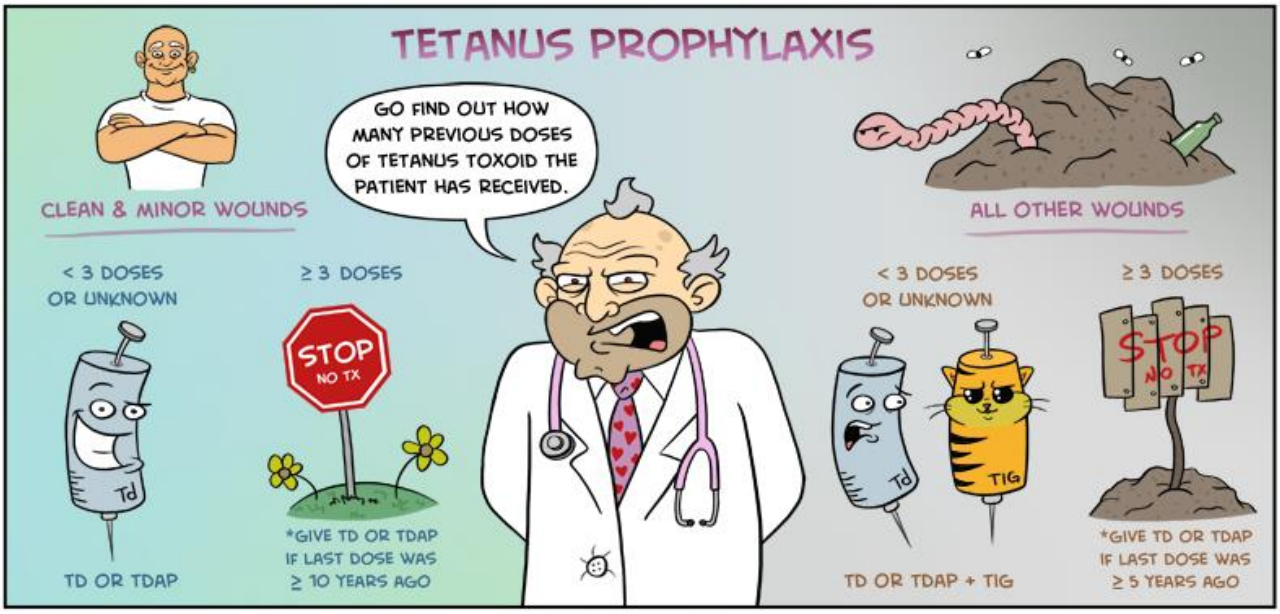


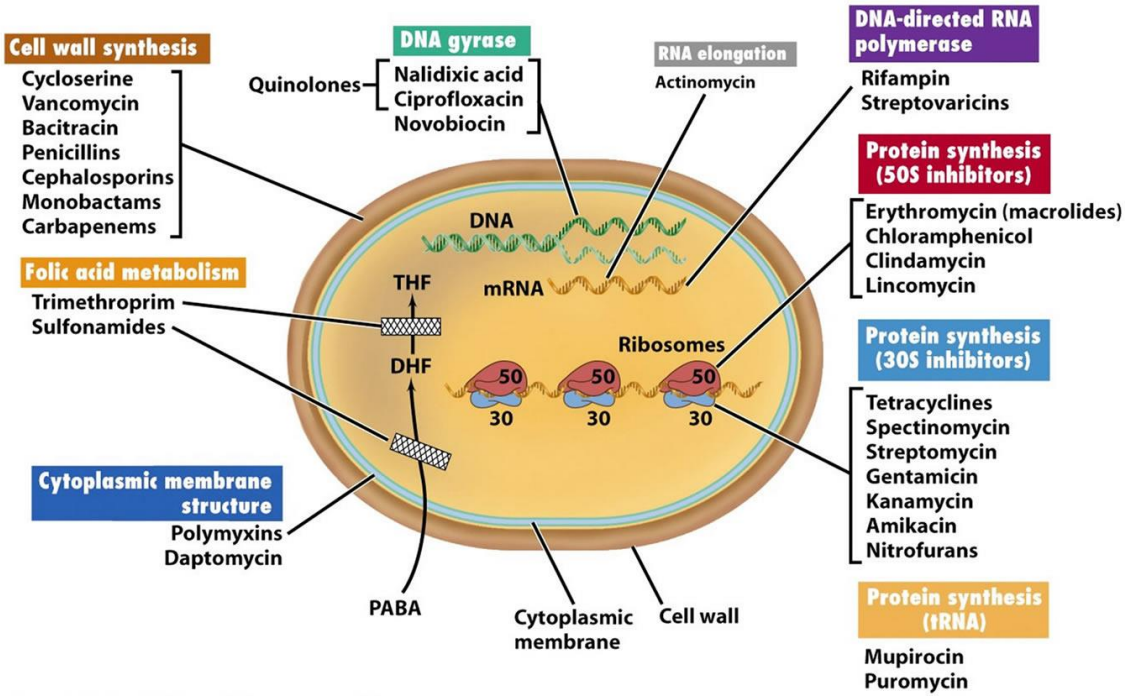
## Antibiotics: Mechanism of Action

**Inhibit cell wall formation**
- Penicillins
- Cephalosporins

**Inhibit protein synthesis**
- Aminoglycosides *(cause misreading of mrna)*
- Chloramphenicol
- Macrolides *(e.g. Erythromycin)*
- Tetracyclines
- Fusidic acid

**Inhibit DNA synthesis**
- Quinolones *(e.g. Ciprofloxacin)*
- Metronidazole
- Sulphonamides
- Trimethoprim

**Inhibit RNA synthesis**
- Rifampicin




## MRSA

Methicillin-resistant Staphylococcus aureus (MRSA) was one of the first organisms which highlighted the dangers of hospital-acquired infections.

**Who should be screened for MRSA?**
- All patients awaiting **elective admissions** (exceptions include day patients having terminations of pregnancy and ophthalmic surgery. Patients admitted to mental health trusts are also excluded)
- In the UK **all emergency admissions** are currently screened

**How should a patient be screened for MRSA?**
- Nasal swab and skin lesions or wounds
- The swab should be wiped around the inside rim of a patient's nose for 5 seconds
- The microbiology form must be labelled 'MRSA screen'

**Suppression of MRSA from a carrier once identified**
- Nose: mupirocin 2% in white soft paraffin, TDS for 5 days
- Skin: chlorhexidine gluconate, od for 5 days. Apply all over but particularly to the axilla, groin and perineum

**The following antibiotics are commonly used in the treatment of MRSA infections:**
- Vancomycin
- Teicoplanin

**Some strains may be sensitive to the antibiotics listed below but they should not generally be used alone because resistance may develop:**
- **Rifampicin**
- Macrolides
- Tetracyclines
- Aminoglycosides
- Clindamycin

