Infectious Diseases
2015

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Director of Infectious Diseases & Microbiology
The Stamford Hospital
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Outline

• Overview
• Antibiotic resistant infections
• New Enterovirus infections
• Ebola
• MERS
• Arbovirus infections
Complexity of human infectious diseases on a global scale:

*pity the infectious diseases specialist!*

- 342 human infectious diseases
- 2000 pathogens
- 240 diagnostic tools
- 65 vaccines
- 269 anti-infective drugs
- 9979 drug trade names
- 220 countries
## Newly identified infectious diseases

<table>
<thead>
<tr>
<th>Year</th>
<th>Disease Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>Powassan, Heartland, Bourbon virus</td>
</tr>
<tr>
<td>2014</td>
<td>Enterovirus D68</td>
</tr>
<tr>
<td>2013</td>
<td>Chikungunya</td>
</tr>
<tr>
<td>2012</td>
<td>MERS</td>
</tr>
<tr>
<td>2009</td>
<td>H1N1pdm influenza</td>
</tr>
<tr>
<td>2005</td>
<td>H7N9 and H9N2 influenza</td>
</tr>
<tr>
<td>2004</td>
<td>ESBL / CRE infections</td>
</tr>
<tr>
<td>2003</td>
<td>SARS</td>
</tr>
<tr>
<td>2002</td>
<td>VRSA</td>
</tr>
<tr>
<td>1999</td>
<td>Nipah virus</td>
</tr>
<tr>
<td>1999</td>
<td>West Nile Virus (new world)</td>
</tr>
<tr>
<td>1997</td>
<td>H5N1 influenza</td>
</tr>
<tr>
<td>1996</td>
<td>nCJD (mad cow disease)</td>
</tr>
<tr>
<td>1995</td>
<td>HHV-8 (Kaposi sarcoma virus)</td>
</tr>
<tr>
<td>1994</td>
<td>Hantavirus</td>
</tr>
<tr>
<td>1992</td>
<td>MDR-Tuberculosis</td>
</tr>
<tr>
<td>1989</td>
<td>Hepatitis C</td>
</tr>
<tr>
<td>1988</td>
<td>Hepatitis E, HHV-6</td>
</tr>
<tr>
<td>1983</td>
<td>HIV/AIDS, Helicobacter</td>
</tr>
<tr>
<td>1983</td>
<td>E. coli O157:H7, Lyme disease</td>
</tr>
<tr>
<td>1980</td>
<td>HTLV I, II</td>
</tr>
<tr>
<td>1978</td>
<td>Clostridium difficile colitis</td>
</tr>
<tr>
<td>1976</td>
<td>Ebola, Legionnaires disease</td>
</tr>
</tbody>
</table>
A Historical Perspective

- Greece and Egypt accounts describe epidemics of smallpox, leprosy, tuberculosis, meningococcal infections and diphtheria prior to 1000 BC.
- Smallpox and plague killed 25% to 90% of naïve populations from Athens to Europe to North and South America from 400BC to 1600 AD.
- These plagues contributed greatly to collapse of Spartans, Roman Empire, Aztec civilization.
- Although the epidemiology of infectious diseases was well described by John Snow (cholera in London) and Ignatz Semmelweiss (puerperal fever in Vienna) microbial causes were not apparent.
- It remained for Louis Pasteur in 1857 and Robert Koch in 1867 to introduce the concept that microorganisms were pathogens and could cause disease.
A Historical Perspective

- In the 18th and 19th century, TB ("consumption") was the leading cause of death in the US, the life expectancy was 40 years, and infant mortality was astronomical.
- There were no effective medicinal treatments.
- There were epidemics related to impure foods, contaminated water supplies, inadequate sewage disposal, and poor housing conditions.
- Yellow fever, malaria and smallpox were common in the Northeast U.S.
- Infectious diseases, poverty and squalor became the subjects of great literary works (*The Jungle, Cannery Row*).
- Such ravages led to the “quarantine” system of public health which was instituted in 1873.
Dramatic decline in infectious disease mortality preceded the antibiotic era

FIGURE 1. Crude death rate* for infectious diseases — United States, 1900–1996†

*Per 100,000 population per year.
## EVOLUTION OF ANTIBIOTIC RESISTANCE: Rate of Development

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Year Deployed</th>
<th>Resistance Observed</th>
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<tbody>
<tr>
<td>Sulfonamides</td>
<td>1930s</td>
<td>1940s</td>
</tr>
<tr>
<td>Penicillin</td>
<td>1943</td>
<td>1946</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>1943</td>
<td>1959</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>1947</td>
<td>1959</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>1948</td>
<td>1953</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>1952</td>
<td>1988</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>1956</td>
<td>1988</td>
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<tr>
<td>Methicillin</td>
<td>1960</td>
<td>1961</td>
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<tr>
<td>Ampicillin</td>
<td>1961</td>
<td>1973</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>1960s</td>
<td>late 1960s</td>
</tr>
</tbody>
</table>

Table 20.2 Microbiology: A Clinical Approach (© Garland Science)
Factors known to increase prevalence of resistance

- Appropriate antibiotic prescribing
- Inappropriate antibiotic prescribing
- Excessive treatment
  - Chronic treatment
  - Repeated courses of rx
- Overuse, particularly in a health care facility
- Inadequate dosing
- Inadequate surgery / drainage
- Poor infection control practices
- Antibiotic use in animal feed
The crisis in antibiotic resistance 1992

The synthesis of large numbers of antibiotics over the past three decades has caused complacency about the threat of bacterial resistance. Bacteria have become resistant to antimicrobial agents as a result of chromosomal changes or the exchange of genetic material via plasmids and transposons.

