DISCLOSURES

- I do not have (nor does any immediate family member have) a vested interest in or affiliation with any corporate organization offering financial support or grant monies for this continuing education activity, or any affiliation with an organization whose philosophy could potentially bias my presentation.

TECHNICIAN OBJECTIVES

- List SIRS criteria for sepsis identification
- Identify antimicrobials acceptable for use under the new SEP-3 update
- Summarize key changes in the Sepsis Core Measure updates

PROGRESSION OF SEPSIS

SIRS: systemic inflammatory response syndrome

SEVERE SEPSIS
- End-organ damage or hypoperfusion (SBP <90 mmHg or MAP <70 mmHg)

SEPTIC SHOCK
- Severe sepsis with persistent hypotension despite adequate fluid resuscitation

Systemic Inflammatory Response Syndrome
- T: <36 or >38°C, RR: >20 bpm, HR: >90 bpm, WBC: <4 or >12x10^3/mm^3

PHARMACIST OBJECTIVES

- Discuss the core measures required for sepsis management
- Evaluate the efficacy of protocols and bundles in the management of sepsis
- Formulate steps necessary for the implementation of sepsis protocols
- Discuss the role of pharmacists in implementation of sepsis protocols

SEPSIS

- Major cause of morbidity and mortality
- Leading cause of death in non-cardiac intensive care units (ICUs)
- In the United States:
  - >1,000,000 cases/year
  - ~10^6 leading cause of death

Centers for Disease Control and Prevention
SEVERE SEPSIS
• 1 in 10 patients admitted to the ICU has or will develop severe sepsis
• ~3% of hospital discharges
• Incidence expected to increase

NEW CORE MEASURE
• 1 in 10 patients admitted to the ICU has or will develop severe sepsis
• ~3% of hospital discharges
• Incidence expected to increase

SEPSIS CORE MEASURE OVERVIEW
• Adults 18 years and older with a diagnosis of severe sepsis or septic shock
• Addresses:
  • Serum lactate levels to evaluate tissue perfusion
  • Time to obtaining blood cultures
  • Time to initiation of broad spectrum antibiotics
  • Adequate volume resuscitation
  • Vasopressor administration, when indicated
  • Reassessment of volume status and tissue perfusion

DEFINITIONS
• Bacteremia: viable bacteria in blood
• SIRS: widespread inflammatory response
  • Temperature: > 38.3 C or < 36.0 C
  • Heart rate > 90 beats per minute
  • White blood cell count > 12,000 cells/mm³ or < 4,000 cells/mm³ or 10% bands
  • Respiratory rate > 20 breaths per minute
• Sepsis: suspected infection with ≥ 2 positive SIRS criteria
• Severe sepsis: sepsis with ≥ 1 organ dysfunction
  • SBP < 90 mmHg or MAP < 65 mmHg, or decrease in SBP of 40 mmHg
  • Serum creatinine >2.0 mg/dL or UOP < 0.5 mL/kg/hr x2h
  • Total bilirubin > 3 mg/dL
  • Platelets < 100,000 or INR > 1.5 or aPTT > 60 sec
  • Lactate > 2 mmol/L
• Septic shock: severe sepsis + tissue hypoperfusion persisting after resuscitation as evidenced by:
  • SBP < 90 mmHg or MAP < 65 mmHg or decrease in SBP by 40 mmHg OR lactate > 4 mmol/L

WHAT IS A CORE MEASURE?
• Centers for Medicare & Medicaid Services (CMS)
• Set of standards, proven to improve patient outcomes
• “…meaningful to patients, consumers, and physicians, while reducing variability in measure selection, collection burden, and cost.” -CMS

DEFINITIONS
• Severe sepsis: sepsis with ≥ 1 organ dysfunction
  • SBP < 90 mmHg or MAP < 65 mmHg, or decrease in SBP of 40 mmHg
  • Serum creatinine >2.0 mg/dL or UOP < 0.5 mL/kg/hr x2h
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• Septic shock: severe sepsis + tissue hypoperfusion persisting after resuscitation as evidenced by:
  • SBP < 90 mmHg or MAP < 65 mmHg or decrease in SBP by 40 mmHg OR lactate > 4 mmol/L
**CMS Core Measure Criteria**

**Within 3 hours**
- Severe sepsis and septic shock
- Initial lactate level
- Blood cultures drawn prior to antibiotics
- Broad spectrum antibiotics

**Septic Shock**
- Resuscitation with 30 mL/kg of crystalloids (actual body weight)
- Normal saline or Lactated Ringer’s ONLY
- Plasmalyte does NOT count

**Within 6 hours**
- Severe sepsis and septic shock
- Repeated lactate level if initial lactate is elevated >4 mmol/L

**Septic Shock**
- Vasopressors initiated if hypotension persists after fluid challenge
- Repeat volume status and tissue perfusion assessment

**A focused exam including:**
- Vital signs
- Cardiopulmonary exam
- Capillary refill evaluation
- Peripheral pulse evaluation
- Skin examination

