TOXIC SHOCK SYNDROME AND STREPTOCOCCAL TOXIC SHOCK:

TOXIC SHOCK SYNDROME:

- A toxin-mediated, severe, life-threatening syndrome characterised by h igh fever, profound hypotension, diffuse erythroderma, mucous membrane hyperaemia, pharyngitis, diarrhoea and constitutional symptoms
- Rapidly progresses to MODS with severe electrolyte disturbances, renal failure and shock
- Many risk factors:
    - No longer related to tampon use and menses

Table 145-2 Risk Factors for Toxic Shock Syndrome
Current menstruation
Cutaneous lesions, including burns
Recent surgical procedure
Postpartum/postabortion status
Other less common reported associations:
Sinusitis
Intrauterine device use
Pharyngitis

Table 145-1 Case Definition of Toxic Shock Syndrome
An illness with the following findings:
1. Fever: temperature ≥38.9°C (≥102.0°F)
2. Rash: diffuse macular erythroderma
3. Desquamation: 1–2 wk after onset of illness, particularly on the palms and soles
4. Hypotension: systolic blood pressure ≤90 mm Hg for adults or less than fifth percentile by age for children aged <16 y; orthostatic drop in diastolic blood pressure ≥15 mm Hg from lying to sitting, orthostatic syncope, or orthostatic dizziness
5. Multisystem involvement (*three or more of the following*):
a. GI: diarrhea and/or vomiting at onset of illness
b. Muscular: severe myalgia or creatine phosphokinase level at least twice the upper limit of normal
c. Mucous membrane: vaginal, oropharyngeal, or conjunctival hyperemia
d. Renal: blood urea nitrogen or creatinine level at least twice the upper limit of normal for laboratory, or urinary sediment with pyuria (≥5 leukocytes per high-power field) in the absence of urinary tract infection
e. Hepatic: total bilirubin, alanine aminotransferase enzyme, or aspartate aminotransferase enzyme levels at least twice the upper limit of normal for laboratory
f. Hematologic: platelet count <100,000/mm3
g. Central nervous system: disorientation or alterations in consciousness without focal neurologic signs when fever and hypotension are absent
6. Laboratory criteria: negative results on the following tests, if obtained:
Blood, throat, or cerebrospinal fluid cultures (blood culture may be positive for *Staphylococcus aureus*)
Rise in titer to Rocky Mountain spotted fever, leptospirosis, or measles
Case classification:
Probable: a case in which five of the six specified criteria described above are present
Confirmed: a case in which all six of the specified criteria described above are present, including desquamation, unless the patient dies before desquamation occurs

- Staphylococcus aureus has been isolated form the vaginas of 98% of women with toxic shock syndrome vs 8-10% of controls

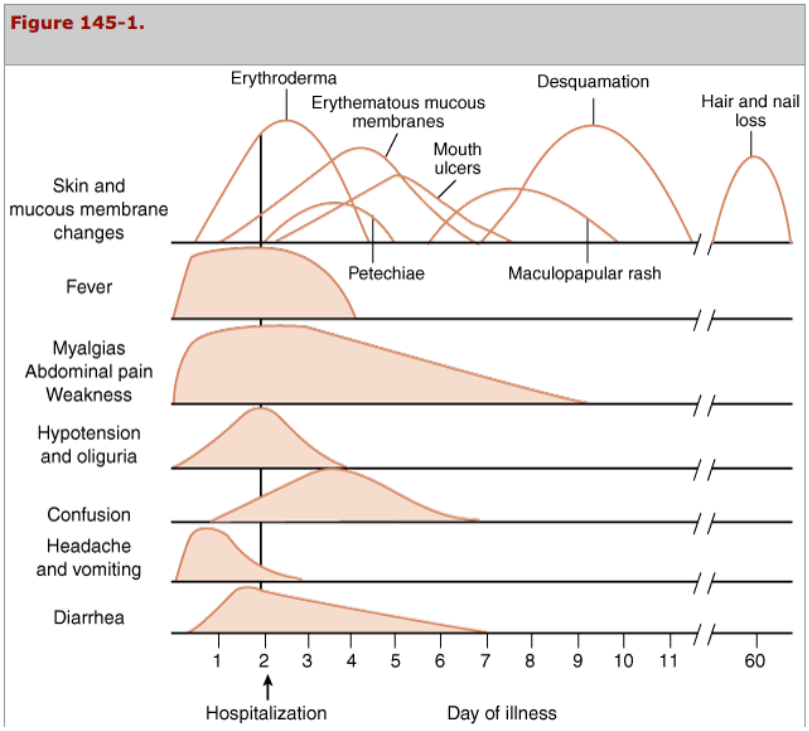
PATHOPHYSIOLOGY:

- The toxin causes direct toxic effects as well as stimulating secondary mediators → toxin is known as TOXIC SHOCK SYNDROME TOXIN-1 (responsible for most-menstruation-related toxic shock, where Staph aureus is the causative agent)
- The amount of toxin produced is favoured by vaginal conditions, especially during menstruation

- The most impressive aspect is MASSIVE VASODILATATION AND RAPID MOVEMENT OF SERUM PROTEINS AND FLUIDS FROM THE INTRAVASCULAR SPACE TO THE EXTRAVASCULAR SPACE
    - Hypotension is due to decreased vasomotor tone, non-hydrostatic leakage of fluid into the interstitium, depressed cardiac function and total body water deficits from vomiting, diarrhoea and fever
- Renal failure is multifactorial:
    - Direct toxic effect
    - Rhabdomyolysis
    - Volume depletion/hypotension

CLINICAL FEATURES:

- Consider toxic shock syndome in patients with any unexplained febrile illness associated with ERYTHRODERMA, HYPOTENSION AND DIFFUSE ORGAN PATHOLOGY → i.e. an acutely ill patient with erythroderma and no obvious source of sepsis
- Diffuse myalgias/muscle weakness, rhabdomyolysis and profuse watery diarrhoea/vomiting
- 50-75% have pharyngitis with strawberry-red tongue
- Rash associated is diffuse, blanching erythroderma → "PAINLESS SUNBURN"
- In all cases, a fine, generalised desquamation of the skin, with peeling over the soles, fingers, toes and palms occurs from 6-14 days after onset of illness



DIAGNOSIS:

- Should be considered in all patients before all criteria are met as desquamation does not occur until late
- Other systemic illnesses characterised by fever, rash, diarrhoea, myalgias and MODS resemble toxic shock syndrome

Table 145-3 Differential Diagnosis of Toxic Shock Syndrome	
Acute pyelonephritis	Acute viral syndrome
Septic shock	Leptospirosis
Acute rheumatic fever	Systemic lupus erythematosus
Streptococcal scarlet fever	Rocky Mountain spotted fever
Staphylococcal scarlet fever	Tick typhus
Staphylococcal scalded skin syndrome	Gastroenteritis
Legionnaire disease	Kawasaki disease
Pelvic inflammatory disease	Reye syndrome
Hemolytic uremic syndrome	Toxic epidermal necrolysis
Clostridium-associated toxic shock	Erythema multiforme

TREATMENT AND DISPOSITION:

- Most important aspects in initial treatment:
  - Aggressive management of circulatory shock (usually in ICU setting)
    - Can require 4-20L of crystalloid and FFP
    - Beware development of APO/ALI/ARDS due to fluid resuscitation → may need intubation and ventilation
  - Remove foreign bodies (tampons, nasal packing, surgical packing)
- ANTIBIOTICS DUE DOT AFFECT OUTCOME OF THE ACUTE ILLNESS BUT THEY ARE GIVEN TO ERADICATE TOXIN-PRODUCING STAPHYLOCOCCI AND DECREASE RECURRENCE RATE → IV anti-staphylococcal penicillin or cephalosporin for at least three days or until patient improves clinically
- A 2009 review recommended IV Ig if no clinical improvement is seen after 6 hours of aggressive supportive therapy
- Most patients become afebrile and normotensive within 48 hours of admission
  - Neurologic deficits are common → 50% exhibit residual memory deficits

