



# MSS

## Microbiology

LEC no. 1



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# Cutaneous infections that manifest in maculopapular rashes (2)

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# Lecture overview

Category	Diseases	
Childhood Exanthems	Enteroviral rashes	
	Erythema infectiosum (Fifth disease/Slapped-cheek syndrome)	
	Roseola infantum (Exanthem subitum)	
	Scarlet fever	
	Rubeola (Measles)	
	Rubella	
Other Conditions	Infectious mononucleosis	EBV
	Secondary syphilis	Treponema pallidum
	Rocky Mountain spotted fever	Rickettsia transmitted via a tick bite.
	Toxic shock syndrome	mediated by s.aureous or s.pyogenes toxin

● Dr said "the cutaneous manifestations of each disease are extremely important. ▼"  
 ● Colored & underlined words and activities are also very important.

Other conditions cause **Maculopapular rashes**

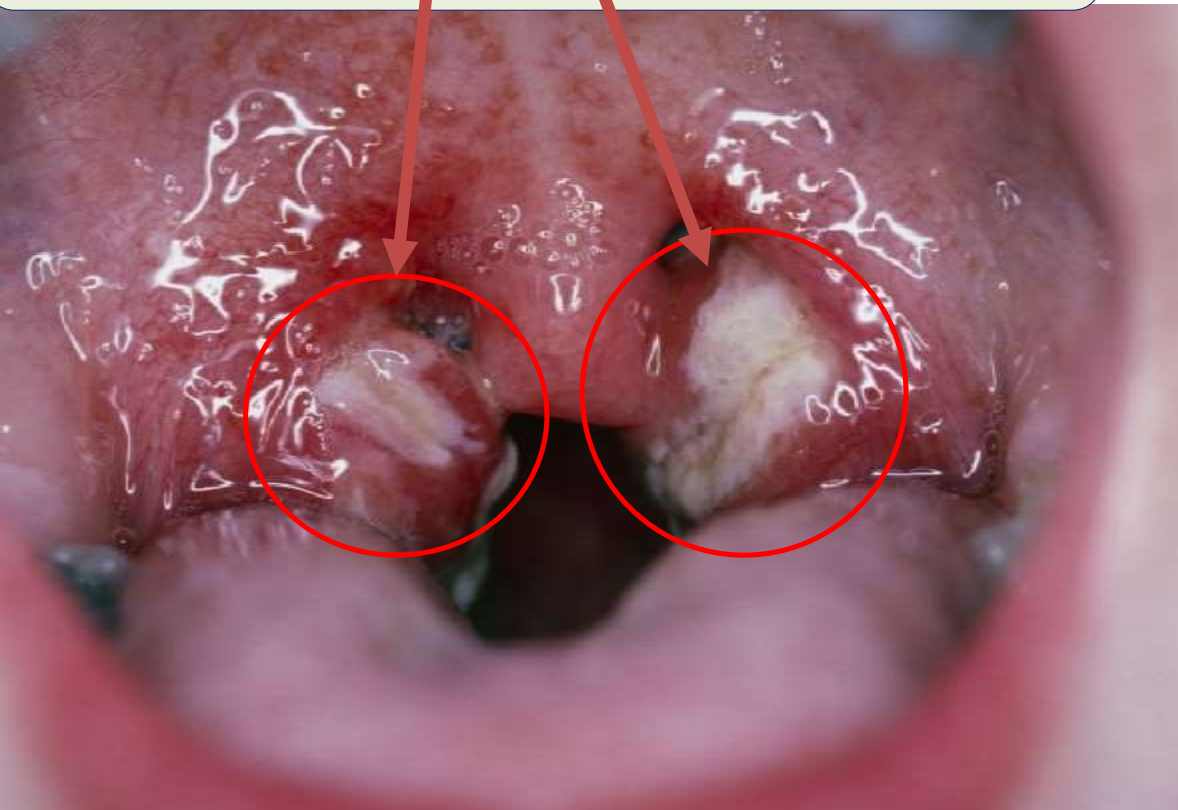
# 1. Infectious Mononucleosis

- Infectious mononucleosis can cause a rash in a certain subset of patients.
- Epstein-Barr virus (EBV) causes this disease and usually causes a regional lymphadenopathy due to its ability to infect B lymphocytes.  
Cutaneous Manifestations are important 🖱️ !!
- **1. Petechiae (نمش) on the hard and soft palates can be seen in 25-60% of patients.**
- **2. A maculopapular rash is usually faint, widely scattered, and erythematous, and occurs in 10-15% of patients. The rash is more common in young children.**



# Infectious Mononucleosis

Petechiae on the hard and soft palates  
With signs of **pharyngitis** !!