*Relatively new antibiotics such as linezolid, quinupristin/dalfopristin combinations and tigecycline have activity against MRSA but should be reserved for resistant cases*

*Staphylococcus aureus*

- Facultative anaerobe
- Gram positive coccus
- Haemolysis on blood agar plates
- Catalase positive
- 20% population are long term carriers
- Exo and enterotoxin may result in toxic shock syndrome and gastroenteritis respectively (*enterotoxin is pre-formed* → ***rapid onset of symptoms.***)
- Ideally treated with penicillin although many strains now resistant through beta Lactamase production. In the UK less than 5% of isolates are sensitive to penicillin.
- Resistance to methicillin (and other antibiotics) is mediated by the mec operon, essentially penicillin binding protein is altered and resistance to this class of antibiotics ensues
- Common cause of cutaneous infections, abscesses, **surgical site infections**. Common cause of **lactational mastitis**
- Most common cause of **septic arthritis**.

*Staphylococcus* ***epidermidis***
Tends to colonise plastic devices and forms a **biofilm** which allows colonisation with other bacterial agents. It is notoriously difficult to eradicate once established and the usual treatment is removal of the device.

*Streptococcus pyogenes*

- Gram positive, forms chain like colonies, Lancefield Group A *Streptococcus*
- Produces beta haemolysis on blood agar plates
- Rarely part of normal skin microflora
- Catalase negative
- Releases a number of proteins/ virulence factors into host including hyaluronidase, streptokinase which allow rapid tissue destruction
- Releases superantigens such as pyogenic exotoxin A which results in scarlet fever
- Remains sensitive to penicillin, macrolides may be used as an alternative.