<u>STREPTOCOCCAL TOXIC SHOCK SYNDROME:</u>

- Infection with Group A Streptococci WITH INVASIVE SOFT TISSUE INVOLVEMENT, EARLY ONSET OF SHOCK AND ORGAN FAILURE
  - Similar to toxic shock syndrome except that Streptococcal Toxic Shock Syndrome occurs IN ASSOCIATION WITH A SEVERE SOFT TISSUE INFECTION AND RESULTS OF CULTURES OR TISSUE BIOPSY ARE **POSITIVE FOR STREPTOCOCCUS PYOGENES**
- This disease commonly affects individuals between 20-50, who may be without predisposing illnesses
- Other risk factors:
  - Extremes of age
  - Diabetes
  - Alcoholism
  - Drug abuse
  - Treatment with NSAIDS
  - Immunodeficiency
- Portal of entry for Strep is skin, pharynx, mucosa or vagina in 50% cases

CLINICAL FEATURES:

- Soft tissue pain OUT OF PROPORTION TO PHYSICAL FINDINGS and fever are the most common initial manifestations
- Muscle pain, erythema, and tenderness can quickly lead to compartment syndrome
- USUAL FINDING IS SOFT TISSUE INFECTION OF EXTREMITIES
- Shock may be refractory to treatment or require massive volume replacement
- Development of vesicles and bullae with progression blue discolouration is an ominous sign for necrotizing fasciitis
- ARDS develops in 55%

Table 145-4 Case Definition of Streptococcal Toxic Shock Syndrome
An illness with the following clinical manifestations occurring within the first 48 h of hospitalization or, for a nosocomial case, within the first 48 h of illness:
Hypotension defined by a systolic blood pressure ≤90 mm Hg for adults or less than the fifth percentile by age for children <16 y
Multi-organ involvement characterized by two or more of the following:
1. Renal impairment: creatinine level ≥2 milligrams/dL (≥177 micromoles/L) for adults or greater than or equal to twice the upper limit of normal for age; in patients with preexisting renal disease, a greater than twofold elevation over the baseline level
2. Coagulopathy: platelet count ≤100,000/mm^3 (≤100 $_x$ 10^6/L) or disseminated intravascular coagulation, defined by prolonged clotting times, low fibrinogen level, and the presence of fibrin degradation products
3. Liver involvement: alanine aminotransferase, aspartate aminotransferase, or total bilirubin levels greater than or equal to twice the upper limit of normal for the patient's age; in patients with preexisting liver disease, a greater than twofold increase over the baseline level
4. Acute respiratory distress syndrome: defined by acute onset of diffuse pulmonary infiltrates and hypoxemia in the absence of cardiac failure or by evidence of diffuse capillary leak manifested by acute onset of generalized edema, or pleural or peritoneal effusions with hypoalbuminemia
5. A generalized erythematous macular rash that may desquamate
6. Soft tissue necrosis, including necrotizing fasciitis or myositis, or gangrene
Laboratory criteria for diagnosis:
Isolation of group A streptococcus
Case classification:
Probable: a case that meets the clinical case definition in the absence of another identified etiology for the illness and with isolation of group A streptococcus from a nonsterile site (e.g., throat, vagina, sputum)
Confirmed: a case that meets the clinical case definition and with isolation of group A streptococcus from a normally sterile site (e.g., blood or cerebrospinal fluid or, less commonly, joint, pleural, or pericardial fluid)

DIAGNOSIS:

- **See above table for diagnostic criteria**
- WCC >13 WITH PROFOUND BANDAEMIA
- LFT anomalies
- DIC
- Renal function → progressive dysfunction that often requires dialysis
- Blood cultures are positive for GAS in 60% patients and >90% of tissue cultures show positive findings
- IF NECROTISING FASCIITIS or streptococcal myositis is suspected, IMMEDIATE SURGICAL CONSULT SHOULD BE OBTAINED → CT/MRI may assist but should not delay consultation

TREATMENT:

- Initial treatment is aggressive management of shock with volume replacement and early use of vasopressors
- BEGIN ANTIBIOTICS IMMEDIATELY → PENICILLIN IV PLUS CLINDAMICIN 900MG TDS OR LINEZOLID 600MG Q12H
    - If penicillin allergic → CEFTRIAXONE 2G Q12H PLUS CLINDAMICIN 900MG TDS
- Although antibiotics is important, PROMPT AND AGGRESSIVE EXPLORATION AND DEBRIDEMENT OF SUSPECTED DEEP-SEATED STREPTOCOCCUS PYOGENES INFECTION SITES IS **MANDATORY**