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A maculopapular rash is usually faint, widely scattered, and erythematous



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# Infectious Mononucleosis

- Infectious mononucleosis can be misdiagnosed as a streptococcal pharyngitis, with subsequent treatment with amoxicillin or ampicillin.
- About 80% of patients with EBV mononucleosis treated with amoxicillin or ampicillin develop **a widely scattered maculopapular rash** as a result of drug reaction .
- To avoid treating infectious mononucleosis with antimicrobial agent, *Streptococcus pyogenes* pharyngitis should be ruled out (استبعاد).

**Unnecessary antibiotic** use can lead to drug reaction developing an additional rash besides the EBV rash!!

## ADDITIONALLY:

Drug reactions occur if your body responds badly to a medicine.

Before giving any antibiotic, you should confirm the absence of *S. Pyogenes* through either a rapid strep test (via throat swab) or culture !!

# Infectious Mononucleosis - Epidemiology

- EBV is found worldwide and is common and relatively mild in children. The disease is usually more severe in young adults.
- **A skin rash develops in 10-15% of patients with infectious mononucleosis.** Not all of the Patients would develop a skin rash however it stills a common condition !!
- Most people are seropositive for EBV by age 25.

Why is EBV commonly known as the kissing disease??

- EBV is transmitted via saliva, sexual contact, organ transplantation, or blood transfusions from infected or convalescent persons.

# Infectious Mononucleosis - Pathogenesis

EBV is a Herpes virus that will be latent through out the life of infected individual

What is the site of infection and the site of latency for EBV?

**B cells**

Additionally: The RES is also known as the mononuclear phagocyte system, is a part of the immune system that is mainly present in the liver and spleen and takes up foreign bodies from the circulation to protect the body from their harmful effects.

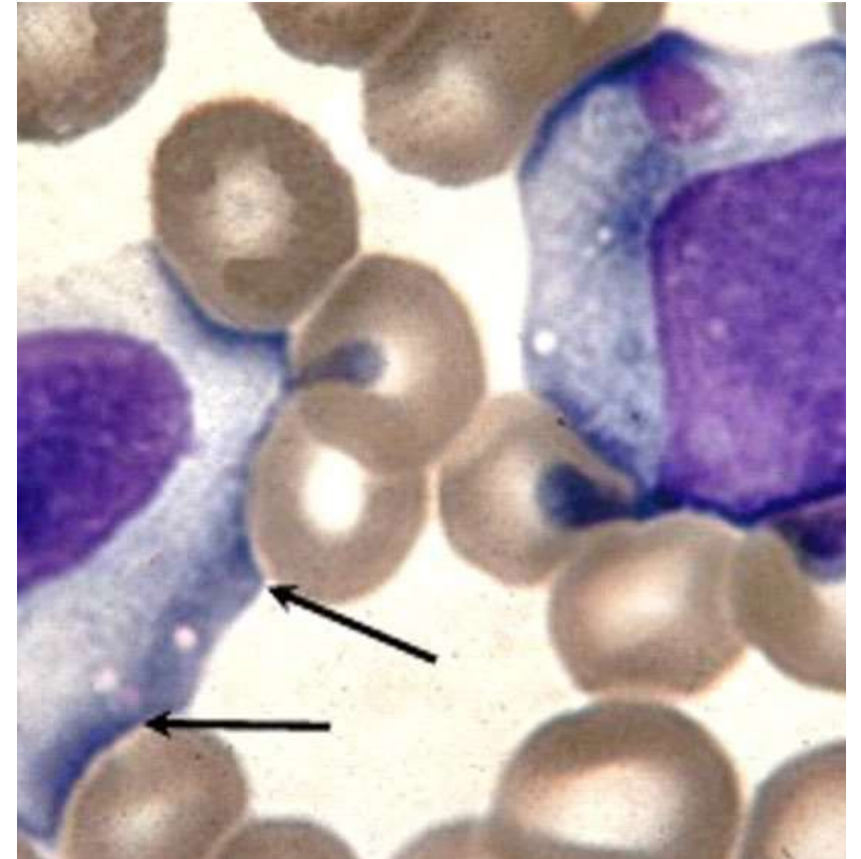
- EBV infects the B cells in the oropharyngeal epithelium, then the B cells spread the infection throughout the reticuloendothelial system.
- EBV infection of B cells results in humoral and cellular (**mainly**) responses. Some of the B cells (**humoral response**) produce antibodies that react with EBV antigens; **specific diagnose**  
however, other activated B cells produce antibodies that do not react with EBV antigens but react with antigens from other mammals (heterophile antibodies). **Non-specific diagnose**
- The virus is usually present in immune complexes responsible for the arthralgia and rash that occurs during the acute phase of the disease.
- The T-cell response (**cellular response**) is essential in the control of EBV infection.