*Escherichia coli*
*(see later… 'Bacterial Gastroenteritis')*

*Campylobacter jejuni*
*(see later… 'Bacterial Gastroenteritis')*

*Streptococcus viridans*

- Affects heart valves

*Streptococcus bovis*

- Septicaemia is associated with carcinoma of the colon.
- Can also cause endocarditis.

*Helicobacter pylori*

- Gram negative, helix shaped rod, microaerophilic
- Produces hydrogenase that can derive energy from hydrogen released by intestinal bacteria
- Flagellated and mobile
- Those carrying the cag A gene may cause ulcers
- It secretes urease that breaks down gastric urea → $CO_2$ & $NH_3$→ Ammonium → Bicarbonate (simplified!). The bicarbonate can neutralise the gastric acid.
- Usually colonises the gastric antrum and irritates resulting in increased gastrin release and higher levels of gastric acid. These patients will develop duodenal ulcers. In those with more diffuse H-Pylori infection gastric acid levels are lower and ulcers develop by local tissue damage from H-Pylori- these patients get gastric ulcers.
- Diagnosis may be made by serology (approx. 75% sensitive). Biopsy urease test during endoscopy probably the most sensitive.
- In patients who are colonised 10-20% risk of peptic ulcer, 1-2% risk gastric cancer, <1% risk MALT lymphoma.

*Actinomycosis spp*

- Gram positive bacilli.
- **Facultative anaerobes.**
- May be difficult to culture. Direct visualisation of organisms and sulphur granules from lesions themselves is the easiest way to make a diagnosis.
- It remains a differential of conditions such as hydradenitis suppurativa, particularly if it is occurring in odd locations and with deeper abscesses than usual.

Mnemonic to remember some encapsulated pathogens is: ***'Even Some Super Killers Have Pretty Nice Big Capsules'***
**E**scherichia coli, **S**treptococcus pneumoniae, **S**almonella, **K**lebsiella pneumoniae, **H**aemophilus influenzae, **P**seudomonas aeruginosa, **N**eisseria meningitidis, **B**acteroides fragilis, and the yeast **C**ryptococcus neoformans

## Bacterial Gastroenteritis

| Causative organisms | Features |
|---|---|
| *Shigella* spp. | • Members of the Enterobacteriaceae<br>• Gram negative bacilli<br>• Clinically causes dysentery<br>• *Shigella* sonnei is the commonest infective organism (mild illness)<br>• Usually self-limiting, ciprofloxacin may be required if individual is in a high risk group |
| *Salmonella* spp. | • Facultatively anaerobic, gram negative, Enterobacteriaceae<br>• Infective dose varies according to subtype<br>• Salmonellosis: usually transmitted by infected meat (especially poultry) and eggs |
| *Yersinia enterocolitica* | • Gram negative, coccobacilli<br>• Typically produces a protracted **terminal ileitis** that may mimic Crohn's disease<br>• **Δ Δ acute appendicitis**<br>• May progress to septicaemia in susceptible individuals<br>• Usually sensitive to quinolone or tetracyclines |
| Vibrio cholera | • Short, gram negative rods<br>• Transmitted by contaminated water, seafood<br>• Symptoms include sudden onset of effortless vomiting and profuse watery diarrhoea<br>• Correction of fluid and electrolyte losses are the mainstay of treatment<br>• Most cases will resolve, antibiotics are not generally indicated |
| *E. coli* | • Gram negative rod<br>• Facultative anaerobe, non sporing<br>• Wide range of subtypes and some are normal gut commensals<br>  ○ ***Enteropathogenic (EPEC):*** childhood diarrhea<br>  ○ ***Enteroinvasive (EIEC):*** dysentery, large **bowel necrosis/ulcers**<br>  ○ ***Enterotoxigenic (ETEC):*** small intestine, **traveler's diarrhoea**<br>  ○ ***Enterohaemorrhagic (EHEC):*** *subtype 0157*, cause **haemolytic uraemic $**, haemorrhagic colitis, and thrombotic thrombocytopaenic purpura<br>• They are resistant to many antibiotics used to treat gram positive infections and acquire resistance rapidly and are recognised as producing beta lactamases<br>• Most common organism implicated in **cholangitis** infections.<br>• Implicated in **Fournier's gangrene** along with bacteroides |
| *Campylobacter jejuni* | • Spiral / curved, gram negative rods, non sporulating bacteria<br>• Most common cause of acute infective diarrhoea<br>• Produces enteritis which is often diffuse and blood may be passed<br>• Usually infects caecum and terminal ileum. Local lymphadenopathy is common<br>• May mimic appendicitis as it has marked RIF pain **(differential for RIF pain with diarrhoea)**<br>• Reactive arthritis is seen in 1-2% of cases<br>• Self-limiting infection so antibiotics are not usually advised. However, the quinolones are often rapidly effective.<br>• Birds are recognized reservoirs of campylobacter. |