**Or any two of the following four:**
- Central venous pressure measurement
- Central venous oxygen measurement
- Bedside cardiovascular ultrasound
- Passive leg raise or fluid challenge

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**Time to Antimicrobial Therapy**

- To meet the core measure requirement for receipt of antimicrobial therapy within 3 hours, one of the following antibiotics must be administered:
  - Amoxicillin-clavulanic acid
  - Ampicillin-sulbactam
  - Ceftriaxone
  - Cefepime
  - Piperacillin-tazobactam
  - Levofloxacin
  - Aztreonam + vancomycin

- For patients with severe beta-lactam allergies:
  - Amoxicillin-clavulanic acid
  - Ampicillin-sulbactam
  - Ceftriaxone
  - Cefepime
  - Piperacillin-tazobactam
  - Levofloxacin
  - Aztreonam + vancomycin

**What Starts the Clock?**

**Severe Sepsis (documented within 6 hours)**
- Documentation of a suspected source of clinical infection
- Two or more (SIRS) criteria
  - Temperature >38.3 or <36.0
  - Heart rate (pulse) >90
  - Respiration >20 per minute
  - White blood cell count >12,000 or <4,000 or >10% bands

**Organ dysfunction**
- Hypertension
- Creatinine >2.0, or urine output <0.5 mL/hour for 2 hours
- Bilirubin >2 mg/dL
- Platelet count <100,000
- INR >1.5 or aPTT >60 sec
- Lactate >2 mmol/L

**Septic Shock (documented within 6 hours)**
- MD/PA/ARNP documents septic shock
- Severe sepsis criteria or MD/PA/ARNP documents severe sepsis
- Persistent hypotension or lactate ≥4 mmol/L

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**Time to Antimicrobial Therapy**

- Must be administered within 3 hours of severe sepsis and septic shock recognition
- Timely processing and dispensing of these orders is imperative
- Surviving Sepsis Campaign recommends ‘within first hour of recognition of septic shock and severe sepsis’
HOW TO REMEMBER IT ALL?

PROTOCOLS & BUNDLES

ORIGIN OF MEDICAL BUNDLES

• Voluntary Hospital Association (VHA)
• Institute of Healthcare Improvement (IHI)
• 2001: Idealized Design of the Intensive Care Unit (IDICU)

• Goal: “...achieve the highest levels of reliability in critical care processes and resultant outcomes, while at the same time introducing concepts of enhanced teamwork and communication.”

IHI/VHA CHANGE STRATEGY

• Patient care bundles
• Grouping of care elements for particular symptoms, treatments, or procedures
• Strong science, good methodology, poor process
• Enhance care, reduce harm

BUNDLE DESIGN GUIDELINES

• 3-5 elements with strong clinician agreement
• Elements are relatively independent
• Defined patient population
• Multidisciplinary care team development
• Descriptive – allowing for appropriate clinical judgement
• Compliance measured with all-or-none approach

CHALLENGES WITH BUNDLES

• Never ‘complete’
• Avoiding a checklist mentality
• Complexity
• Having an owner
SUCCESSFUL BUNDLES

VENTILATOR ASSOCIATED PNEUMONIA
- Reduction in VAP incidence by 10%
- Head of bed elevation
- Daily sedation vacation
- Peptic ulcer disease prophylaxis
- Deep venous thrombosis prophylaxis
- Daily oral care

EARLY GOAL DIRECTED THERAPY
- Reduction in mortality by 16%
- Fluid challenge 30mL/kg
- Achieve CVP 8-10mmHg
- Svo2 > 70%
- MAP ≥ 65
- UOP ≥ 0.5mL/kg/hr

FIRST STEPS
- Determine the goal of the protocol
- Administration buy-in
- Determine resources needed
- Develop a team!

BUNDLE
- All components are necessary and sufficient
- Straightforward
- Same time and space continuum
- All – or – nothing
- Work Smarter, Not Harder

PICKING YOUR TEAM
- Is there an administrator responsible for the success of the initiative?
- How will this administrator be involved in the process longitudinally?
- Who has something at stake?

DESIGNING A PROTOCOL

FIRST STEPS
- Determine the goal of the protocol
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- All components are necessary and sufficient
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DESIGNING A PROTOCOL
GATHERING A TEAM OF STAKEHOLDERS

- Physicians
- Nursing
- Pharmacy
- Department Leaders
- Quality
- IT

Find people who are influential among their peers.

IMPLEMENTATION

- Go-live date
- Education of all involved parties
- Hype!

PLAN, DO, STUDY, ACT

- Analyze the data to understand the impact of the change
- Compare observed and predicted results
- Adjust the plan
- Implement changes to improve process
- Collect the information required to measure the change
- How will you achieve the goal? What steps are necessary?
- Plan how to measure the effect of the change
- Adjust the plan
- Implement changes to improve process
- Institute for Healthcare Improvement

AND REMEMBER...

- Use your resources!
- Have similar institutions implemented a similar process?
- Network!