# Infectious Mononucleosis - Diagnosis

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- In CBC with differential, leukocytosis with lymphocytosis is seen, with the presence of at least 10% atypical lymphocytes.
- Since other etiologic agents can cause similar CBC results, serologic testing must be performed.
- Serologic findings for EBV includes **1.** positive heterophile antibody tests (Monospot and Paul-Bunnell tests) and **2.** EBV-specific serology (VCA IgM, EA IgG, EBNA IgG).



Credit: Author: Peter Maslak; Susan McKenzie; American Society of Hematology (ASH); <https://imagebank.hematology.org/image/1867/infectious-mononucleosis--1>

# 2. Secondary Syphilis

- Syphilis manifests in three stages: primary, secondary, and tertiary. The stage with the most prominent skin lesions is secondary syphilis with many maculopapular lesions that cover most of the body.
- Syphilis is caused by *Treponema pallidum*, a spiral-shaped bacterium with a characteristic corkscrew motility so it can invade the skin.
- *T. pallidum* is too thin to be stained and observed with conventional light microscopy. The most rapid method of visualizing *T. pallidum* is darkfield microscopy.



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# Secondary Syphilis - Clinical Manifestations

What distinguishes secondary syphilis from neonatal/congenital syphilis ??

- In neonatal syphilis, the lesions can be vesicular, bullous حويصلات, or maculopapular.
- Unlike the childhood exanthems and infectious mononucleosis, lesions in secondary syphilis can be seen on the palms and soles.
- Other symptoms include condyloma lata **wart-like overgrowth** in the anogenital region (**mainly**), and/or on the oral, pharyngeal, and nasal mucosa.