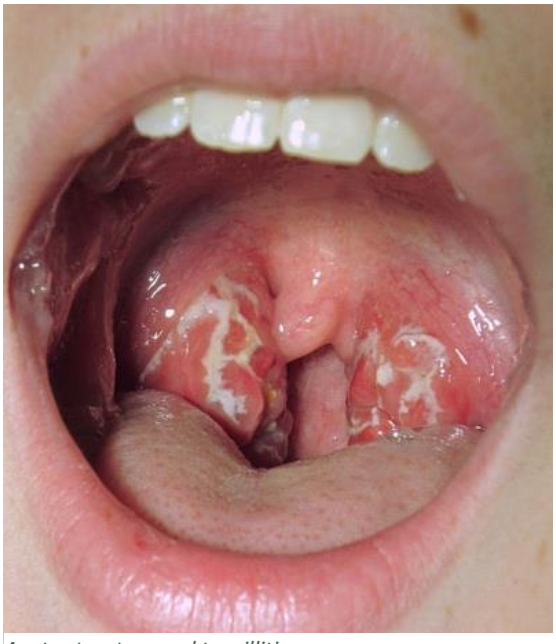
# Gastro Intestinal Parasitic Infections

Common infections

| | |
|---|---|
| **Enterobiasis** | • Due to organism *Enterobius vermicularis*<br>• Common cause of **pruritus ani**<br>• Diagnosis usually made by placing scotch tape at the anus, this will trap eggs that can then be viewed microscopically<br>• Treatment is with mebendazole |
| **Ancylostoma duodenale** | • **Hookworms** that anchor in proximal small bowel<br>• Most infections are asymptomatic although may cause iron deficiency anaemia<br>• Larvae may be found in stools left at ambient temperature, otherwise infection is **difficult to diagnose**<br>• Infection occurs as a result of cutaneous penetration, migrates to lungs, coughed up and then swallowed<br>• Treatment is with mebendazole |
| **Ascariasis** | • Due to infection with **roundworm** *Ascaris lumbricoides*<br>• Infections begin in gut following ingestion, then penetrate duodenal wall to migrate to lungs, coughed up and swallowed, cycle begins again<br>• Diagnosis is made by identification of **worm or eggs** within faeces<br>• Treatment is with mebendazole |
| **Strongyloidiasis** | • Due to infection with *Strongyloides stercoralis*<br>• Rare in west<br>• Organism is a nematode living in duodenum of host<br>• Initial infection is via skin penetration. They then migrate to lungs and are coughed up and swallowed. Then mature in small bowel are excreted and cycle begins again<br>• An auto infective cycle is also recognised where larvae will penetrate colonic wall<br>• Individuals may be asymptomatic, although they may also have respiratory disease and skin lesions<br>• Diagnosis is usually made by stool microscopy<br>• In the UK mebendazole is used for treatment |
| **Cryptosporidium** | • Protozoal infection<br>• Organisms produce cysts which are excreted and thereby cause new infections<br>• Symptoms consist of diarrhoea and cramping abdominal pains. Symptoms are worse in immunosuppressed people *(for e.g. following transplant)*<br>• Cysts may be identified in stools<br>• Treatment is with metronidazole |
| **Giardiasis** | • Diarrheal infection caused by *Giardia lamblia* (protozoan)<br>• Infections occur as a result of ingestion of cysts *(resists chlorination → risk of transfer in swimming pools)*<br>• Symptoms are usually gastrointestinal with abdominal pain, bloating and passage of soft or loose stools *(causes fat malabsorption → greasy stools)*<br>• Diagnosis is by serology or stool microscopy<br>• First line treatment is with metronidazole |