*Streptococcus pneumoniae, Staphylococcus aureus*, organisms that cause respiratory and cutaneous infections; and members of the *Enterobacteriaceae* and Pseudomonas families, organisms that cause diarrhea, urinary infection, and sepsis, are now resistant to virtually all of the older antibiotics.

The extensive use of antibiotics in the community and hospitals has fueled this crisis. Mechanisms such as antibiotic control programs....and better hygiene....need to be adopted in order to limit bacterial resistance.

ID Physicians Warn of Brewing “Superbug” Crisis

Infectious Diseases Society of America Proposes Federal Measures to Spur Antibiotic Development

http://www.idsociey.org
What you need to know
WHO's first global report on antimicrobial resistance, with a focus on antibiotic resistance, reveals that it is no longer a prediction for the future. Antibiotic resistance - when bacteria change and antibiotics fail - is happening right now, across the world.

The report is the most comprehensive picture to date, with data provided by 114 countries.

Looking at 7 common bacteria that cause serious diseases from bloodstream infections to gonorrhoea.

High levels of resistance found in all regions of the world.

Significant gaps exist in tracking of antibiotic resistance.

Over the last 30 years, no major new types of antibiotics have been developed.

What does this mean?
Without urgent action we are heading for a post-antibiotic era, in which common infections and minor injuries can once again kill.

How can infections be prevented in the first place to reduce the need for antibiotics?

- Better hygiene
- Access to clean water and sanitation
- Infection control in healthcare facilities
- Vaccination

What you can do
- Use antibiotics only when prescribed by a health professional
- Complete the full prescription, even if you feel better
- Never share antibiotics with others or use leftover prescriptions
Crisis in Antimicrobial Drug Development

Dramatic Decrease in Antibiotic Drug Approvals

Source: Spellberg, CID 2004, Modified

New Antibiotic Drug Approvals

Years

'83-'87 '88-'92 '93-'97 '98-'02 '03-'07 '08-'12

0 2 4 6 8 10 12 14 16

Trends in Antimicrobial Resistance 2015: ESCAPE pathogens

- *Enterococcus* (VRE)
- *Staphylococcus aureus* (MRSA and VISA)
- *Carbapenem resistant Enterobacteriaceae (CRE) E coli, Klebsiella, Enterobacter* (and others: NDM-1, etc)
- *Acinetobacter* (multi-drug resistant)
- *Pseudomonas* (FQ resistant)
- *Extended spectrum beta-lactamase producing GNR (ESBL positive E. coli, Klebsiella, Enterobacter)*
  - plus
- *Clostridium difficile* (NAP-1 strains, and others)
Staphylococcal Infections
A Nasty Bug Breaks Out
Drug-resistant staph bacteria now stalk even students

By Lindsay Lyon

The trouble started in May, when a 12-year-old boy had a temperature of 104°F and was fighting for her life. She was taken to a hospital in California where the MRSA (methicillin-resistant Staphylococcus aureus) bacteria was suspected. The treaters were surprised to find out that the bacteria was resistant to most antibiotics.

MRSA is a common bacteria that can cause skin infections such as boils and abscesses. In severe cases, it can lead to blood infections and even death. The bacteria has become resistant to many antibiotics, making it difficult to treat.

The bacteria has spread rapidly in recent years, particularly in hospitals and other health care facilities. It is transmitted through contact with infected people or contaminated objects.

The bacteria can be prevented by washing hands with soap and water, using hand sanitizer, and avoiding touching the face.

The bacteria has become a major concern for public health officials, who are working to control its spread. Schools are also implementing new policies to prevent the spread of MRSA, such as requiring students to wash their hands before eating and avoiding close contact with sick students.

Infectious Disease

The Advocate Stamford student has staph infection

By Ethan, 10th grade

Stamford High School was recently hit by a case of MRSA (methicillin-resistant Staphylococcus aureus) bacteria, which is a type of staph infection that can cause skin abscesses and bloodstream infections. The bacteria is resistant to many antibiotics, making it difficult to treat.

The bacteria has spread rapidly in recent years, particularly in hospitals and other health care facilities. It is transmitted through contact with infected people or contaminated objects.

The bacteria can be prevented by washing hands with soap and water, using hand sanitizer, and avoiding touching the face.