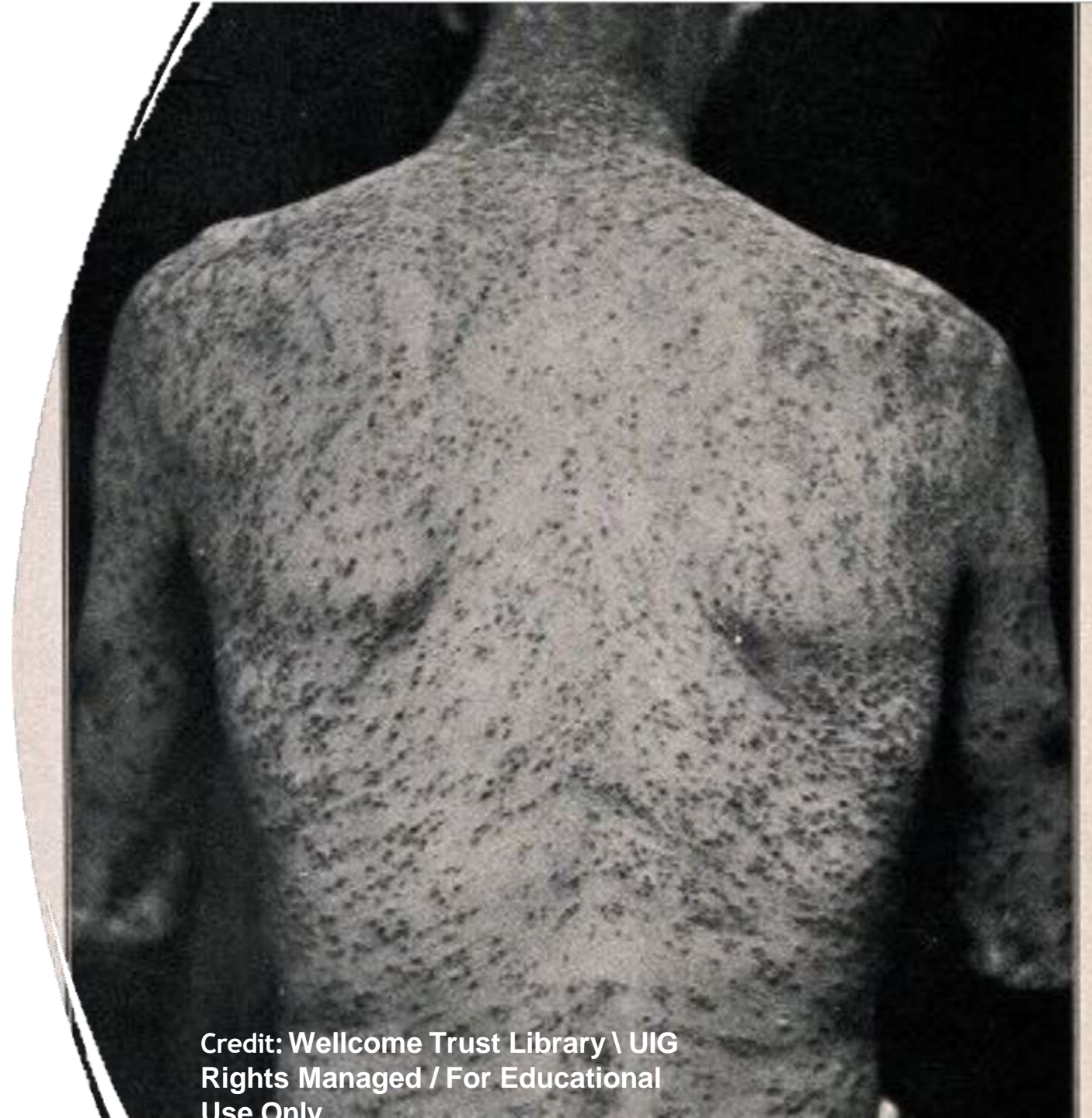


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# Secondary Syphilis - Clinical Manifestations

- In adults, secondary syphilis develops about 6-8 weeks after the appearance of the primary chancre (**painless ulcer**) and has a wide range of presentations such as malaise, fever, lymphadenopathy, myalgias, and arthralgias, **with a generalized erythematous maculopapular rash** over the entire body, **including the palms and soles** **!!**.
- The lesions regress **يختفي** without treatment, but relapses of the rash can occur in 20% of untreated patients.



# Syphilis - Epidemiology/Pathogenesis

- Syphilis is an STI. Sexually transmitted infection , it can also be transmitted from infected mother to her fetus during pregnancy
- The incidence of secondary syphilis is highest in sexually active men and women aged 20-45 years.
- Following contact with a break in the skin, *T pallidum* penetrates the lower layers of the skin and multiplies
- An inflammatory reaction occurs causing a **hard chancre** (**raised edematous ulcer**) (**primary syphilis**) . Histologic examination of the chancre demonstrates endarteritis and periarteritis and infiltration of the ulcer with macrophages and PMNs.



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Additionally:  
Endarteritis:inflammation of the inner lining of an artery.  
Periarteritis:inflammation around an artery.