## Streptococci

Streptococci may be divided into alpha and beta haemolytic types



*Acute streptococcal tonsillitis*

### Alpha haemolytic streptococci

The most important alpha haemolytic streptococcus is Streptococcus pneumoniae (pneumococcus). Pneumococcus is a common cause of pneumonia, meningitis and otitis media. Another clinical example is Streptococcus viridans

### Beta haemolytic streptococci

These can be subdivided into group A and B

#### Group A

- most important organism is Streptococcus pyogenes
- responsible for erysipelas, impetigo, cellulitis, type 2 necrotizing fasciitis and pharyngitis/tonsillitis
- immunological reactions can cause rheumatic fever or post-streptococcal glomerulonephritis
- erythrogenic toxins cause scarlet fever

#### Group B

- Streptococcus agalactiae may lead to neonatal meningitis and septicaemia

## Acute Tonsillitis

- Characterised by pharyngitis, fever, malaise and lymphadenopathy.
- Over half of all cases are bacterial with *Streptococcus pyogenes* the most common organism
- The tonsils are typically oedematous and yellow or white pustules may be present
- Infectious mononucleosis may mimic the condition.
- Treatment with penicillin type antibiotics is indicated for bacterial tonsillitis.
- Bacterial tonsillitis may result in local abscess formation (quinsy)

## Salmonella

The Salmonella group contains many members, most of which cause diarrhoeal diseases. They are facultative anaerobes, Gram negative rods which are not normally present as commensals in the gut.

Typhoid is caused by **Salmonella typhi** and paratyphoid is caused by **Salmonella paratyphi** (types A, B & C).
They are often termed enteric fevers, producing systemic symptoms such as headache, fever, arthralgia

### Features

- Initially systemic upset as above
- Relative bradycardia
- Abdominal pain, distension
- Constipation: although salmonella is a recognised cause of diarrhoea, constipation is more common in typhoid
- Rose spots: present on the trunk in 40% of patients, and are more common in paratyphoid

### Possible complications include

- Osteomyelitis (especially in **sickle cell disease** where salmonella is one of the most common pathogens)
- GI bleed/perforation
- Meningitis
- Cholecystitis
- Chronic carriage (1%, more likely if adult females)

# Hepatitis B

Hepatitis B is a **double-stranded DNA virus** and is spread through exposure to infected blood or body fluids, including vertical transmission from mother to child. The incubation period is 6-20 weeks.

### Immunization against hepatitis B

- Contains HBsAg absorbed onto aluminium hydroxide adjuvant and is prepared from yeast cells using recombinant DNA technology
- Most schedules give 3 doses of the vaccine with a recommendation for a one-off booster 5 years following the initial primary vaccination
- At risk groups who should be vaccinated include: healthcare workers, intravenous drug users, sex workers, close family contacts of an individual with hepatitis B, individuals receiving blood transfusions regularly, chronic kidney disease patients who may soon require renal replacement therapy, prisoners, chronic liver disease patients
- Around 10-15% of adults fail to respond or respond poorly to 3 doses of the vaccine. Risk factors include age over 40 years, obesity, smoking, alcohol excess and immunosuppression
- Testing for anti-HBs is only recommended for those at risk of occupational exposure (i.e. Healthcare workers) and patients with chronic kidney disease. In these patients anti-HBs levels should be checked 1-4 months after primary immunization
- The table below shows how to interpret anti-HBs levels:

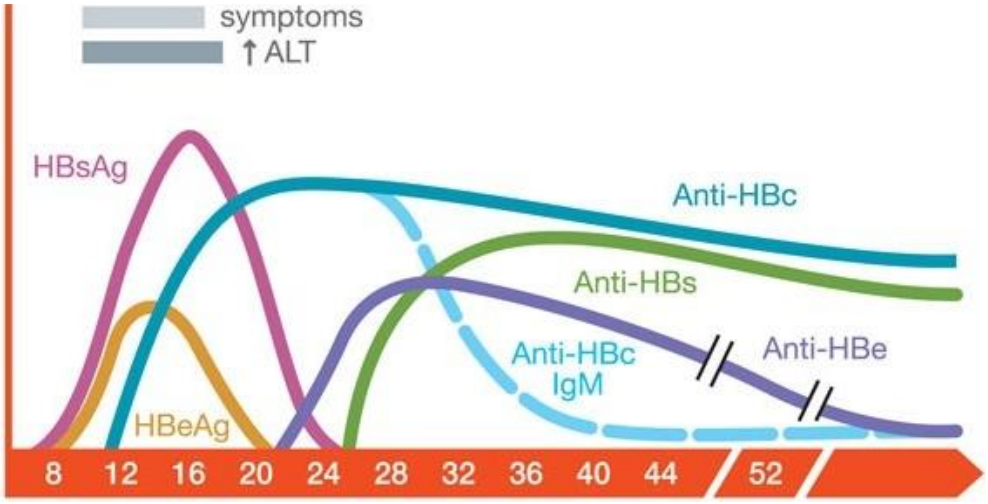
| Anti-HBs level (mIU/ml) | Response |
|---|---|
| > 100 | Indicates adequate response, no further testing required. Should still receive booster at 5 years |
| 10 - 100 | Suboptimal response - one additional vaccine dose should be given. If immunocompetent no further testing is required |
| < 10 | Non-responder. Test for current or past infection. Give further vaccine course (i.e. 3 doses again) with testing following. If still fails to respond then HBIG would be required for protection if exposed to the virus |

### Complications of hepatitis B infection

- Chronic hepatitis (5-10%)
- Fulminant liver failure (1%)
- Hepatocellular carcinoma
- Glomerulonephritis
- Polyarteritis nodosa
- Cryoglobulinemia

### Management of hepatitis B

- PEGylated interferon-alpha used to be the only treatment available. It reduces viral replication in up to 30% of chronic carriers. A better response is predicted by being female, < 50 years old, low HBV DNA levels, non-Asian, HIV negative, high degree of inflammation on liver biopsy
- However, due to the side-effects of PEGylated interferon it is now used less commonly in clinical practice. Oral antiviral medication is increasingly used with an aim to suppress viral replication (not in dissimilar way to treating HIV patients)
- Examples include lamivudine, tenofovir and entecavir



## Hepatitis C

Hepatitis C is likely to become a significant public health problem in the UK in the next decade. It is thought around 200,000 people are chronically infected with the virus. At risk groups include intravenous drug users and patients who received a blood transfusion prior to 1991 (e.g. haemophiliacs).

### Transmission

- The risk of transmission during a needle stick injury is about 2%
- The vertical transmission rate from mother to child is about 6%
- Breast feeding is not contraindicated in mothers with hepatitis C
- The risk of transmitting the virus during sexual intercourse is probably less than 5%

### Features

- After exposure to the hepatitis C virus less than 20% of patients develop an acute hepatitis

### Complications

- Chronic infection (80-85%) - only 15-20% of patients will clear the virus after an acute infection and hence the majority will develop chronic hepatitis C
- Cirrhosis (20-30% of those with chronic disease)
- Hepatocellular cancer
- Cryoglobulinemia

### Management of chronic infection

- Currently a combination of PEGylated interferon-alpha and ribavirin are used
- Up to 55% of patients successfully clear the virus, with success rates of around 80% for some strains

### Complications of treatment

- Ribavirin - side-effects: haemolytic anaemia, cough. Women should not become pregnant within 6 months of stopping ribavirin as it is teratogenic
- Interferon alpha - side-effects: flu-like symptoms, depression, fatigue, leukopenia, thrombocytopenia

## HIV Testing

HIV seroconversion is symptomatic in 60-80% of patients and typically presents as a glandular fever type illness. Increased symptomatic severity is associated with poorer long term prognosis. It typically occurs 3-12 weeks after infection

### Features

- Sore throat
- Lymphadenopathy
- Malaise, myalgia, arthralgia
- Diarrhoea
- Maculopapular rash
- Mouth ulcers
- Rarely meningoencephalitis

### Diagnosis

- Antibodies to HIV may not be present
- HIV PCR and p24 antigen tests can confirm diagnosis