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Infectious Disease

The New York Times

Dead Student Had Infection, Officials Say

By KIMBERLY KU and SARAH KERSHAW

New York City health officials said yesterday that a Brooklyn middle school student who died on Oct. 14 had become infected with a new, resistant strain of bacteria that is primarily spread in hospital settings.

The infection, which is resistant to multiple antibiotics, has been found in patients in several regions of the city. The health officials, who said they were unable to confirm the source of the infection, added that the school was not closed.

The infection is a major concern for public health officials, who are working to control its spread. Schools are also implementing new policies to prevent the spread of MRSA, such as requiring students to wash their hands before eating and avoiding close contact with sick students.

Infectious Disease
MRSA
(methicillin-resistant *Staphylococcus aureus*

- First appeared in 1959
- Hospital-acquired (HA-MRSA)
  - Patients in the hospital
- Healthcare associated (HA-MRSA)
  - Patients who have visited the hospital
  - Nursing home
  - Infusion Center or dialysis outpatients
  - Visited relatives or friends in hospital
  - Discharged from the hospital
- Community acquired (CA-MRSA)
  - Patients with none of the above risk factors
Burden of *Staphylococcus aureus* Infections in the United States

- 292,045 inpatient stays per year in US due to Staph infections (CDC)
  - 0.8% of all inpatients
  - 120,000 cases MRSA per year
- MRSA accounts for up to 70% of hospital-acquired Staph. aureus infections
- Patients with MRSA infection have
  - 3 times length of hospital stay (14.3 vs 4.5 days)
  - 3 times total charges ($48,824 vs $14,141)
  - 5 times risk of hospital death (11.2% vs 2.3%)

Emergence of MRSA over 20 years Stamford Hospital Microbiology Lab data

(community and hospital strains)
Community Acquired MRSA in athletes

- Football, rugby, wrestling
- Towel, soap, razor sharing
- Turf burns, other sites of abrasion
- Body shaving
- Suboptimal hygiene in players, trainers
- High BMI (e.g. linemen)
- Prior antibiotic use
- Poor maintenance of equipment (e.g. whirlpools)
Outpatient purulent cellulitis: Empiric Rx for CA-MRSA

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult Dose</th>
<th>Evidence / Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMP-SMX</td>
<td>1-2 DS BID</td>
<td>All</td>
</tr>
<tr>
<td>Doxycycline, Minocycline</td>
<td>100 BID</td>
<td>All</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>300-450 TID</td>
<td>All</td>
</tr>
<tr>
<td>Linezolid</td>
<td>600 BID</td>
<td>All</td>
</tr>
</tbody>
</table>

Infectious Diseases Society of America (IDSA) Guidelines 2014
Recurrent MRSA SSTI: Decolonization Regimens

• Mupirocin (Bactroban) nasal + any other colonized site
  – twice daily x 10 days
• Chlorhexidine bathing or wipes
  – Daily x 10 days
• Systemic antibiotic active at skin surface
  – Rifampin, TMP/SMX, minocycline x 10 days
• 70% response rate
  – Risk of recolonization
Predictive Value of MRSA Nasal Swab PCR Assay for MRSA Pneumonia
Benjamin Dangerfield, Andrew Chung, Brandon Webb, and Maria Teresa Seville
Mayo Clinic and University of Utah. AAC February 2014 vol. 58 no. 2 859-864

ABSTRACT
Pneumonia due to methicillin-resistant Staphylococcus aureus (MRSA) is associated with poor outcomes and frequently merits empirical antibiotic consideration despite its relatively low incidence. Nasal colonization with MRSA is associated with clinical MRSA infection and can be reliably detected using the nasal swab PCR assay. In this study, we evaluated the performance of the nasal swab MRSA PCR in predicting MRSA pneumonia. A retrospective cohort study was performed in a tertiary care center from January 2009 to July 2011. All patients with confirmed pneumonia who had both a nasal swab MRSA PCR test and a bacterial culture within predefined time intervals were included in the study. These data were used to calculate sensitivity, specificity, positive predictive value, and negative predictive value for clinically confirmed MRSA pneumonia. Four hundred thirty-five patients met inclusion criteria. The majority of cases were classified as either health care-associated (HCAP) (54.7%) or community-acquired (CAP) (34%) pneumonia. MRSA nasal PCR was positive in 62 (14.3%) cases. MRSA pneumonia was confirmed by culture in 25 (5.7%) cases. The MRSA PCR assay demonstrated 88.0% sensitivity and 90.1% specificity, with a positive predictive value of 35.4% and a negative predictive value of 99.2%. In patients with pneumonia, the MRSA PCR nasal swab has a poor positive predictive value but an excellent negative predictive value for MRSA pneumonia in populations with low MRSA pneumonia incidence. In cases of culture-negative pneumonia where initial empirical antibiotics include an MRSA-active agent, a negative MRSA PCR swab can be reasonably used to guide antibiotic de-escalation.
MRSA pneumonia: Vancomycin vs. Linezolid?


