India	5%	<5%
· Lacunar cells – RS variant · Nodules · Collagen bands	· RS cells ++ · Mixed inflammatory background	RS cells scattered in background of small lymphocytes	· RS predominant · depleted on non-neoplastic BG lymphocytes
Females > Males	HIV/AIDs association	Older males	· Liver & marrow involved · Relative sparing of peripheral nodes
· Mediastinal masses · Peripheral nodes	· Retroperitoneal mass (+)	· Localised to peripheral nodes	Strongest a/i HIV/AIDs
<10% EBV (+)	70-90% EBV (+)	~40% EBV	>90% EBV
2ND BEST PROGNOSIS	GOOD PROGNOSIS	· FEWER RELAPSES EXCELLENT PROGNOSIS	· AGGRESSIVE COURSE · WORST PROGNOSIS

TYPES OF RS cells

1) Popcorn - NLPHL
2) Lacunar - NS-HL
3) Pleomorphic - LD-HL
4) Mononuclear - any HL

MODE OF SPREAD

1) HL almost always originates in a LYMPHNODE

   Whenever a primary diagnosis of HL is made in an extranodal site WITHOUT CONTIGUOUS NODAL INVOLVEMENT, THE DIAGNOSIS SHOULD BE HIGHLY SUSPECTED WITH THE EXCEPTION OF HIV(+) INDIVIDUALS

2) HL spreads in an ORDERLY FASHION through the lymphatic system by CONTIGUITY

   Histological variants other than NS often skip MEDIASTINUM & disease appears in neck & abdomen

3) AXIAL LYMPHATIC SYSTEM >> DISTAL SITES (Epitrochlear / Popliteal)

4) Hematogenous dissemination occurs late in the course
   → characteristic of LD subtype

SITES OF INVOLVEMENT

1) PERIPHERAL NODES

- Cervical / Supraclavicular lymphadenopathy > 70% (Level IV & V)
  - (L) Supraclavicular ⇒ Abdominal involvement (spleen)
- Axillary & inguinal nodes - less frequently involved
- Waldeyer ring / extranodal lymphoid tissue seldom involved

2) THORAX

MEDIASTINUM (ANTERIOR) > HILAR → Contiguity → Lung involvement
Hematogenous ↗

Pleural effusion, SVC S° (↓↓)

3) ABDOMEN

- Spleen, splenic hilar nodes, celiac nodes → easiest abdominal sites of involvement in infradiaphragmatic HL
  - 25% of clinically not-enlarged spleens harbor occult HL
- Liver - involved only after spleen

4) RETROPERITONEUM

Supradiaphragmatic HL → late involvement of RP

Inguinal presentation of HL → early RP involvement

5) BONE MARROW

↳ involvement rare at the time of diagnosis

↑ RISK OF BONE MARROW INVOLVEMENT

- Advanced stage disease
- Systemic symptoms
- Mixed Cellularity / Lymphocyte Depleted histology

↓ BONE MARROW BIOPSY > Aspirate

6) BONE - Osseous involvement - OSTEOBLASTIC REACTION

7) OTHER EXTRANODAL SITES

- Very rare in HL
- if present ⇒ advanced disease

STAGING

ANN-ARBOR STAGING - COTSWOLD MODIFICATION

Stage I : INVOLVEMENT OF SINGLE LYMPHNODE REGION / LYMPHOID STRUCTURE

Stage II : INVOLVEMENT OF ≥ 2 LYMPHNODE REGIONS ON SAME SIDE OF DIAPHRAGM

Stage III : INVOLVEMENT OF LYMPHNODE REGIONS ON BOTH SIDES OF DIAPHRAGM

- Stage III 1: Splenic / hilar / celiac / Portal nodes
- Stage III 2: Para-aortic / Iliac / Mesenteric nodes

Stage IV : INVOLVEMENT OF ≥ 1 EXTRANODAL SITE IN ADDITION TO THE SITE FOR WHICH DESIGNATION 'E' WAS USED

DESIGNATIONS

A : No symptoms

B : Fever (>38°C)
Night Sweats
> 10% weight loss ≤ 6 months

X : Bulky disease [Nodal mass > 10cm
Mediastinal mass > 1/3rd Transverse diameter of chest]

E : Involvement of single extranodal site contiguous / proximal to a known nodal site

PROGNOSTIC FACTORS

Adverse prognostic factors

1) Age ≥ 45y
2) Male gender
3) Stage IV disease
4) Anemia (Hb < 10.5g%)
5) TLC > 15,000/μL
6) Lymphocyte count < 8% of TLC
   < 600/μL
7) Serum albumin < 4g/dL
8) Eosinophilia, Lymphocyte depletion, RS cell atypia

[EVALUATION - COMMON TO ALL LYMPHOMAS - REFER NOTES]

CLINICAL FEATURES

- Painless lymphadenopathy
- Systemic symptoms: Fever, night sweats, weight loss
  - → PEL-EBSTEIN FEVER
  - Pruritus
- Pain - Alcohol-induced pain - infrequent but characteristic
  Bone pain, neurogenic pain, back pain

