

1. Staphylococci survival

**The Staphylococci are able to survive in the environment for long periods of time.**

Non spore-forming  
Dessication resistant  
Heat resistant  
Resistant to high salt concentrations

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2. Human Pathogens (1)

## **Human Pathogens**

*Staphylococcus aureus*

**Responsible for a broad spectrum of clinical syndromes**

*Staphylococcus epidermidis*

**Medical device-related infection**

*Staphylococcus saprophyticus*

**Urinary tract infection**

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3.

## History

# History

A 39 year-old IV drug user with no significant past medical history presents to the ER with a two day history of high fevers, shaking chills, night sweats, and increasing shortness of breath. He last injected himself with cocaine three days prior to admission. He injected with a clean needle.

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4.

## Physical Exam

# Physical Exam

You note an ill-appearing, immobile young man. Vital signs are temp 104.5, pulse 108, respirations 20, and BP 120/60. Rales are noted in the right lower lung field. A II/VI systolic murmur is heard at the lower left sternal border. You notice a red, warm, fluctuant 3 cm area over a vein on the dorsal surface of the right hand suggestive of an abscess.

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5.

Further Work-up

## Further Work-up

- You order a pulmonary arteriogram. This demonstrates a perfusion defect in the right lower lobe suggestive of an embolus.
- You order a cardiac echo.

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Valves

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## 7. The Encounter

### The Encounter

The reservoir for *S. aureus* in adults is the human axillae, nares, external genitalia. In neonates, *S. aureus* is found in umbilical stump, perineal area, skin, and gastrointestinal tract.

The carriage rate is approximately 30% in the general population. Health care workers as well as diabetics, intravenous drug users, and patients on hemodialysis have higher carriage rates.

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## 8. Intranasal mupirocin: Prevention of Clinical Infection

### Intranasal mupirocin: Prevention of Clinical Infection

- Ability to prevent *S. aureus* infection is modest
- Flora of nares is altered
- Increase in infections caused by gram-negative organisms
- Mupirocin-resistant strains

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## 9. Entry/Multiplication

### **Entry**

*S. aureus* gains entry to deeper tissues after trauma, surgery, or instrumentation breach integrity of the skin or mucous membranes.

### **Multiplication**

*S. Aureus* is specialized for survival in the host as an extracellular pathogen

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## 10. Treatment and Resistance

### **Treatment And Resistance**

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13. Vancomycin-intermediate (VISA) and Vancomycin-resistant (VRS...

**Vancomycin-intermediate (VISA) and  
Vancomycin-resistant (VRSA) *S. aureus***

VISA

Is the result of a thickened peptidoglycan layer  
Vancomycin is unable to penetrate peptidoglycan  
to reach the cell membrane  
Several reports in US, all MRSA as well

VRSA

Is the result of the *vanA* gene from vancomycin-resistant enterococcus  
Makes D-alanine-D-lactate instead of D-alanine-D-alanine  
Two cases in US have come from patients harboring VRE

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14. Vancomycin-resistant MRSA

**Vancomycin-resistant MRSA**

Linezolid

Inhibits bacterial protein synthesis by binding to 23S rRNA,  
Bacteriostatic against *Staphylococci*  
Resistance is uncommon and involved a point mutation of 23S rRNA

Daptomycin

Depolarizes the cell membrane of susceptible bacteria=no energy  
Inhibits DNA/RNA/protein synthesis  
Bactericidal

Synercid: dalbapristin/ quinupristin

Inhibitor of protein synthesis

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15. Virulence factors (1)

## **Virulence Factors**

**Cell-associated adhesins  
(colonization of tissues)**

**Secreted proteins  
(creation of a hospitable extracellular milieu)**

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16. Secreted Proteins

### **Secreted Proteins**

- 1) Proteases
  - 2) Lipases
  - 3) Thermostable DNase
- } (Nutrients from extracellular matrix)

4) Fatty Acid-Modifying Enzyme (FAME): Esterifies long-chain, bacteriocidal fatty acids, which are found in abscesses, to alcohols. Found in 80% of SA strains. May prolong bacterial survival in abscesses

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17. Other Secreted Proteins of Note

## Other Secreted Proteins of Note

Coagulase: Non-enzymatic activator of thrombin resulting in the conversion of fibrinogen to fibrin. Coagulase is the traditional marker for distinguishing *S. aureus* from *S. epidermidis*.

Staphylokinase: Non-enzymatic activator of plasminogen resulting in thrombolysis. Related protein streptokinase used for dissolution of clots.

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18. Exotoxins

## Exotoxins

(secreted toxins)

### Membrane-damaging agents

\* $\alpha$ -toxin  
 $\beta$ -toxin  
 $\delta$ -toxin  
 $\gamma$ -toxin  
Leukocidin  
\*Panton-Valentin leukocidin

### Superantigens

TSST-1  
Staphylococcal enterotoxin  
Exfoliative toxins

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19.

$\alpha$  -toxin

## $\alpha$ -toxin:

- Most potent membrane-damaging toxin of *S. aureus*.
- Binds to the membrane of platelets and monocytes
- Forms pores through which monovalent cations may pass.
- End result is release of cytokines.
- Responsible for septic shock that occurs during severe infections caused by *S aureus*.

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Panton-Valentin leukocidin

## Panton-Valentin leukocidin

- Leukotoxic
- Non-hemolytic
- 2% of all *S. aureus* isolates express P-V leukocidin
- 90% of dermonecrotic lesions express P-V leukocidin
- Thought to be important in necrotizing skin infections

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21.