Infectious Diseases Society of America (IDSA) Guidelines 2014
Hospital Isolation Process for Patients with MRSA

• Contact precautions – whether infected or colonized
  – Hand hygiene, gown, gloves
  – Soap and water or alcohol gel

• Remove from isolation if two negative screening cultures at least 48 hours apart
  – Must be off topical and systemic abx
  – Nasal culture (or PCR) plus previously positive sites

• Isolate on readmission if previously positive
  – Flagging system in admissions office
  – Remove from isolation if new screening cultures are negative

• Reason for isolation is to prevent spread to health care workers and transmission within the hospital
Hospital-acquired MRSA Infections
Stamford Hospital Overall

Hospital-acquired MRSA Infection Rate and Hand Hygiene

MRSA rate  HH rate
Multi-drug resistant organisms
MDRO Infections

Gram-negative infections
Enterobacteriaceae

- Family of bacteria -- primarily of intestinal origin
- Common causes of community and healthcare acquired infections.
- *E. coli* is the most common cause of outpatient urinary tract infections.
- Penicillins and cephalosporins have been the mainstay of treating infections caused by *Enterobacteriaceae*.
- However, resistance to many beta-lactams emerged several years ago and has continued to rise, due to enzymes which destroy the drugs.
- These resistance enzymes are called beta-lactamases.
Beta-lactamases

- Beta-lactamases destroy penicillin and cephalosporin antibiotics
- Found in all types of bacteria
- More than 700 chemical types are described to date
  - Varying structures with complex epidemiology
  - Preference for different beta-lactam antibiotics
- Extended spectrum beta-lactamases (ESBLs)
  - Broad spectrum of activity
  - ESBLs confer resistance to all penicillins and cephalosporins including the newest and most potent agents
  - Increasingly prevalent in hospitals and SNFs
Infection Control Issues for ESBL-producing bacteria

- Evidence indicates that patients acquire ESBL-producing organisms while in hospital
- Treatment failures occur due to resistance to primary treatment regimen and comorbidities
- These organisms transiently colonize the hands of hospital staff members
- The intestinal tract constitutes the main reservoir for ESBL-producing *Enterobactericeae*
- Environmental sources are rarely found
- Growing prevalence in the community

Paterson et al., Annals Internal Med 2004
Infection due to ESBL+ Klebsiella
ESBL-positive isolates at Stamford
DEADLY BACTERIA THAT DEFY DRUGS OF LAST RESORT

A new family of antibiotic-resistant bacteria, known as CRE, is raising concerns across the medical community because of its ability to cause infections that defy even the strongest antibiotics. The antibiotic resistance is spread by mobile pieces of DNA that can move between different species of bacteria, creating new drug-defying bugs.

Where the organisms can infect the body

How a resistance gene moves between bacteria

When antibiotic-resistant bacteria are present in the body and antibiotics are introduced ...

Antibiotics and resistant bacteria
Resistant bacteria dominate
The resistance gene
Pili bridge
Resistance gene transfer

Source: Source: University of Virginia Health System
By Frank Pompe, USA TODAY

Liz Szabo and Peter Eisler, USA TODAY | 5pm EST March 6, 2013

Health officials are raising concerns that it may soon be too late to stop superbugs.
CRE (Carbapenem resistant Enterobacteriaceae)

- Newest concern
  - 2006 described in NYC
  - 2009 described in India (NDM)
  - Numerous cases associated with medical tourism
- Clusters now occurring in hospitals in most states
  - NIH outbreaks; ERCP associated
  - Transmitted on the hands of personnel > environmental
  - Very difficult to treat
- Resistant to all beta-lactams including carbapenems
  - Usually co-resistant to multiple other classes
- Stamford experience
  - Sporadic single cases
  - 2/3 outpatients
  - No spread or trend yet
CRE isolates at Stamford

KPC Totals
CRE Infections
Outcome data from NYC

Overall Mortality

<table>
<thead>
<tr>
<th>Cases</th>
<th>Controls</th>
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</thead>
<tbody>
<tr>
<td>48</td>
<td>20</td>
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$P < 0.001$

Attributable Mortality

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<td>12</td>
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$P < 0.001$

Infection due to CRE + Klebsiella

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Result</th>
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<tbody>
<tr>
<td>URINE CULTURE</td>
<td>Verified 01/03/15-1124</td>
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<tr>
<td>Final</td>
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</tr>
<tr>
<td>Source: URINE</td>
<td></td>
</tr>
<tr>
<td>NEPHROSTOMY</td>
<td></td>
</tr>
<tr>
<td>LEFT</td>
<td></td>
</tr>
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</table>

The Klebsiella pneumoniae **ESBL** activity cannot be determined due to increased resistance of this organism.

The Klebsiella pneumoniae exhibits carbapenemase **KPC** production. The clinical efficacy of the carbapenems and other beta lactams has not been established for treating infections caused by Enterobacteriaceae that demonstrate carbapenemase production in vitro. Consider Infectious Diseases consultation.