MANAGEMENT

- Surgery - limited to Dx - biopsy in most cases

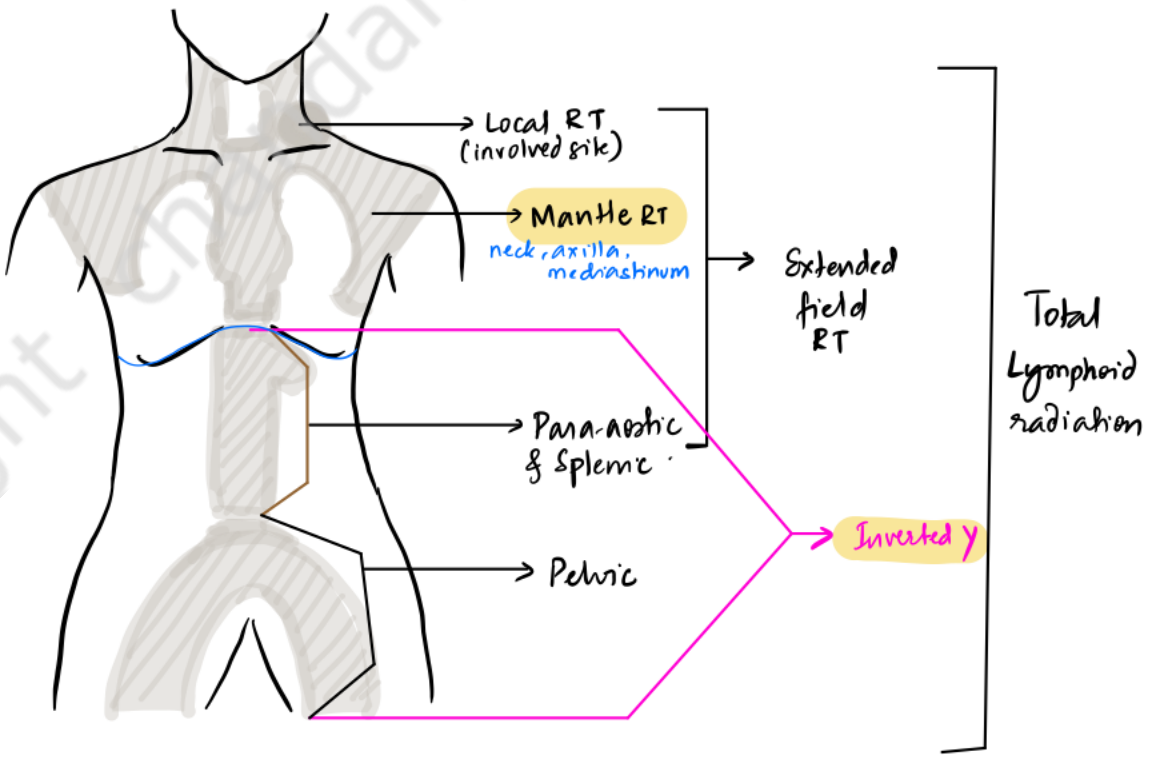
  in the past - staging laparotomy was done - now superceded by non-invasive staging investigations

  ROLE OF SPLENECTOMY
  - occasionally exists for 1) Symptomatic splenomegaly
    2) Thrombocytopenia & Leukopenia (Hypersplenism features) which result in chemotherapy delays

- RT - Early stage HL - Predominantly RT - 30-40Gy

Newer modalities of RT

1) IFRT → Involved field RT
2) ISRT → Involved site RT
3) INRT → Involved node RT



- Chemotherapy

ABVD - Adriamycin (DOXORUBICIN) Bleomycin Vinblastine Dacarbazine
EBVP - Epirubicin Bleomycin Vinblastine Prednisone
MOPP - Mechlorethamine, Oncovin (Vincristine), Procarbazine, Prednisone
COPP - Cyclophosphamide, Oncovin (Vincristine), Procarbazine, Prednisone
MOPP-ABV -
BEACOPP - Bleomycin, Etoposide, Doxorubicin, Cyclophosphamide, Oncovin, Procarbazine, Prednisone

NON HODGKIN'S LYMPHOMA

Non Hodgkin's Lymphomas are neoplastic transformations of B-cells, T-cells & NK cells

Epidemiology

1) Incidence 8x that of HL

2) Age
   - SLL → elderly
     - ↳ (tissue/nodal counterpart of CLL)
   - Lymphoblastic lymphoma - male adolescents, young adults
   - Follicular lymphoma - middle age
   - Burkitt lymphoma - young age

3) Infectious agents a/i NHL
   - RNA viruses - HTLV-1 → Adult T cell leukemia - lymphoma
     - HIV → High grade B cell lymphomas
     - HCV → Indolent B cell lymphoma
   - DNA virus - EBV - Burkitt Lymphoma
     - Nasal T cell lymphoma
     - NK cell lymphoma
   - H. pylori → Gastric lymphoma

4) Immunodeficiency
   - AIDS
   - Organ transplant recepients
   - Congenital immunodeficiencies - Agammaglobulinemia
     - Ataxia telangectasia
     - Wiskott Aldrich Syndrome
   - Autoimmune disorders - Sjögren's Syndrome
     - RA
     - SLE
     - Hashimoto thyroiditis

5)
   - Phenytoin
   - Toxins

WHO / REAL CLASSIFICATION OF NHL

PRECURSOR B AND T CELL NEOPLASMS

1) Precursor B lymphoblastic Leukemia / lymphoma
2) Precursor T lymphoblastic Leukemia / lymphoma

MATURE B CELL NEOPLASMS

1) CLL / SLL
2) B cell prolymphocytic leukemia
3) Mantle cell lymphoma
4) Marginal zone lymphoma
   - MALT
   - Nodal
   - Splenic
5) Burkitt lymphoma
6) Follicular lymphoma
7) DLBCL
8) Hairy cell leukemia
9) Plasmacell neoplasms
   - Multiple Myeloma
   - Plasmacytoma
   - MGUS

MATURE T & NK CELL NEOPLASMS

1) T-ALL
2) T-cell large granular lymphocytic leukemia
3) Cutaneous T cell lymphoma
4) Mycosis fungoides
5) Extranodal NK / T cell lymphoma
6) Anaplastic large cell lymphoma

POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDERS (PTLD)

1) Plasmacytic hyperplasia
2) Polymorphic PTLD
3) Monomorphic PTLD

WORKING FORMULATION CLASSIFICATION

LOW GRADE

- Small lymphocytic
- Follicular - small cleaved cell
- Follicular - mixed - small cleaved + large cell

INTERMEDIATE GRADE

- Follicular - large cell
- Diffuse
  - Small cleaved
  - Mixed
  - Large cell

HIGH GRADE

- Large cell immunoblastic (B / T cell)
- Lymphoblastic
- small - non cleaved (Burkitt / Non-Burkitt)

RAPPAPORT CLASSIFICATION

Architectural pattern

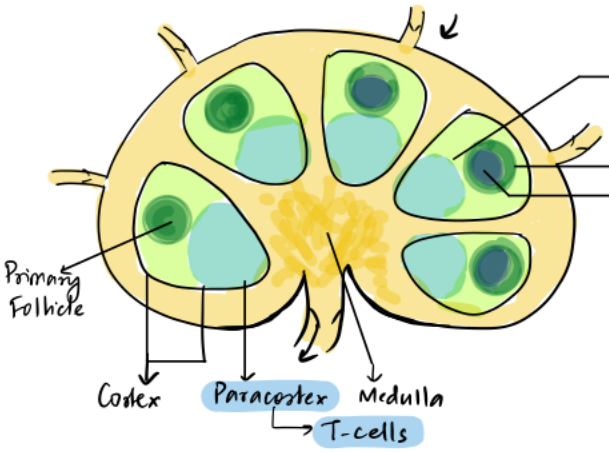
NODULAR

- lymphocytic (small cell)
- Histiocytic (large cell)

DIFFUSE

- lymphocytic (small cell)
- Histiocytic (large cell)