# Secondary Syphilis Pathogenesis

- After skin penetration, *T. pallidum* enters the blood with spread to almost every organ, including **the skin**.
- The immune response causes the mucocutaneous lesions with maculopapular lesions on the skin, and condyloma latum.
- **All these lesions contain viable *T. pallidum* and are highly infectious because those lesions are formed as a result of body response against *T. pallidum*.**
- If the patient remains untreated, significant damage to the CNS, skin, and vasculature can occur, resulting in tertiary syphilis.

# Secondary Syphilis Diagnosis

- The diagnosis of secondary syphilis involves a complete history, physical exam, serologic tests (**mainly**), and darkfield microscopy of fluids from lesions. Two different serologic tests are used: screening tests and confirmatory tests.
- The **screening test** is a non-treponemal **Non specific test** test that detects the presence of antibodies reactive with cardiolipin. The non-treponemal serologic tests include the venereal diseases research laboratory (**VDRL**) and rapid plasma reagin (**RPR**) tests. False-positive results can occur; therefore, a confirmatory test is required following a positive result.
- **Confirmatory** or treponemal **specific test** tests include the *Tpallidum* immobilization (**TPI**), fluorescent treponemal antibody absorption (**FTA-ABS**), and micro-hemagglutination assay for *Tpallidum* (**MHA-TP**).

If the screening test gives positive result while the confirmatory test gives negative result. In such cases the secondary syphilis should be excluded

There is much false positive in screening tests.  
القرار النهائي لل confirmatory test

# Secondary Syphilis Treatment and Prevention

- **Benzathine penicillin** is the antibiotic of choice for treatment of primary and secondary syphilis.

**Jarisch-Herxheimer reaction** is a normal reaction ,you should **not** stop the treatment

- Many treated patients will develop a **Jarisch-Herxheimer reaction** within 6-12 hours after initial antibiotic treatment This reaction usually includes malaise, fever, headache, and temporary exacerbation of the skin lesions. The reaction usually subsides within 24 hours.
- The non-treponemal tests are helpful to determine the efficacy of the antibiotic treatment with declining antibody levels after successful treatment. Antibody levels to treponemal antigens remain detectable for the lifetime even following successful treatment.
- Preventive measures identifying and treating their sexual contacts and avoiding sexual contact with other syphilitic patients.

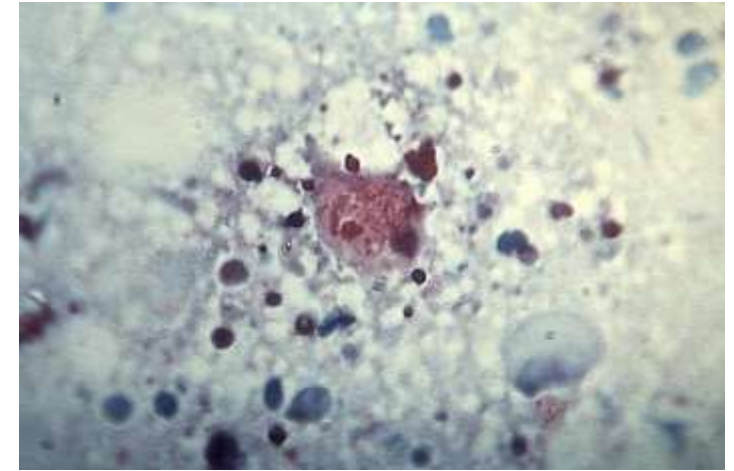
# 3. Rocky Mountain spotted fever (RMSF)

!! Pay attention :

What the most common tick-borne infection in the United States?

Answer: lyme disease also has cutaneous manifestations

- Rocky Mountain spotted fever (RMSF) is **the most common rickettsial tick-borne infection in the United States.**
- RMSF is caused by Rickettsia rickettsii which is an obligate intracellular bacterium transmitted via a **tick bite.**



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# RMSF - Manifestations

- 5-10 days after a tick bite, fever, nausea and vomiting, severe headache, myalgia, and anorexia can occur.
- The majority of RMSF patients present with a rash 3 days after the bite. A unique manifestation of this disease is that the rash begins as erythematous macules on the wrists and ankles.
- Damage to the blood vessels can cause partial paralysis of the lower extremities; gangrene requiring amputation of fingers, toes, arms, or legs; and conditions including hearing loss, loss of bowel or bladder control, movement disorders, or language disorders.