Organism 1
- Colony Count: 

Organism 2
- Colony Count: 

Organism 3
- Colony Count: 

<table>
<thead>
<tr>
<th>Organism</th>
<th>Colony Count</th>
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<th>RX</th>
<th>ESC COLI</th>
<th>MIC</th>
<th>RX</th>
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<tr>
<td>KLEBSIELLA</td>
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<tr>
<td>PNEUMONIAE <strong>KPC</strong></td>
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<td>&gt;100,000 COL./CC.</td>
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<td>ESCHERICHIA COLI</td>
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<td>DIPHTHEROID</td>
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<table>
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<th>KLEB KPC</th>
<th>ESC COLI</th>
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<td>MIC</td>
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<td>CEFAZOLIN</td>
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<tr>
<td>CEFOTAXIME</td>
<td>&gt;32</td>
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<tr>
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<td>&gt;32</td>
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<td>CEFUROXIME</td>
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<td>CIPROFLOXACIN</td>
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<tr>
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<tr>
<td>NITROFURANTOIN</td>
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<tr>
<td>TETRACYCLINE</td>
<td>&gt;8</td>
</tr>
<tr>
<td>PIP/TAZO</td>
<td>&gt;64</td>
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</table>
CDC Action Plan for CRE

• Surveillance
  – ICP education
• Laboratory detection
  – Lab education
• Mandatory Reporting
• Rigid isolation / contact tracing / screening
• Antibiotic stewardship
• Controlled use of rx: polymixin, fosfomycin, tigecycline, ceftazidime + avibactam (Avycaz®)
Clostridium difficile
Changing Epidemiology of C. diff

• Recent outbreaks of severe disease caused by new epidemic strain of *C. difficile* with increased virulence, antibiotic resistance (NAP-1)
• ≥95% CDI pts have received antibiotic therapy
  – Fluoroquinolones>cephalosporins>penicillins
  – PPIs an important risk factor
• Although elderly (over 75) are still most greatly affected, more disease reported in “low-risk” persons
  – Healthy persons, pregnant women
• Community-acquired cases becoming more common
• High relapse rate -- 20% (importance of microbiome)
• *C. difficile* carried on hands and skin and persists in the environment
• Asymptomatic patients carry *C. difficile*
  – Community 5-10%
  – SNF and LTAC 50%
CONTRIBUTING FACTORS

(a) Infection through fecal-oral route

(b) Drug destroys normal flora giving pathogen an opportunity to grow

(c) Pathogen grows and produces increased infection and disease

*Normal flora important to maintain intestinal balance*
*Potential pathogen resistant to drug but unable to grow because of inhibition by normal microbial flora*
Incidence of Hospital acquired *Clostridium difficile* Infection.

Estimated U.S. Burden of *Clostridium difficile* Infection (CDI), According to the Location of Stool Collection and Inpatient Health Care Exposure, 2011.

Risk of *C. difficile* with Antibiotics Given for Surgical Prevention

Carignan, Sherbrooke Hospital, Quebec. SHEA abstract 001, 2007

- 7256 class 1 and 2 surgeries
- CDAD rate 9.2/1000 cases
  - 5.1 / 1000 cases after only PAP
  - 21.8 / 1000 cases after treatment
- Equivalent rates for cefazolin, cefoxitin, other PAP
  - No cases after vancomycin prophylaxis
- Risk increased with hip surgery, higher Charlson score, case since 2003
- Risk related to number of antibiotic doses received

<table>
<thead>
<tr>
<th>Doses</th>
<th>Cases</th>
</tr>
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<tbody>
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<td>0 cases</td>
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<tr>
<td>1 dose</td>
<td>1.6/1000 days</td>
</tr>
<tr>
<td>2 doses – 48 hours</td>
<td>3.4/1000 days</td>
</tr>
<tr>
<td>&gt;48 hours</td>
<td>13.0/1000 days</td>
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</table>
Persistence of *C. difficile*
During and After Treatment

Percentage of positive cultures for *C. difficile* before, during, and after treatment

Prior to treatment  
Day 3 of treatment  
Resolution of diarrhea  
End of treatment  
1-6 weeks after treatment

Percent Positive

Stool  
Skin  
Environment

C. difficile “bundle”
Hospital Methods to Attempt Control

✓ Barrier Precautions
  • Handwashing with soap and water, gloves, gowns
  • Duration of hospitalization
✓ Single room isolation or patient cohorting
✓ Patient bathing with chlorhexidine
✓ Environmental cleaning and disinfection
  • Patient room disinfection
  • Bleach
✓ Disposables
  • Disposable rectal thermometers, etc
✓ Antibiotic use – restriction policies
  • Use probiotics
  • Creative regimens: prolonged, taper, pulse, fidaxomycin
  • Fecal transplantation for multiple recurrences
  • Avoid antibiotics for 6-12 months
Executive Order -- Combating Antibiotic-Resistant Bacteria

EXECUTIVE ORDER

........

