Disclosure
My Background at Penn

• My Background at Penn:
  – 1980-1987 Ph.D. Studies
  – 1994- Instructor, School of Dental Medicine
  – 1995-1997 Adjunct Asst. Prof. (Geriatrics – Risa Mourey)
  – 2007- Pres Adjunct Asst. Prof. (Geriatrics – Jerry Johnson)

• Other:
  – 1970-1976 Army National Guard
  – 1976-1978 Grad. Teaching Asst for Master’s Degree – West Chester University
  – 1982-1988 Smithkline Beecham
  – 1996 Founder Of PA Osteoporosis Society
Device Implants and New Concepts of Bacterial Resistance – The Mystery

Al Giovenella, Ph.D.
December 14, 2012
Bacteria been able to survive for so many eons because:

1. they have resistance to threats from the environment
2. they have virulence factors for defense or aggression
3. they have means of adaptation to change
4. all of the above
Bacterial Evolution

- Millions of years in days
- Why have they persisted for so long?
  - Resistance to threats from environment
  - Virulence factors for aggression or defense
  - Adaptation to change
Which bacterial species is the most frequent isolate from diseases of the elderly?

1. Escherichia coli
2. Staphylococcus aureus
3. Pseudomonas aeruginosa
4. Mycobacterium tuberculosis
In Diseases of Elderly

- Numerous diseases, but focusing on bone, prosthetic devices
  - Osteomyelitis
  - Septic Arthritis
- Bacteria of highest incidence
  - Staphylococcus aureus
  - Staphylococcus epidermidis
  - Streptococcus faecalis (Enterococci)
  - Streptococcus pyogenes

- Wright JA and Nair SP, Int J Med Micro 2010; (300): 193-204
The number of hip replacements & knee replacements done each year are:

1. 10,000 hip / 50,000 knee
2. 1500 hip / 2500 knee
3. 250,000 hip / 400,000 knee
4. 1 million hip / 3 million knee
By 2030, these numbers are expected to increase by:

1. 100%
2. 20%
3. 50%
4. 200%
Joint Replacements

• In the USA alone, 250,000 hip replacements and 400,000 knee replacements are performed every year.

• These numbers are expected to double before the year 2030 because of
  – The general increase in average age globally
  – Growing demands for a higher quality of life

WBCs

Staphylococcus aureus

Streptococcus faecalis (Enterococci)

Vancomycin resistance genes

Streptococcus faecalis (Enterococci)

Adapted from Granulocyte (Google Wikimedia Commons): Neutrophil2.jpg

-Bacteria – Giovenella A
Traditional Means of Becoming Resistant

Small Colony Variants (SCVs) and Biofilms

e.g. resistant organisms
Adapted from Sendi P and Proctor RA, *Cell* 2004 (Jan): 54-58
Staphylococcus aureus, Biofilms, and Small Colony Variants

- Prosthesis
- Biofilm around prosthesis
- Additional (or same) Niche
- V - Resistance
- Vancomycin (V) 5 min → 1 Hr
- Slowly-increasing concentration of V
- SCVs
- Section through biofilm
- Stress Response
- Additional (or same) Niche
- e.g. S. epidermidis at HUP

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Staphylococcus aureus, Biofilms, and Small Colony Variants

- Prosthesis
- Biofilm around prosthesis
- Additional (or same) Niche
- V - Resistance
- Staph DNA

Vancomycin (V)

5 min ➤ 1 Hr

Slowly-increasing concentration of V

SCVs

Section through biofilm

Stress Response

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MULTI-SPECIES:
Staphylococcus aureus, Candida albicans
Biofilms, and Small Colony Variants

Vancomycin (V) 5 min 1 Hr
Slowly-increasing concentration of V
SCVs
Section through biofilm
Prosthesis
Biofilm around prosthesis
Quorum-sensing, auto-inducers
S. aureus
C. albicans
Additional (or same) Niche
Staph DNA

V - Resistance
Stress Response

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Case Report

- A patient with pacemaker endocarditis:
  - A man aged 56 years was admitted with a 4-day history of nausea, vomiting, and shaking chills. Physical examination showed a temperature of 39.3 degrees C and tenderness in his upper right quadrant. *Staphylococcus aureus* grew from blood cultures. He was treated intravenously with 12 gm cloxacillin daily for 4 weeks. 1 week after discharge he developed nausea, vomiting, fever, and sweating. Again, *S. aureus* grew from blood cultures. For 6 weeks he was treated with 12 gm intravenous cloxacillin daily and with 600 mg oral rifampicin daily. There were no signs of endocarditis. He promptly responded to antibiotic therapy, but was readmitted a third time 9 days after discharge with the same symptoms. Once again, *S. aureus* grew from blood cultures. The entire pacing system was removed and intravenous cloxacillin was continued for 4 weeks. He remained well thereafter. Swabbing of the infected pacemaker lead recovered *S. aureus*, and examination by electron microscopy showed localized accretions of coccoid bacteria.

Vaccine Fails to Prevent Infections in Heart Surgery
by Ed Susman, Contributing Writer, MedPage Today (Oct. 21, 2012)

- Vaccine developed to prevent surgical wounds from infection with *Staph aureus*
- 201 of 3,958 patients who were inoculated with the S.aureus vaccine V710 died – a rate of **5.7 per 100 person/years** -- compared with 177 deaths (**5.0 per 100 person/years**) among 3,967 patients given placebo
  – Vance Fowler Jr, M.D., M.P.H., Prof of Med. At Duke University School of Medicine

- V710 was not efficacious in preventing S. aureus bacteremia and/or deep sternal wound infection, despite eliciting a robust antibody response.
  – Fowler

- The vaccine may have actually increased mortality when compared with placebo.
- Among patients who developed infection, those who were given the vaccination were more likely to develop multiple organ failure.
  – Fowler, Susman

- Susman E, MedPage Today 2012 (Oct 21)
Summary

• Infections of implants are growing in number because of the increase in the aging of the population, and the numbers of procedures being done.

• The infecting organisms, mainly Staphylococcus aureus, have made a considerable number of evolutionary adaptations that make them a challenging etiology.

• We will meet these challenges if we pay attention to the organisms virulence factors that make these such difficult to treat infections.

• It is felt by a group of scientists that these non-routine factors make this infection an important potential model for the treatment of cancer.

- Giovenella A 2012
Answers

1. 4

2. 2

3. 3

4. 1