LYMPHNODE



Naive B cell

Marginal zone - Post GC B-cell
- Marginal cell lymphoma
- Hairy cell leukemia

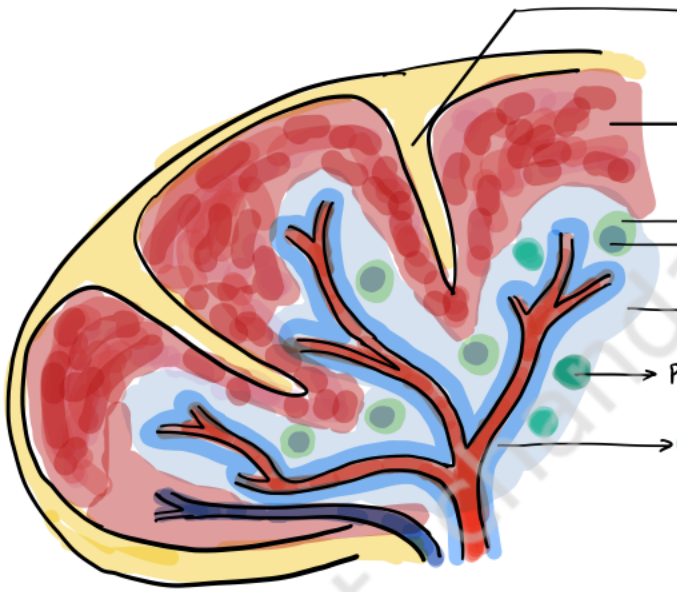
Secondary follicle
- Mantle zone (Mantle cell lymphoma)
- Germinal centre (GC)
  - Centroblasts (Burkitt)
    - Immunoblasts (DLBCL)
    - centrocytes (Follicular lymphoma)

Memory B cell

Circulating B cell
- CLL

BONE MARROW
- Plasma cell → Multiple Myeloma

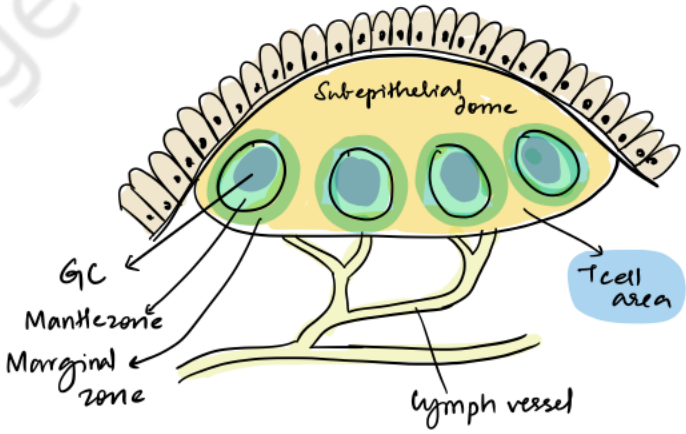
SPLEEN



- trabeculae
- RED PULP : sinusoids
- Mantle zone, Germinal centre → Secondary follicle
- Marginal zone
- Primary follicle
- Periarteriolar lymphoid sheath (PALS) → Tcells

→ White pulp

MUCOSA ASSOCIATED LYMPHOID TISSUE

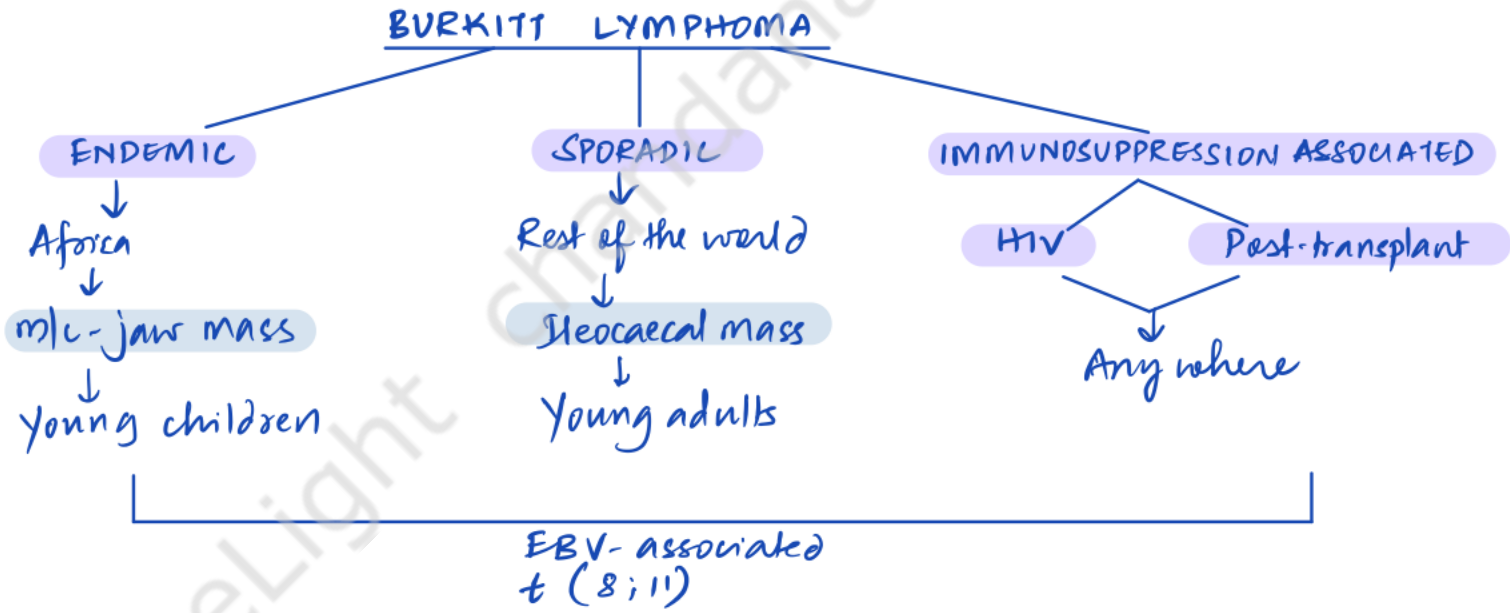


MALTomas - group of extranodal lymphomas that arise in the parafollicular or marginal zone cells that surround the mantle zone (B cell)

- Often follow a pre-existing organ-associated autoimmune disease
  - SJÖGREN SO (LACRIMAL/ PAROTID)
  - HASHIMOTO THYROIDITIS
- Gastric MALTOma - H. pylori infection → m/c MALTOma
  2/3rds of cases - regress after H. Pylori eradication