Gangrene due to the blood vessels occlusion

# RMSF - Pathogenesis

The Manifestations are due to the replication of rickettsia inside the cells, it is an obligate intracellular

- After the tick bite, *Rickettsia* spread via lymphatics to the blood and attach to endothelial cells.
- Pathology in RMSF is due to increased vascular permeability with a subsequent host mononuclear cell response.
- The increased vascular permeability can lead to edema and hypovolemia. The rash is due to what?
- Eventually, the classic petechial rash of RMSF develops due to hemorrhage of the capillaries.
- Vascular damage can cause CNS, GI, renal, and hepatic manifestations.

# RMSF - Diagnosis

- Culturing for the organism is rarely performed.
- An indirect immunofluorescence assay (IFA) can be performed on blood samples.
- Immunostaining of a biopsy of the rash can also be performed.
- PCR is now performed on blood and skin biopsies.
- Routine laboratory test results suggestive of RMSF include leukocytosis, thrombocytopenia, hyponatremia, or elevated liver enzyme levels.

# RMSF - Treatment and Prevention

Fatal disease!!

PAY attention: Doxycycline is contraindicated for pregnant

- Because of the severity of RMSF, treatment with doxycycline should be initiated immediately when there is a suspicion of the disease.
- Chloramphenicol is prescribed for patients who are pregnant.
- Treatment should not be delayed until laboratory confirmation is obtained.
- An important method of preventing disease is for anyone exposed to tick-infested areas to promptly and carefully inspect and remove attached ticks. It usually takes several hours for an attached tick to transmit the RMSF bacterium; therefore, prompt removal of attached ticks can prevent transmission of the disease.

# 4. Toxic shock syndrome (TSS)

Toxin mediated

- Toxic shock syndrome (TSS) is an uncommon but severe systemic life-threatening disease that follows exposure to a bacterial superantigen produced by certain strains of *S. aureus* and *S. pyogenes*.
- The most common cause of TSS is *S. pyogenes* strains producing either superantigen SPE A or C.
- *S. aureus* also causes TSS. Staphylococcal TSS can occur during menstruation or following a localized staphylococcal infection (non-menstrual TSS). Staphylococcal TSS is caused by the superantigen exotoxin TSS toxin-1 (TSST-1) or enterotoxins.

-*S. pyogenes* TSS is more severe than *Staph aureus* TSS  
-Superantigen causes non-specific T cells activation.



# Toxic shock syndrome - Clinical Manifestations

- Streptococcal TSS is defined as any group A streptococcal infection associated with the early onset of shock and organ failure.
- A diffuse scarlatina-like erythema is seen in only about 10% of patients with streptococcal TSS.
- Staphylococcal TSS is an acute-onset illness characterized by fever, hypotension, and **rash** and can lead to multi-organ failure and shock.
- **The rash appears later in the disease and has a sunburn-like appearance.** Desquamation frequently is seen in patients who survive. The desquamation is especially prominent on the palms and soles.

# Toxic shock syndrome - Epidemiology

- People of any age can be affected, and many do not have any predisposing conditions. In some cases, viral infections such as chickenpox and influenza have provided a portal for infection.
- The mortality rate of streptococcal TSS is 30-70%. Streptococcal TSS occurs after an invasive infection (e.g., bacteremia, pneumonia).
- Infection begins at a site of minor local trauma. Many cases have developed within 24-72 hours of minor non-penetrating trauma.

# Toxic shock syndrome - Epidemiology

- Non-menstrual staphylococcal TSS commonly follows superinfection of an upper respiratory tract after viral infection. Other staphylococcal infections can cause non-menstrual TSS (e.g., infected surgical wounds, abscesses, infected burns, and deep and superficial soft tissue infections).
- Menstrual staphylococcal TSS is defined as occurring during menstruation or within the 2 days preceding its onset or the 2 days following its cessation. This form of TSS is associated with tampon use.
- The mortality rate is about 5% for both menstrual and non-menstrual TSS.