#### *HIV antibody test*

- Most common and accurate test
- Usually consists of both a screening ELISA (Enzyme Linked Immuno-Sorbent Assay) test and a confirmatory Western Blot Assay
- Most people develop antibodies to HIV at 4-6 weeks but 99% do by 3 months

#### *p24 antigen test*

- Usually positive from about 1 week to 3 - 4 weeks after infection with HIV
- Sometimes used as an additional screening test in blood banks

# Meleney's Gangrene and Necrotising Fasciitis

## Necrotising fasciitis

- Advancing soft tissue infection associated with fascial necrosis
- Uncommon, but can be fatal
- In many cases there is underlying background immunosuppression e.g. Diabetes
- Caused by polymicrobial flora (aerobic and anaerobic) and MRSA is seen increasingly in cases of necrotising fasciitis
- *Streptococcus* is the commonest organism in isolated pathogen infection (15%)

## Meleney's gangrene

- Meleney's is a similar principle but the infection is more superficially sited than necrotising fasciitis and often confined to the trunk

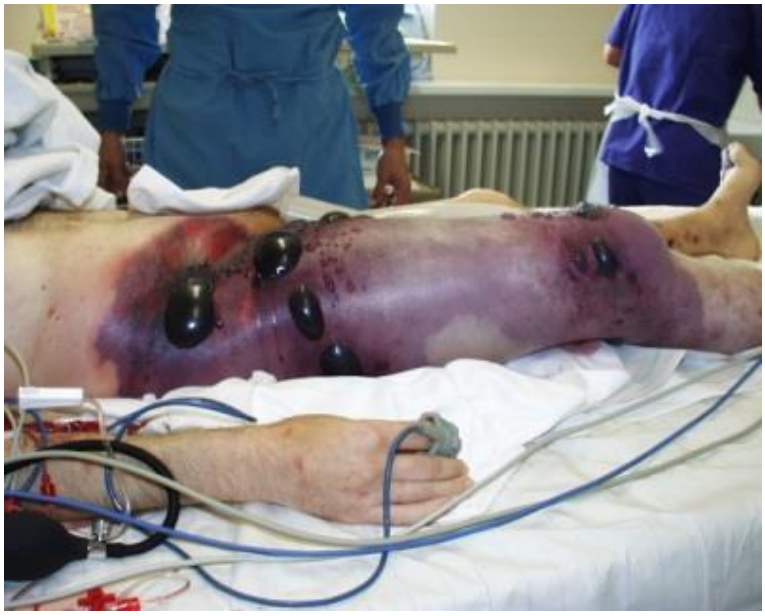
## Fournier's gangrene

- Necrotising fasciitis **affecting the perineum**
- Polymicrobial with **E-coli and Bacteroides** acting in synergy