DLBCL
- AIDs related NHLs
- PTLD
- Primary effusion Lymphoma

Breast implants - Anaplastic Large cell lymphoma



℞ 1) Cyclophosphamide - monotherapy for endemic Burkitt

2) Hyper CVAD ± Rituximab

3) 2 (CODOX-M) + 2(IVAC)

GENERAL APPROACH TO LYMPHOMAS

History

1) painless lymphadenopathy

2) Systemic symptoms - 'B' symptoms

Pruritus & Pel Ebstein fever → HL

3) pain - alcohol induced pain → HL

abdominal pain - splenomegaly
Bowel involvement / adenopathy
Hydronephrosis d/t external compression

Bone pain - Marrow infiltration

Neurogenic pain - Myelopathy / Plexopathy / Radiculopathy
Meningeal involvement
Varicella reactivation → Herpes Zoster

Examination

Lymphnodes -

regions involved - contiguous (HL) / non contiguous (NHL)
number
consistency - rubbery

Tonsils & Oropharynx - Waldeyer's ring - NHL

Splenomegaly

Hepatomegaly

Effusions

Retroperitoneal nodes

CLINICAL EVALUATION

1) Complete hemogram & peripheral smear

Diagnostically abnormal circulating lymphoid cells

↳ Flow cytometry - immunological study

Monoclonality by κ:λ ratios / gene rearrangement

2) ↑ Acute phase reactants

↑ ESR
↑ Fibrinogen
↑ Haptoglobulin

↑ S. Copper

3) LFT

HL → Paraneoplastic s/o - Cholestatic picture - ↑ ALP

Porta hepatis lymphoma - Obstructive jaundice

4) LDH - tumor bulk & turnover → ↑ → poor prognosis

5) S. immunoglobulins - Polyclonal hypergammaglobulinemia (HL + NHL)

Monoclonal spikes → NHL

6) RFT

↑ BUN / Creat → Hydronephosis

Direct renal involvement

Tumor lysis syndrome → Uric acid nephropathy → aggressive NHLs
Hypercalcemia → aggressive NHLs

↓

Renal insufficiency

HL → Paraneoplastic s/o → Nephrotic s/o

BIOPSY PROCEDURES (Surgeon's role in lymphoma; apart from splenectomy)

Biopsy > FNAC

- Biopsy → better for characterisation
- FNAC → Only for
  - Staging evaluation
  - Proving recurrence

1) Peripheral node biopsy - Largest accessible node is excised or sampled
   - Inguinal nodes - generally affected by chronic inflammation
     - chosen ONLY if no other site available or involvement is clearly anticipated

2) Bone marrow biopsy - in abnormal circulating cells / cytopenias

3) Mediastinoscopy / Limited thoracotomy - for mediastinal masses

4) Laparoscopy / Laparotomy - Random biopsy / Staging

5) Endoscopic gastric biopsy - H. Pylori, MALTOMA

6) Retroperitoneal mass - Image guided tru-cut

7) Thoracocentesis + Pleural biopsy

SPECIMEN HANDLING

1) Touch preparation
2) Immunologic phenotyping - Flow cytometry, IHC
3) Cytogenetics / Molecular analysis

IMAGING

1) CXR - mediastinal / hilar lymphadenopathy
- pleural effusions
- parenchymal lesions

2) CT - chest

3) USG Abdomen - too insensitive to pick up abdominal lymphadenopathy
→ may help characterise liver / spleen lesions - solid vs cystic

4) CT / MRI abdomen - intraabdominal nodes, splenomegaly, liver & other visceral lesions

5) Upper GI scopes, endoscopies in NHL - especially Marginal zone & mantle cell lymphomas

6) CNS evaluation

Burkitt lymphoma } - CSF tap to s/o meningeal involvement
Lymphoblastic lymphoma
AIDS related lymphoma
High grade lymphoma involving testes / PNS
→ CT / MRI brain

7) Nuclear imaging

18 FDG PET > Gallium scan - extent of disease

Characteristic	HODGKIN LYMPHOMA	NON-HODGKIN LYMPHOMA
ORIGIN	Malignancy of proliferating germinal centre cell (B-cell)	Monoclonal proliferation of B/T lymphocytes
NEOPLASTIC CELL	Reed Sternberg cell or its variants	B/T-cells in various stages of maturation
INCIDENCE	Less common	More common
AGE	BIMODAL MEDIAN AGE ~30y - Younger	Older
SITE OF ORIGIN	Nodal	Extranodal (10-35%)
NODAL DISTRIBUTION	Axial	Extra-axial - epitrochlear nodes - mesenteric nodes Generalised
NODAL SPREAD	Contiguous	Non-contiguous
CNS INVOLVEMENT	<1%	Upto 10%
HEPATIC INVOLVEMENT	Uncommon	Common (>50%)
BONE MARROW INVOLVEMENT	Uncommon (<10%)	Common (>50%)
MANAGEMENT	• RADIATION FOR LOCALISED DISEASE • CHEMO/CT+RT for advanced disease	Radiation + Chemotherapy
OVERALL PROGNOSIS	FAVORABLE ~80% of patients i HL are cured by regimens using conventional and salvage strategies	UNFAVORABLE <50% are cured by Rx

CANCER RADIOTHERAPY

RADIOTHERAPY

A modality for locoregional tumor control which utilizes ionizing radiation.

TYPES OF RADIATION USED CLINICALLY

PHOTONS
- Electromagnetic waves
  - X-Rays → Generated by LINAC → Bremsstrahlung X-Rays
  - γ-Rays → Emitted by radioactive isotopes (collimated) Eg: COBALT 60

ELECTRONS

β rays (e^-)
- dissipate their energy rapidly as they enter tissue.
- Relatively short depth of penetration
- used for superficial lesions

OTHERS
- Protons - 'Bragg peak'
- Neutrons - ↑ LET, ↓ OER
- Heavy ions - ↑ LET, ↓ OER, Bragg peak (Carbon anions)

'Relative Biologic Effectiveness' (RBE)
'Linear energy transfer' (LET)
'Oxygen Enhancement Ratio' (OER)'

- **Linear Energy transfer**: Rate of energy lost by the beam per length of path traversed

  Heavy ions → ↑ LET - densely ionising
  Photons, electrons → ↓ LET - sparsely ionising

- **Relative biologic effectiveness** - ratio of doses needed to produce same biologic endpoint between a std ↓ LET photon beam (250 keV xray) & another radiation of different LET

  ↑ LET ⇒ ↑ RBE up to 100 keV/μ → after this RBE ↓ due to wastage of further transfer

- **Oxygen enhancement Ratio**:

  Radiation → O_2 → Oxygen free radicals → Cytotoxic
  ↓ LET → ↑ dose of rays for cellular damage → ↑ OER