Toxin-related disease

## Toxin-related disease

- Staphylococcal Scalded skin syndrome: intra-epidermal blisters, scalding in neonates and children (exfoliative toxin)
- Toxic Shock Syndrome: fever, skin rash, hypotension, multi-system failure (Caused by superantigens: TSST-1 or one of staphylococcal enterotoxins)  
Menstrual-associated with vaginal colonization with TSST-1 producing SA  
Non-menstrual: correlated with SA infection elsewhere in body
- Food poisoning: leading cause of food-borne microbial intoxication world-wide; caused by enterotoxins in improperly stored food; characterized by nausea, vomiting, diarrhea-onset 4 hrs after eating, lasts 24 hours,

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22.

Pyrogenic Toxins

### Pyrogenic Toxins: Staphylococcal enterotoxins and TSST-1

- **Agents of toxic shock syndrome when the bacterium is present as colonizer or pathogen.**
- **Staphylococcal enterotoxins are agents of food poisoning when only the toxin is present in food.**

### Exfoliative Toxins

- **Cause intra-epidermal peeling probably due to enzymatic degradation of matrix proteins.**
- **Also act as superantigens, but 100 times less potent than Staphylococcal enterotoxin and TSST-1.**

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23. Regulation of Virulence Factors

## Regulation of Virulence Factors:

### *agr* locus

- encodes a signalling system activated by a bacterial density-sensing peptide
- negatively regulates synthesis of cell surface proteins
- activates secreted factors

### *sar* locus

- encodes a DNA-binding protein
- activates hemolysins
- activates fibronectin binding proteins
- activates lipase

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24. Epidemiology

## Epidemiology

*S. epidermidis* is a normal inhabitant of human skin.

In the normal host, *S. epidermidis* cannot cause infection in the absence of a foreign body, even if the skin has been compromised. Exceptions are neonates, IV drug users

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Virulence Factors (2)

## Virulence Factors

### Adherence to biomaterials

Fimbriae: SSP-1, SSP-2

AtIE: surface-associated autolysin

Capsular Polysaccharide/Adhesin (slime)

**Role of Extracellular Enzymes and Toxins in pathogenesis has not been established.**

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26.

Patient history

**The patient is a 70 year old man status post a coronary artery bypass who has been hospitalized for one week. Sternal instability is noted and determined to be due to breakage of sternal wires. Sternum is opened, cultures are taken, and metal plates are inserted to stabilize the sternum. Approximately one week later, a rectangular area of redness is noted centered about the sternal incision. The patient is treated with vancomycin, but area of redness continues to spread.**

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27.

Therapy (1)

## Therapy

1) Removal of the foreign body

2) Vancomycin, synercid, linezolid

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Staphylococcus saprophyticus

*Staphylococcus saprophyticus*

Urinary tract infections

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29.

Therapy (2)

## Therapy

No different than any other urinary tract pathogen!  
Tmp/SMX, ampicillin, cephalosporins, quinolones

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30.

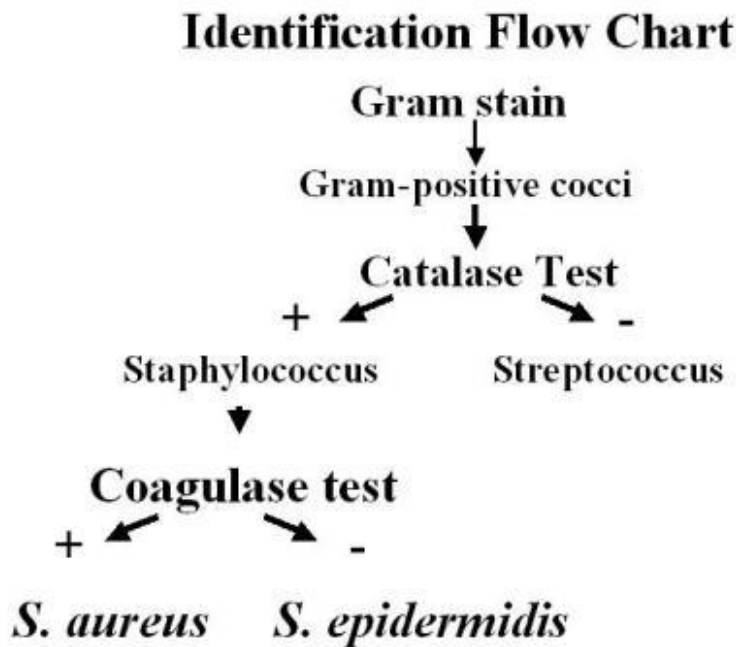
Identification of Staphylococcal Species

## Identification of Staphylococcal Species

- 1) clinical presentation
- 2) colony morphology: *S. aureus*: golden,  
 $\beta$ -hemolytic colonies, *S. epidermidis*: white,  
non-hemolytic
- 3) gram stain: Is it gram-positive or gram-negative?  
Is it a coccus or a rod? Is it in clusters?

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31. Identification Flow Chart



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32. Human Pathogens (2)

## Human Pathogens

*Staphylococcus aureus*

**Abscess formation**  
**Toxin production**  
**Food poisoning**

*Staphylococcus epidermidis*

**Medical device-related infection**

*Staphylococcus saprophyticus*

**Urinary tract infection**

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