COMBATING ANTIBIOTIC-RESISTANT BACTERIA

By the authority vested in me as President by the Constitution and the laws of the United States of America, I hereby order as follows:

Sec. 5. Improved Antibiotic Stewardship. (a) By the end of calendar year 2016, HHS shall review existing regulations and propose new regulations or other actions, as appropriate, that require hospitals and other inpatient healthcare delivery facilities to implement robust antibiotic stewardship programs that adhere to best practices, such as those identified by the CDC. HHS shall also take steps to encourage other healthcare facilities, such as ambulatory surgery centers and dialysis facilities, to adopt antibiotic stewardship programs.

BARACK OBAMA

THE WHITE HOUSE,
September 18, 2014.
Enteroviruses

- Family Picornavirus
- RNA Viruses
- Include
  - Coxsackie viruses
  - Polio viruses
  - Echo viruses
  - Other enteroviruses
Clinical manifestation of Enterovirus Infections

- Aseptic meningitis
- Nonspecific febrile illness
- Colds
- Conjunctivitis
- Pharyngitis
- Herpangina
- Hepatitis
- Exanthems
- Encephalitis
- Paralytic polio
- Vomiting
- Diarrhea
- Pericarditis
- Myocarditis
- Hand-foot-mouth syndrome
Epidemiology

• Transmission from person to person
  – Fecal-Oral
  – Respiratory
  – Food and water

• Peak incidence: Summer & Fall

• Male = Female

• Age: Young children

• Incubation period: 3-6 Days
Hand-foot-mouth syndrome

Small intraoral ulcers and macular or vesicular lesion on hands and feet & buttock

Neurologic complications described
Enterovirus D68

- Outbreak started in Midwest in 2014
  - Missouri, Illinois, Kansas; nationwide, including CT
- Children with severe respiratory illness
  - Runny nose, cough, sneezing, SOB
  - Age range 10 months to 18 years
  - Up to 15% require PICU care
  - Usually afebrile (80%)
  - Many have predisposing asthma
  - Spread by droplet and contact with secretions
- Diagnosis by viral culture/PCR from NP sample
  - EV-D68 confirmation by CDC
- Supportive care
Acute Limb Weakness complicating Enterovirus D68 infection

- Children, age range 1-18 years
- URI followed 2 weeks later with focal limb weakness or cranial nerve palsies
- MRI and CSF c/w spinal cord infection
- CSF samples negative for virus
- Residual weakness and atrophy – like polio
Viral Hemorrhagic Fever

- Viruses of four distinct families
  - Arenaviruses (Lassa)
  - Filoviruses (Ebola)
  - Bunyaviruses (Hantavirus)
  - Flaviviruses (Dengue)

- RNA viruses
  - Enveloped in lipid coating

- Animal or insect host is the natural reservoir
**Ebola Virus Ecology**

**Enzootic Cycle**
New evidence strongly implicates bats as the reservoir hosts for ebolaviruses, though the means of local enzootic maintenance and transmission of the virus within bat populations remain unknown.

**Ebola Viruses:**
- Ebola virus (formerly Zaire virus)
- Sudan virus
- Tai Forest virus
- Bundibugyo virus
- Reston virus (non-human)

**Epizootic Cycle**
Epizootics caused by ebolaviruses appear sporadically, producing high mortality among non-human primates and duikers and may precede human outbreaks. Epidemics caused by ebolaviruses produce acute disease among humans, with the exception of Reston virus which does not produce detectable disease in humans. Little is known about how the virus first passes to humans, triggering waves of human-to-human transmission, and an epidemic.

Human-to-human transmission is a predominant feature of epidemics.

Following initial human infection through contact with an infected bat or other wild animal, human-to-human transmission often occurs.
CENTRE DE TRAITEMENT
EBOLA
Pathogenesis - how does Ebola cause disease?

• Virus enters the body through infected blood/body fluid in contact with a mucus membranes or a break in skin.
• Virus multiplies in monocytes/macrophages which facilitate dissemination of the virus throughout the body.
• Rapid viral growth in hepatocytes, endothelial and epithelial tissues.
• Strong cytokine/inflammatory mediators; release of TNF-α.
• Leads to endothelial damage, increased vascular permeability and shock.
• This results in the multi-organ failure.
• Diffuse intravascular coagulopathy (DIC) leads to hemorrhage.
Ebola Symptoms

- Incubation period, is 2 to 21 days; average is 8 to 10 days.
- Onset: Abrupt – Fever, Headache, Myalgia
- Soon Thereafter:
  - Rash,
  - Nausea, Vomiting, Abdominal Pain, Diarrhea
- Ongoing:
  - Jaundice, Pancreatitis
  - CNS – Somnolence, Delirium, Coma
  - Bleeding (1/3) – Petechiae, Hemorrhages
- Laboratory
  - Electrolyte abnormalities – sodium and potassium loss
  - Liver failure → low serum protein → edema
  - Bleeding from low platelets
- Fatality rate, current outbreak: ~50%
Ebola Awareness