- **Bragg peak**: a peak on the Bragg curve (plot energy loss of ionizing radiation during its travel through matter

  Eg: For protons / α-rays - Bragg peak occurs immediately before the particles come to rest

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Mechanisms of cellular damage

INDIRECT ACTION
↓
Generation of hydroxyl radicals from water
↓
Hydrolysis of chemical bonds in DNA

DIRECT ACTION
↓
Breakage of chemical bonds by direct deposition of radiation energy
- Base damages
- cross-links
- single-strand / Double-strand breaks

Lethality

Mitotic death - loss of reproductive integrity
Interphase death
Apoptosis

Models
LQ - linear quadratic
SHMT - Single Hit Multi Target

FRACTIONATION

- Division of the total radiation dose into smaller fractions in order to balance tumor control and normal tissue damage

fractions → 1.8 - 2.25 Gy/d

Fractionation Radiobiology - 4 'R's

REOXYGENATION

Radiation damage d/t hydroxyl radicals depends on the availability of O_2 molecules in close proximity

Fractionation allows O_2 to diffuse into the usually hypoxic center of an expanding tumor during the interval between fractions

↓

Enables more tumor-cell killing during subsequent treatments

REPOPULATION

Repopulation by mitotic growth in the interval between fractions

- Normal tissue → Recovery
- TUMOUR TISSUE → accelerated repopulation in acute-responding cells

fast dividing cells which express acute effects of irradiation

REPAIR

Initial part of radiation damage can be repaired by cell machinery

↓

SUBLETHAL DAMAGE REPAIR (SLD)

Decreasing fraction dose to allow for complete SLD repair

↓

↑ in total dose of radiation required.

Late responding tissues show higher SLD repair capacity

REDISTRIBUTION

Cells exhibit differential sensitivities towards RT at different phases of cell cycle

Sensitivity ↑ at G_2-M junction

Resistant at 'S' phase

Fractionation allows more cells to enter sensitive phase

Fast cycling cells (Mucosa, tumors) are more prone to RT Killing than slow / dormant cells (Connective tissue)

Conventional Fractionation scheme - 1.8-2 Gy / fraction to the total dose

ALTERED FRACTIONATION SCHEMES

HYPERFRACTIONATION

Total dose : same / ↑
Dose / fraction : ↓
Number of fractions : ↑
Overall time : same

↓ dose / fraction → reduces late effects

↑ Total dose - ↑ tumor kill

Local control - better
Acute toxicity - ↑
Late toxicity - ↓

ACCELERATED FRACTIONATION

Total dose : ↓
Dose / fraction : ↓ / same
Number of fractions - same
Interval between fractions is REDUCED

↓

Overall treatment time ↓

Reduced interval - ↓ tumor repopulation
↑ acute toxicity

↓ Dose / fraction - ↓ late effects

HYPOFRACTIONATION / SINGLE DOSE

Total dose : ↓
DOSE / FRACTION : ↑
Number of fractions : ↓
Overall time : ↓

Reduced interval - ↓ tumor repopulation
↑ Late toxicity

↓ Dose → ↓ local control
↓ acute toxicity

Generally used for palliation in poor PS
Not good for slow-responding tissues

MODES OF RADIATION DELIVERY

EXTERNAL BEAM RADIOTHERAPY (Teletherapy)

- **PRECISION ORIENTED RT** - Computerized planning & delivery

1) **CONFORMAL RT** → dose coverage conforms to the target volume in a 3-D fashion (3D-CRT)

2) **IMRT - Intensity modulated RT:**
Photon beam intensity can be modulated to deliver specific doses to irregular shaped target volumes while sparing organs at risk
Can be used to deliver tumor bed boost
IMRT
- Fixed field approach
- VMAT (Volumetric modulated arc therapy)

3) **Particle therapy - Eg: PROTON BEAM THERAPY**
- utilizes the principle of Bragg Peak to deliver RT precisely to the desired location

4) **STEREOTACTIC IRRADIATION** - utilises 3D coordinate system

Stereotactic Radiosurgery (SRS)	Stereotactic Radiotherapy (SRT)	Stereotactic Body RT (SBRT) or Stereotactic Ablative Body RT (SABR)
↓	↓	↓
'Gammaknife'	Stereotactic principles + Conventional fractionation	Stereotactic principles + HYPOFRACTIONATION
For CNS tumors	for larger lesions	↓
		for extra CNS lesions (lung, liver, prostate)

- **FUNCTIONAL IMAGE GUIDED RT** - PET / MR Spectroscopy + IMRT / PBT

- **IGRT - Image Guided RT** - precise tracing of RT target in order to compensate for daily setup & motion uncertainties both inter & intra fractionated sessions
(target lesion moves day to day through long RT course)
uses technologies like 'On board imaging'
'Fiducial marker seeds'
'Respiratory gating'

- **ADAPTIVE RT** - uses daily dynamic image verifications to map the changes in tumor bulk during RT

BRACHYTHERAPY

Radioactive sources are inserted into the tumor bearing area

Eg:
1) Interstitial [Embedded in soft tissue]
2) Intraluminal [Eg: Esophagus / tracheal / rectum]
3) Intracavitary [Eg: Vaginal vault]

RADIOISOTOPES USED
Ir-192, I-125, Pd-103, Cs-137, Sr-90, Co-60, Au-198 [Historically, Ra-226]

Based on rate of dose delivery, these are 2 types of Brachytherapy

LOW DOSE RATE (LDR)	HIGH DOSE RATE (HDR)
• Permanent implants	Exclusively via temporary implants
↓	↓
LDR source seeds inserted manually via needle implant	Afterloading done using an electronically controlled unit
↓	↓
Radioactivity spontaneously decays	Single highly Radioactive source within a shielded container
• Temporary implants - Afterloading technique - Hollow catheters → source seeds are loaded	

RADIATION UNITS

Units of RADIOACTIVITY

- Curie (Ci)
- Becquerel (Bq)

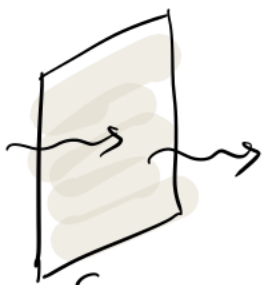
1 Ci = Radioactivity of 1g of Ra 226
= 3.7×10^{10} decays/s

1 Bq = 1 decay/second
= 2.703×10^{-11} Ci

Units of Radiation Exposure

- Roentgen (R)
- Coulomb/Kg

1 Roentgen
= 2.58×10^{-4} C/kg



Units of Absorbed dose (Depends on tissue)