## Clinical features

- Fever
- Pain
- Cellulitis
- Oedema
- Induration
- Numbness

*Muscles are relatively spared*



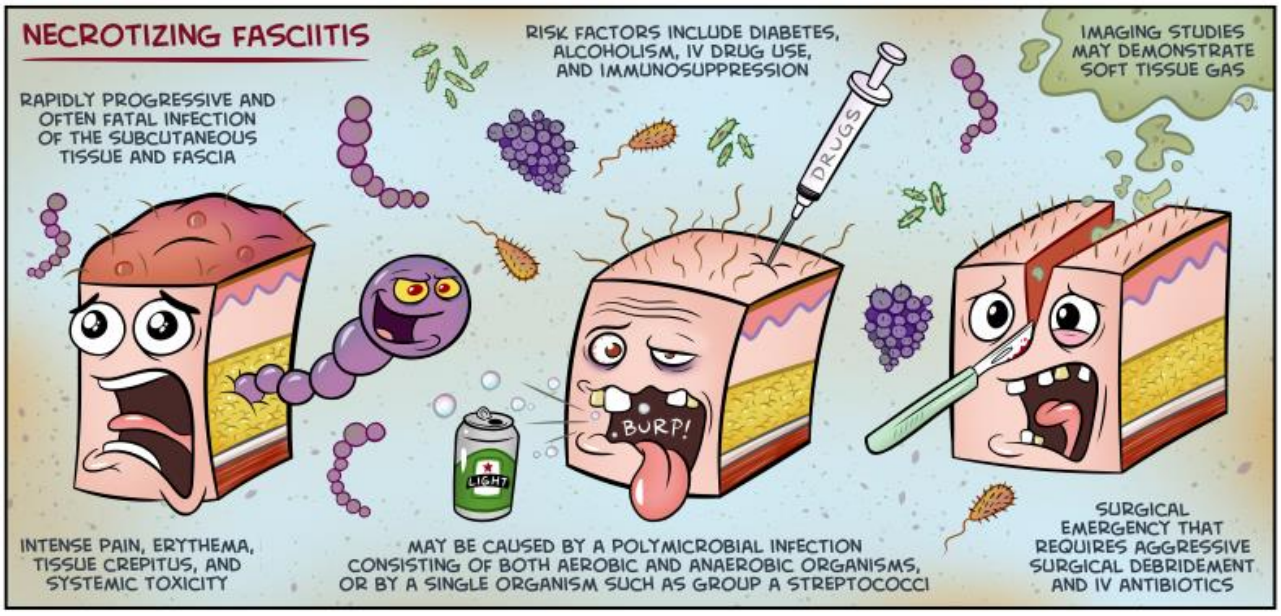
## Late findings

- Purple/black skin discolouration
- Blistering
- Haemorrhagic bullae
- Crepitus *(maybe present in 35%)*
- Dirty Dishwater fluid discharge
- Septic shock

## Diagnosis is mainly clinical

## Management

- Radical surgical debridement forms the cornerstone of management
- Sterile dressing is used to dress the wound
- Reconstructive surgery is considered once the infection is completely treated (**further surgery** after 24-48h).



# Osteomyelitis

Infection of the bone

**Causes**

- S aureus and occasionally Enterobacter or *Streptococcus*species
- In sickle cell: *Salmonella* species

**Clinical features**

- Erythema
- Pain
- Fever

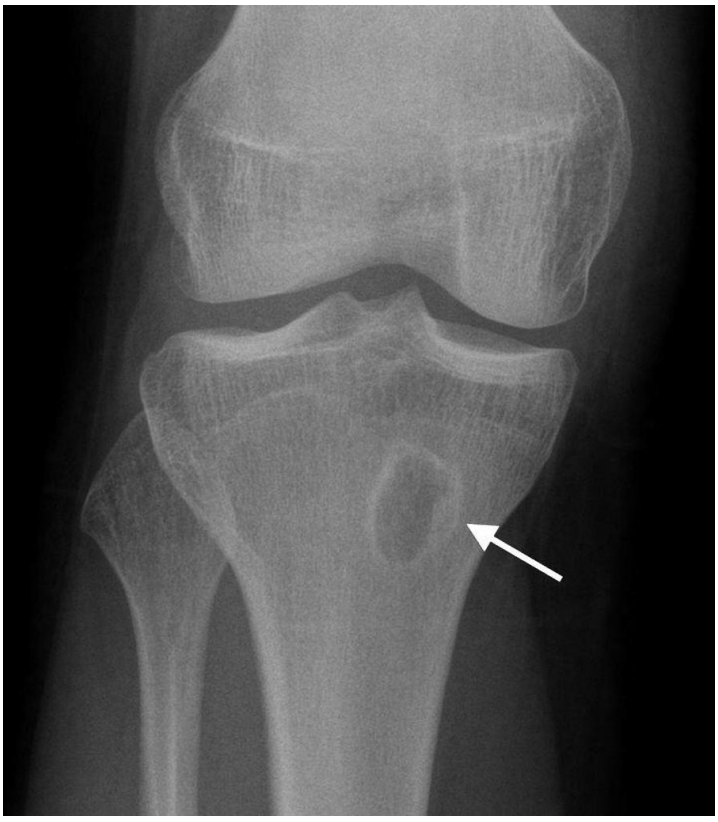
**Investigation**

- X-ray: lytic centre with a ring of sclerosis
- Bone biopsy and culture

**Treatment**

- Prolonged antibiotics
- Sequestra may need surgical removal

The ***Lautenbach procedure*** involves debridement, intramedullary reaming and the insertion of double-lumen tubes to establish both a local antibiotic delivery system and cavity analysis for volume and culture.



*Brodie Abscess*