- >27,000 cases, >11,000 deaths
- Border closures, airport closures, martial law, curfews, country lockdown
- Ongoing cases
- Supportive treatment
- Prevention by PPE / avoiding high risk contact
- Cultural barriers to infection control
- Travelers still arriving
WHO Epidemiologic Histogram (8/9/15)

Figure 1: Confirmed, probable, and suspected EVD cases worldwide (data up to 9 August 2015)

- Guinea: 3787 Cases, 2524 Deaths
- Liberia: 4808 Cases, 10672 Deaths
- Sierra Leone: 3951 Cases, 13470 Deaths
- Italy: 1 Case, 0 Deaths
- Mali: 86 Cases, 0 Deaths
- Nigeria: 20 Cases, 8 Deaths
- Senegal: 1 Case, 0 Deaths
- Spain: 0 Cases, 1 Death
- United Kingdom: 1 Case, 0 Deaths
- United States of America: 4 Cases, 1 Death

Total: 11298 Cases, 27965 Deaths
Ebola Response

• Ebola preparation meetings
• Screening questionnaire
  – Registration, EMS, ED triage physicians
• Rapid triage plan
• Patient management flow algorithm
• High risk isolation signage
• High risk isolation cart
• Upgraded fluid impermeable PPE
• Process for safe laboratory management
• Ongoing training and competency program for staff
Have you travelled outside of the country in the last 3 weeks?
If “yes”, please alert medical personnel upon arrival
## Screening for Ebola

### Patient presentation
- Fever $>101.5$ ($>38.6$)
- Headache
- Muscle aches
- Vomiting or diarrhea
- Abd pain
- Hemorrhage

### Travel History
**West Africa within 21 days:**
- Guinea
- Liberia
- Sierra Leone

### Close Contact
- With anyone sick with Ebola or suspect?
- With blood or body fluids of a person sick with Ebola?
- With remains of a person who died of Ebola?
Number of persons traveling, monitored, and reported to CDC as PUls with concerns about Ebola -- United States, 2014-15

Source: CDC Domestic Clinical Inquiries Team
Middle East Respiratory Syndrome Coronavirus (MERS-CoV)

- Novel coronavirus that emerged in 2012
- Epicenter in Saudi Arabia
- Causes severe acute respiratory illness
- 1368 cases
- 37% fatality rate
MERS-CoV Symptoms

- Severe acute respiratory illness:
  - Fever, cough, shortness of breath
  - ARDS with multiorgan failure
- Incubation period is 10-14 days
- 65% male, mean age 50 (range 9-99)
- Illness initially sporadic, family clusters, HCW, then epidemic peaks in S Korea and Saudi Arabia.
- Some cases have had atypical presentations:
  - Initially presented with abdominal pain and diarrhea and later developed respiratory complications
- Reservoir potential camels, bats
- Healthcare exposure
Confirmed cases of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) (N = 55) reported as of June 7, 2013, to the World Health Organization, and history of travel from the Arabian Peninsula or neighboring countries.
Patient Under Investigation (PUI)

PUI Criteria:

1. Persons who develop severe acute lower respiratory illness of known etiology within 14 days after traveling from the Arabian Peninsula or neighboring countries
2. Persons who develop severe acute lower respiratory illness who are close contacts of a symptomatic traveler who developed fever and acute respiratory illness within 14 days of traveling from the Arabian Peninsula or neighboring countries
3. Acute respiratory infection, may include fever $\geq 100.4^\circ F$ and cough
4. Suspicion of pneumonia or acute respiratory distress syndrome based on clinical or radiological evidence
5. Symptoms not already explained by any other infection or etiology
MERS-CoV Transmission

• Airborne / droplet
  • Gowns, gloves, N-95 mask, eye protection

• Transmission:
  • Transmission between close contacts
  • Transmission from infected patients to healthcare personnel
  • Clusters of illnesses have been reported by six countries
Figure 1. Epidemic curve of MERS-CoV cases (n=1368) (as of 7 July 2015)
Climate Change

- Global average surface temperature has risen at an average rate of 0.15°F per decade since 1901. Average temperatures have risen more quickly since the late 1970s (0.26 to 0.43°F per decade).
- Worldwide, 2014 was the warmest year on record and 2005–2014 was the warmest decade on record since thermometer-based observations began.
- Similar to the rate of warming within the contiguous 48 states. Seven of the top 10 warmest years on record for the contiguous 48 states have occurred since 1998, and 2012 was the warmest year on record.
- Concentrations of heat-trapping greenhouse gases are increasing in the Earth's atmosphere. In response, average temperatures at the Earth's surface are expected to continue rising.
- Annual and seasonal temperature patterns determine the types of animals and plants and insects that can survive in particular locations. Changes in temperature can disrupt a wide range of natural processes, particularly if these changes occur more quickly than species can adapt.
Temperatures Worldwide, 1901–2014


For more information, visit U.S. EPA’s “Climate Change Indicators in the United States” at www.epa.gov/climatechange/indicators.
Temperatures in the Contiguous 48 States, 1901–2014


For more information, visit U.S. EPA’s “Climate Change Indicators in the United States” at www.epa.gov/climatechange/indicators.
Global spread of dengue virus types: mapping the 70 year history
Spread of Arthropod-borne Infections due to Climate Change

Climate Change and Malaria

Distribution of the primary Malaria agent
- Current distribution
- Possible extended distribution by 2050 (suitable climate)
- Presently suitable, but unsuitable climate by 2050

Current distribution represents the maximum extent of the distribution of the *Plasmodium* Malaria parasite. The scenario is based on the high scenario from the HadCM2 experiment.