- Rad
- Gray (Gy) → SI unit

1 Gy = 100 Rad

1 Gy = 1 Joule/Kg

Units of Equivalent dose

- Rem
- Sievert

= absorbed dose × weighting factor

X-Ray, γ-Ray → 1

α → 20

1 Sievert = 100 Rem
↓
SI unit

SIDE EFFECTS OF RADIOTHERAPY

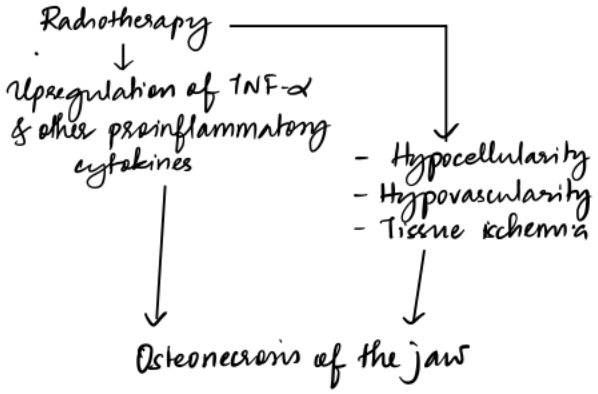
(H&N)

→ Acute, self limiting effects:

- Erythema of skin
- Conjunctivitis
- Mucositis
- Epilation
- Edema
- Rhemitis
- Dysgeusia
- Xerostomia
- Infection - Oral Candidiasis

Long term: Xerostomia
Dysgeusia
Cataract
OSTEORADIONECROSIS
Cervical myelopathy
2ND Malignancies

OSTEORADIONECROSIS



→ Seen in total dose to bone >65Gy

- usually reported following tooth extractions not timed to allow extraction site healing 10-14d before starting RT

- Correlates strongly ↑ Bisphosphonate use, Denosumab use

℞ - pentoxifylline

Antioxidants - Tocopherol

TABLE 129.2

Formulary of Common Treatments for Oral Complications of Cancer Therapya

	Instructions
Prevention of Oral Mucositis	
Amifostine	200 mg/m^2 daily, as 3-min IV infusion 15–30 min before radiation therapy. Hydrate adequately, monitor blood pressure, and use antiemetics.
Cryotherapy Distilled water, 1 gallon	Place ice chips in mouth for 30 min beginning 5 min prior to bolus administration of chemotherapy.
$NAHCO_3$ powder, 3 tablespoons or 11.6 g	Rinse mouth twice a day for 30 s. Do not swallow.
NaCl powder, 3 tablespoons or 11.6 g	Combine all ingredients. Rinse mouth 2–4 times daily. Do not swallow.
Povidone-iodine 0.5% oral rinse	Rinse mouth 2–4 times daily. Do not swallow.
Treatment of Oral Mucositis–Related Pain	
Carafate suspension, 1 g	Rinse mouth 4 times daily. Do not swallow.
Diphenhydramine (Benadryl; McNEIL-PPC, Inc., Fort Washington, PA), 12.5 mg/5 mL; kaolin and pectin (Kaopectate; Chattem, Inc., Chattanooga, TN)	Use equal amounts of each. Rinse mouth with 10–15 mL 4–6 times daily. Do not swallow.
Diphenhydramine (Benadryl), 12.5 mg/5 mL: 30 mL; Maalox (Novartis, Basel, Switzerland), 30 mL; nystatin, 100,000 U/mL: 30 mL	Combine all ingredients. Rinse mouth with 15 mL 4–6 times per day. Do not swallow.
Diphenhydramine (Benadryl), 12.5 mg/5 mL: 30 mL; viscous lidocaine (Xylocaine) 2%, 30 mL; Maalox, 30 mL	Combine all ingredients. Rinse mouth with 15 mL 4–6 times per day. Do not swallow.
Diphenhydramine (Benadryl), 12.5 mg/5 mL: 30 mL; tetracycline, 125 mg/5 mL suspension: 60 mL; nystatin oral suspension, 100,000 U/mL: 45 mL; viscous lidocaine (Xylocaine) 2%, 30 mL; hydrocortisone suspension, 10 mg/5 mL: 30 mL; sterile water for irrigation, 45 mL	Combine all ingredients. Rinse mouth with 15 mL 4–6 times per day. Do not swallow.
Dyclonine hydrochloride 0.5% or 1.0% solution	Rinse mouth with 10–15 mL every 2–3 h. Do not swallow.
Gelclair (Sinclair Pharmaceuticals, Surrey, England)	Mix 1 Gelclair packet per manufacturer's directions with 40 mL or 3 tablespoons of water. Stir and rinse immediately for at least 1 min, gargle, and spit out at least 3 times a day.
Opiates	Oral, transdermal, or parenteral opiates may be used, such as PCA. Use tablet form of oral analgesics. Do not use elixir because alcohol exacerbates oral mucositis.
Viscous lidocaine (Xylocaine) 2% solution	Rinse mouth with 10–15 mL every 2–3 h. Do not swallow.
Xerostomia	
Biotene chewing gum (GlaxoSmithKline, Brentford, England)	Use as needed.
Pilocarpine	5 mg oral 3 times a day

↳ from De Vita

- Bailey & Love 27E, Sabiston 20E

TISSUE ENGINEERING REQUIRES
- Cells
- Scaffolding

Basic idea - cells are isolated and cultured invitro - placed on scaffolds & introduced into the body

Cells used for Tissue engineering
May be → Autologous / Allogenic

Somatic cells (mature cells)
- Epithelial cells
- Chondrocytes
- Smooth muscle cells
- Uroepithelial cells

Stem cells
- Somatic stem cells (SSCs)
- Human embryonic stem cells (ESCs)
- Fetal cells
- induced pluripotent stem cells

Somatic stem cells (SSCs) → **Multipotent** cells which can differentiate into a LIMITED variety of specialized cells
- Hematopoietic stem cells
- Mesenchymal stromal cells
- Endothelial Progenitor cells
- Neural stem cells
- Follicular bulge skin stem cells

→ Most widely used for tissue engineering

Human embryonic stem cells (ESCs) → **Totipotent** cells from inner cell mass of embryo 4-5 d post IVF

ESCs are allogenic - can be rejected

Autologous → donor somatic cell nuclear transfer → enucleate recipient oocyte → cell culture → SCNT → just like 'Dolly'

Fetal cells → **Pluripotent** cells - from blood, bone marrow etc of aborted fetus

induced pluripotent stem cells → **Pluripotent** → induced by lentiviral or retroviral transfection → Expression of specific transcription factors