Which is less than *s.pyogenes*

# Toxic shock syndrome - Pathogenesis

- Production of streptococcal pyrogenic exotoxins A and C cause the signs and symptoms seen in streptococcal TSS.
- Staphylococcal TSS can occur in menstruating women following overgrowth of *S aureus* in superabsorbent tampons or in tampons that remain in the vagina an excessive amount of time.
- *S aureus* is commonly found in the vaginal mucosa; however, only strains that produce TSST-1 can cause TSS.
- In both staphylococcal and streptococcal TSS, superantigens cause overactivation of the immune system, which activates immune cells to produce increased levels of cytokines.

# Toxic shock syndrome - Pathogenesis

The details aren't required

what you need to know that the toxin (superantigen) leads to massive activation of T cells and massive release of cytokines.

- Superantigens activate the immune system by simultaneously binding to MHC class II molecules and the TCR in the V- $\beta$  region.
- Superantigen binding results in the activation of numerous antigen-presenting cells and T cells, with subsequent systemic release of cytokines. Superantigens can stimulate over 20% of all T cells, whereas a conventional antigen stimulates only about 0.01% of the T cells.
- The high levels of cytokine cause the clinical features of both staphylococcal and streptococcal TSS (i.e., fever, hypotension, rash).
- The major cytokines released by superantigens are tumor necrosis factor (TNF)  $\alpha$  and  $\beta$ , interleukin-1 (IL-1), IL-2, and interferon- $\gamma$  (IFN- $\gamma$ ).
- TNF alpha and beta cause capillary leakage leading to peripheral pooling of blood and shock. IL-1 causes fever. IL-2 and IFN- $\gamma$  cause a rash.

# Toxic shock syndrome - Diagnosis

- Streptococcal TSS can be difficult to diagnose
- A set of clinical and laboratory criteria can aid in determining the diagnosis.
- Because of the difficulty in diagnosing TSS, the Centers for Disease Control and Prevention has developed a case definition of characteristic clinical criteria (Criteria for toxic shock syndrome and STSS).



# Toxic shock syndrome - Treatment and Prevention

- Treatment includes **aggressive fluid replacement** and IV treatment with antibiotics (e.g., oxacillin or nafcillin).
- In non-menstrual TSS, removing the localized staphylococcal infection is essential.
- **Unless if there is MRSA (Methicillin-resistant Staphylococcus aureus), Vancomycin should be given.**
- Treatment of streptococcal TSS includes identification of the site of infection and surgical debridement, aggressive fluid replacement, and intravenous antibiotics.
- Frequent handwashing and measures to prevent spread of these superantigen-producing bacteria can be helpful.

-عينٌ على أهل غزّة العزّة:  
تخيّل كطبيب تعمل 4 شهور دون طعام جيّد، بدون راتب، متعب، تواجه ضغطاً نفسياً وعصبياً في كلّ لحظة على مدار اليوم، مهدّد بالقتل، مطالب بالتعامل مع حالات لا حصر لها في السّاعة، لا نوم لا راحة، كلّ عملك في نبش الأعصاب والأوردة والجراحات المعقّدة، أصعب المشاهد تمرّ أمامك في كلّ لحظة ما بين مصاب يتألّم، و جريح ينزف، وآخر روحه تخرج أمامك وانت لا تملك أبسط الأدوات الطبيّة اللازمة لإنقاذه!

اللهم ارض عن أطباء غزّة الأبطال وألبسهم ثياب البركة وحرّم على النّار عيونهم الساهرة على ثغر الدين وهي ترابط في سبيلك وتخفف من آلام عبادك.

أنت على ثغر، فلا نوتينّ من قبلك.

-اللَّهُمَّ رَبَّنَا إِنَّا نَبِرُ إِلَيْكَ مِنْ هَذَا الْخِذْلَانِ، اللَّهُمَّ فَرِّجْ عَنْ أَهْلِنَا وَاخْوَانِنَا الْمَظْلُومِينَ، وَاعصمنا من السير في ركاب الظالمين.

أنت ربّ المستضعفين!  
يا ربّ.

# Thanks for listening!