Aedes mosquito vector distribution in United States

2014 map of the U.S. showing the areas at risk of dengue outbreaks, based on the approximate distribution of dengue mosquito vectors *Aedes aegypti* and *Aedes albopictus*. 
Aedes species transmit:

- Dengue
- Yellow fever
- West Nile
- Eastern Equine Encephalitis
- Zika virus
- Chikungunya
Chikungunya Prevalence

Current or previous local transmission of chikungunya virus
Chikungunya

- Transmitted by Aedes sp. mosquitos
- Incubation period 3-7 days
- Acute onset of fever and polyarthralgia, bilateral, symmetrical
- Debilitating, severe arthritis may occur
- Headache, myalgia, conjunctivitis, rash
- Lymphopenia, thrombytopenia, elevated SCr and ALT
- Complications (rare): uveitis, retinitis, myocarditis, nephritis, encephalitis, hepatitis, bullous skin lesions
- Symptoms typically resolve in 10 days but may persist for months
- Serologic diagnosis (PCR or IgG/IgM)
- Supportive treatment: NSAIDs, corticosteroids
Chikungunya Arthritis
Tick Borne Diseases in the US -- 2015

- Anaplasmosis
- Babesiosis
- *Borrelia burgorferi* (Lyme Disease)
- *Borrelia miyamotoi* infection
- Colorado tick fever
- Ehrlichiosis
- Heartland virus
- Powassan virus
- Bourbon virus
- Rocky Mountain Spotted fever (*Rickettsia rickettsii*)
- Southern tick-associate rash illness (STARI)
- Tick borne relapsing fever
- Tularemia
- *Rickettsia parkeri*
- Rickettsia species 364D
Powassan, Heartland, Bourbon viruses

• Powassan virus (phlebovirus)
  – Fever, headache, vomiting, confusion, seizures
  – CSF pleocytosis (viral meningoencephalitis)
  – Northeast and Great Lakes
  – Ixodes

• Heartland virus (phlebovirus)
  – Fever, myalgias, HA
  – Leukopenia, thrombocytopenia
  – Missouri & Tennessee
  – Lone star tick

• Bourbon virus (orthomyxovirus)
  – Fever, rash, nausea & vomiting, encephalitis
  – Leukopenia, thrombocytopenia
  – Kansas
  – Tick type unclear
## New infectious diseases

<table>
<thead>
<tr>
<th>Year</th>
<th>Disease Name</th>
</tr>
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<tbody>
<tr>
<td>2015</td>
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<tr>
<td>2014</td>
<td>Powassan, Heartland, Bourbon virus</td>
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<tr>
<td>2014</td>
<td>Enterovirus D68</td>
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<tr>
<td>2013</td>
<td>Chikungunya</td>
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<tr>
<td>2012</td>
<td>MERS</td>
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<tr>
<td>2009</td>
<td>H1N1pdm influenza</td>
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<tr>
<td>2005</td>
<td>H7N9 and H9N2 influenza</td>
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<tr>
<td>2004</td>
<td>ESBL / CRE infections</td>
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<tr>
<td>2003</td>
<td>SARS</td>
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<td>2002</td>
<td>VRSA</td>
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<td>1999</td>
<td>Nipah virus</td>
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<tr>
<td>1999</td>
<td>West Nile Virus (new world)</td>
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<tr>
<td>1997</td>
<td>H5N1 influenza</td>
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<tr>
<td>1996</td>
<td>nCJD (mad cow disease)</td>
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<tr>
<td>1995</td>
<td>HHV-8 (Kaposi sarcoma virus)</td>
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<tr>
<td>1994</td>
<td>Hantavirus</td>
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<tr>
<td>1992</td>
<td>MDR-Tuberculosis</td>
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<tr>
<td>1989</td>
<td>Hepatitis C</td>
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<tr>
<td>1988</td>
<td>Hepatitis E, HHV-6</td>
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<td>1983</td>
<td>HIV/AIDS, Helicobacter</td>
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<td>1983</td>
<td>E. coli O157:H7, Lyme disease</td>
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<td>1980</td>
<td>HTLV I, II</td>
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<tr>
<td>1978</td>
<td>Clostridium difficile colitis</td>
</tr>
<tr>
<td>1976</td>
<td>Ebola, Legionnaires disease</td>
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</tbody>
</table>
Thank You!

Questions?