In vitro differentiation of stem cells to mature cells - Activin, BMP-4, FGF-2

TABLE 7-1 Definitions of Stem Cell–Related Terms

TERM	DEFINITION
Totipotent	Ability to form all cell types and lineages of organism (e.g., fertilized egg)
Pluripotent	Ability to form all lineages of the body (e.g., embryonic stem cells)
Multipotent	Ability of adult stem cells to form multiple cell types of one lineage (e.g., mesenchymal stem cells)
Unipotent	Cells form one cell type (e.g., follicular bulge skin stem cells)
Reprogramming	Dedifferentiation into an embryonic state; can be induced by nuclear transfer, genetic manipulation, viral transduction, and related methods

Sabiston 20E

Transcription factors a/i induced Pluripotent SCs

Oct 4
Sox-2
Klf-4
c-myc

} can reprogram fibroblasts to become pluripotent

TABLE 7-2 Reported Clinical Applications of Stem Cells

CLINICAL APPLICATION	CELL TYPE	DELIVERY METHOD
Inflammatory bowel disease (Crohn's disease)[a]	ASC → Adipose derived stem cell	Surgical implantation into perianal fistulas
Muscular dystrophy[b]	Muscle-derived progenitors, CD133+	Local injection
Ischemic cardiomyopathy (MAGNUM Trial)[c]	BM MSC	Surgically implanted three-dimensional collagen matrix
Acute myocardial infarction (BOOST Trial)[d]	Total BM	Intracoronary injection
Acute myocardial infarction (REPAIR-AMI Trial)[e]	Total BM	Intracoronary injection
Acute myocardial infarction (ASTAMI Trial)[f]	BM MNC	Intracoronary injection
Ischemic cardiomyopathy[g]	Total BM	Systemic injection
Tracheobronchomalacia[h]	BM MSC	Differentiated to chondrocytes and surgically implanted
Traumatic calvarial defect[i]	ASC	Surgical implantation in fibrin glue
Achondroplasia[j]	BM MSC	Transplantation concurrently with distraction osteogenesis

MESENCHYMAL STEM/STROMAL CELLS

Mesenchymal stem and stromal cells

MSCs are multipotent stromal cells that can be sourced from a variety of tissues, including bone marrow, adipose tissue and umbilical cord. Morphologically they resemble fibroblasts. They are adherent to plastic, express certain cell surface markers (CD105, CD73 and CD90), and do not express the cell surface markers associated with haematopoietic stem cells (such as CD34 and CD45). MSCs were initially shown to have the ability to be directed to differentiate into a variety of specialised cell types of the mesodermal lineages, including osteoblasts, chondrocytes, adipocytes, tenocytes and myocytes (**Figure 4.2**). Recent studies suggest that they may also be directed into cells of the ectoderm and endoderm lineages.

Of further clinical importance, MSCs have potent trophic and anti-inflammatory properties, attributable to their ability to produce growth factors (including vascular endothelial growth factor (VEGF), insulin-like growth factor (IGF), hepatocyte growth factor (HGF)), and prostaglandin E2. MSCs for therapeutic use can be isolated from bone marrow (iliac crest aspiration) or from subcutaneous fat (liposuction) which is less invasive and gives a high yield of MSCs. In both cases, MSCs are isolated *in vitro* on the basis of their adherence to plastic. They can then be used either immediately, or after expansion of their numbers by *in vitro* culture. Alternatively, MSCs can be differentiated into the desired lineage *in vitro* by addition of suitable growth factors and chemicals.

The relative ease of cell acquisition has meant that autologous MSCs have been used clinically in a variety of settings such as treatment of burns and to repair defects in cartilage. More clinical evidence is required in terms of efficacy and mechanism of action, as it is not entirely clear whether a given clinical effect resulting from MSC administration is attributable to their ability to contribute directly to tissue regeneration, or due to immunomodulatory and paracrine effects resulting from their ability to release trophic mediators that promote tissue repair by recipient cells (**Figure 4.2**).

Mesenchymal stem cells are harvested by

1) Bone marrow aspiration (iliac crest)

2) Liposuction (subcutaneous fat)

Stem cells bring about tissue regeneration by

Immunomodulation
Paracrine effects
Trophic effects (Growth factors)
Regeneration

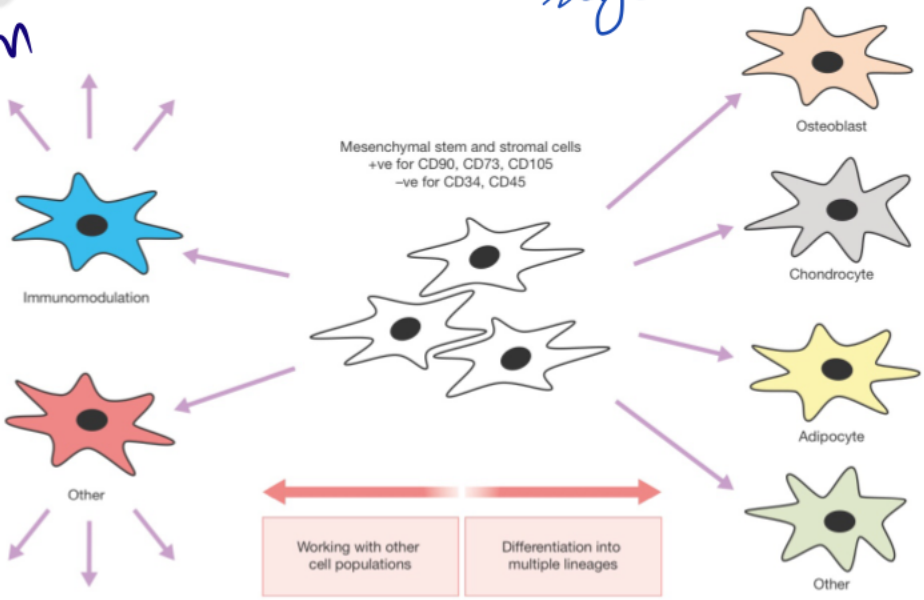


Figure 4.2 Proposed characteristics of mesenchymal stem and stromal cells relevant to tissue engineering and regenerative medicine.

SCAFFOLDS USED FOR TISSUE ENGINEERING

TABLE 4.3 Requirements of a scaffold used in tissue engineering.

- Provide structural support for cells
- Allow cells to attach, migrate and proliferate
- Enable oxygen, nutrients and regulatory factors access to all cells
- Deliver signals to promote cell migration and proliferation
- Biocompatible, non-immunogenic and ideally biodegradable

Summary box 4.2

Regenerative scaffolds can:

- Provide physical support and shape to the engineered tissue
- Guide cell growth, migration and differentiation
- Be natural or artificial

Natural

obtained by treating human / animal tissues i detergent to remove all cellular elements & obtain a **COLLAGEN RICH EXTRACELLULAR MATRIX** (Decellularized organ scaffolds)

Composite biominds 'smart' scaffolds can be made → give biophysical cues & cellular signals

Artificial

Natural Materials

1) Polysaccharides
2) Collagen
3) Fibrin
4) Gelatin
5) Cellulose

Synthetic Materials

1) Polylactide (PLA)
2) Polyglycolide (PGA)
3) Graphene
4) Bioactive Ceramics (Calcium phosphates - hydroxy apatites)
5) Bioactive glasses

Can be crafted into desirable architecture, shape & texture using 3D printing, electrospinning

CELL SEEDING OF SCAFFOLDS

TABLE 4.4 Approaches for seeding cells into scaffolds.	
Static cell seeding	- conc. cell suspension placed in direct contact ĩ scaffold
Dynamic cell seeding	- Rotation of scaffold in cellular medium
Magnetic cell seeding	- cells labelled ĩ supermagnetic beads → magnets used to attract cells onto the scaffold
Pressure and vacuum seeding	- to force cells into pores of scaffold
Photopolymerised hydrogels	- UV rays onto monomer cells suspensions
Bioreactor perfusion systems	

IMPLANTATION OF ENGINEERED TISSUE

Considerations

- Remodelling at target site
- Mechanical stress at target site

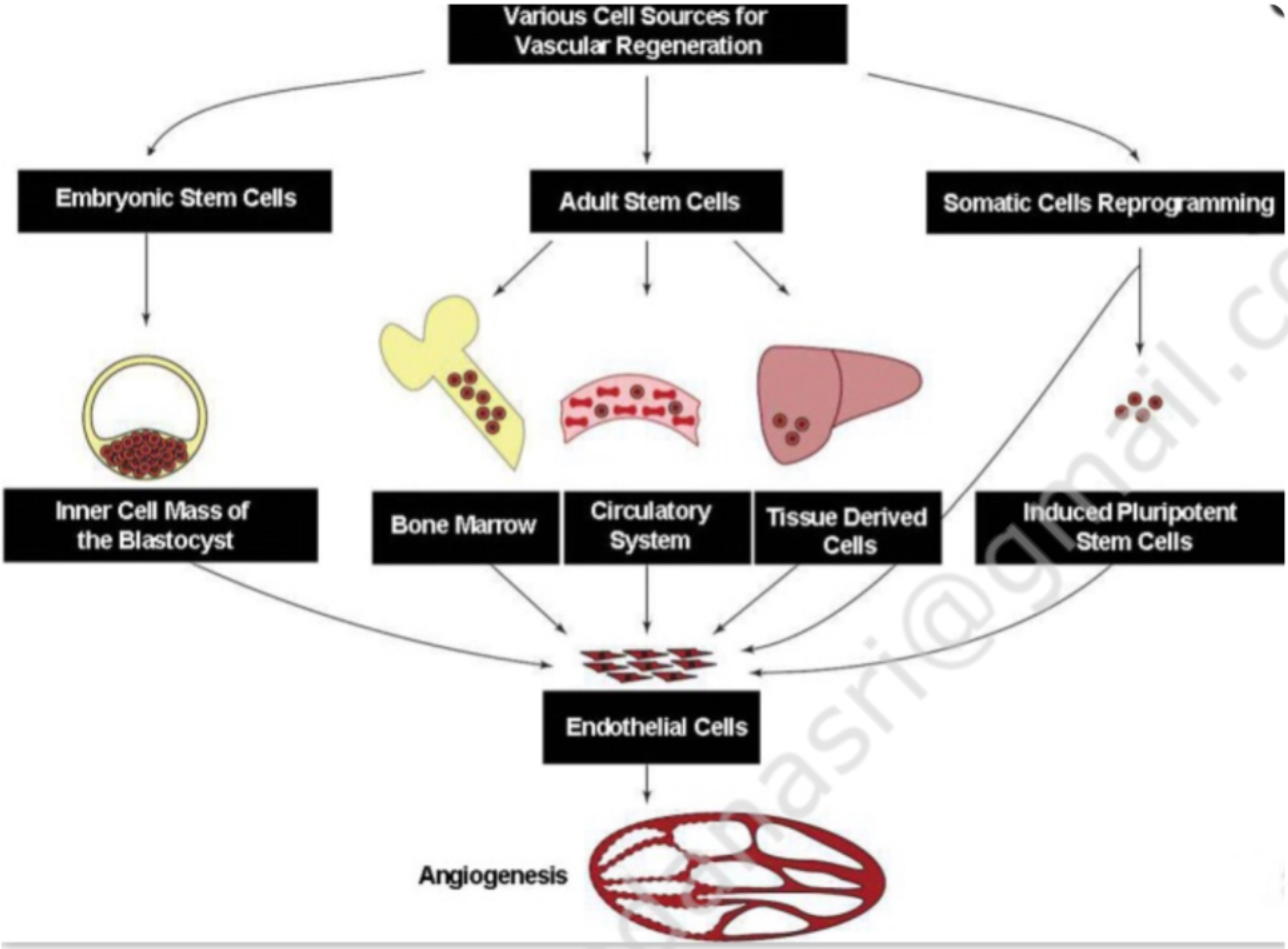
RISKS OF CELL BASED THERAPY

1) Tumor formation
2) Genetic & Epigenetic abnormalities
3) Infection
4) Poor viability / loss of function
5) Differentiation into undesired cell types
6) Rejection
7) Side effects of immunosuppression (in allogenic cells)
8) Ethical considerations

Progress in the field of regenerative medicine

Finding/Experiment
First cell transplantation: Bone marrow transplant (1968)
Discovery of stem cells in human cord blood (1978)
First engineered tissue transplantation: skin (1981)
First in vitro stem cell line developed from mice (1981)
First engineered vessel structure was synthesized (1986)
Adult stem cells were used for vascular regeneration by Asahara (1997)
Isolation of human embryonic stem cells (1998)
First laboratory-grown organ: an artificial bladder implanted in a patient suffering from myelomeningocele (1999)
Implantation of first engineered tubular organs (urine conduits) (2004)
Discovery of stem cells derived from amniotic fluid and placenta (2007)
First solid organ engineered by recycling donor liver (2009)
3D-printed vascular networks direct therapeutic angiogenesis in ischemic condition (2017)

ANGIOGENESIS ENGINEERING



Various cell sources used at the current for vascular regeneration or induction of Angiogenesis. Many cell sources are applicable to regenerate various tissues by affecting angiogenesis and blood support