ROLE OF THE PHARMACIST

- Ensure appropriateness
- Spectrum of activity
- Consider medication allergies
- Optimize dosing
- Expedite preparation and administration
- Mix at bedside
- Procurement of pharmacy-made products
- Advise y-site compatibilities

PHARM-ASSIST

- Go-live date
- Education of all involved parties
- Hype!
PHARM-ASSIST
- Ensure bundle followed
  - Cultures before antibiotics
  - Adequate fluid resuscitation
- Educate
  - Teach patient care team to ensure a more seamless process for the next septic patient
  - Appropriate vasoactive medication

BE A RESOURCE
At the bedside
Order set development

Do the actionable items delivered in an easily understood and easily accessed fashion?

PHARM-ASSIST
- Safety
  - High stress environment
  - Less familiar process
  - High risk of medication errors
- Remain calm!

ORDER SET DEVELOPMENT
Two Order Sets Exist
1. Sepsis
2. Severe Sepsis / Septic Shock

AS EASY AS POSSIBLE!

TYPES OF RECOMMENDATIONS
- Antibiotic Dosing
- Addition of Antimicrobials
- Drug Preparation
- Increasing Fluids
- Drug Information Provided
- Addition of Steroids
- Addition of Vasopressors
- Addition of Insulin

AS EASY AS POSSIBLE!

- Antibiotics (if patient is currently receiving antibiotics)
  - If patient NOT currently receiving antibiotics, choose one of two options below.
  - If patient currently receiving antibiotics, ensure adequate coverage based on known/suspected site(s) of infection.
- Standard antibiotic regimen
  - For broad-spectrum antibiotic coverage (e.g., cefepime, vancomycin, etc.)
- Consider alternate antibiotic agents for patients with previous/known intolerance to agents:
  - Add aminoglycosides if needed for resistant organisms (e.g., suspected intraabdominal, necrotizing soft tissue infections)
  - Consider clindamycin, linezolid, vancomycin, etc.
- Consider IV fluids if patient is dehydrated or hypotensive
- Consider additional diagnostic testing if needed for sepsis
- Revised 08/06/13

ORDER SET REVISION

- Administration instructions
  - “Administer cefepime FIRST”
- “Cultures MUST be obtained prior to initiating antibiotics unless this will result in a delay of therapy greater than 3 hours.”
- Pre-select items frequently omitted

AREAS OF OPPORTUNITY

<table>
<thead>
<tr>
<th>Failure Category</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did not receive required Abx in 3 hours</td>
<td>5</td>
</tr>
<tr>
<td>Abx before baseline culture</td>
<td>1</td>
</tr>
<tr>
<td>No blood cultures in required timeframe</td>
<td>4</td>
</tr>
<tr>
<td>Follow-up exam</td>
<td>3</td>
</tr>
<tr>
<td>No blood cultures in required timeframe</td>
<td>2</td>
</tr>
<tr>
<td>No repeat blood in required timeframe</td>
<td>1</td>
</tr>
<tr>
<td>Venocurett time &gt; 30 minutes</td>
<td>1</td>
</tr>
</tbody>
</table>

INCORPORATE FEEDBACK

- EMR Reminders
- PDA Reminders
- Patient Reminders
- Education
- Awareness
- ADS Inventory

ADS: automated dispensing system
AUTOMATIC DISPENSING SYSTEMS

- All relevant antimicrobials stocked in machines
- Ensure automatic restocking
- Increase stock of NS and LR
- Ensure mini-bags readily available

INCORPORATE FEEDBACK

- EMR Reminders
- ADS Inventory
- Patients, Pharmacy
- Awareness
- Education

PHARMACIST EDUCATION

- Mandatory online education
- Importance of appropriate and timely antimicrobials
- Do not delay therapy to adjust frequency!
  - Dispense one time dose, follow up with provider immediately after
- Identification of Sepsis Alert patients

AWARENESS

- Pharmacies included in sepsis alert pages
- Sepsis alert teams
- Pharmacists on response teams
- BPA fires when waiting room patient SIRS+

PROVIDER EDUCATION

- Physician champion
- Ensure usage of order set
- Education on antimicrobial spectrum of activity
- Feedback on core measure failures
NURSE EDUCATION
• Importance of bundle components
• Administration instructions
• Order of administration of antimicrobials

POSSIBLE FUTURE CHANGES...
• Likely to have long ICU stay or in-hospital death
  • (qSOFA)
  • Respiratory rate of 22/min or greater
  • Altered mentation
  • Systolic blood pressure of 100 mm Hg or less.

CMS uses old definition!

SUMMARY
• It takes a village
• Plan your work, and work your plan
• Improve, improve, improve!

SEPSIS
• Life-threatening organ dysfunction caused by a dysregulated host response to infection
• Organ dysfunction represented by Sequential Organ Failure Assessment (SOFA) score ≥ 2
  • In-hospital mortality >10%

SEPTIC SHOCK
• Vasopressors required to maintain MAP ≥ 65 mm Hg
• Serum lactate >2 mmol/L
• Despite adequate volume resuscitation

POSSIBLE FUTURE CHANGES...
• Likely to have long ICU stay or in-hospital death
• Respiratory rate of 22/min or greater
• Altered mentation
• Systolic blood pressure of 100 mm Hg or less.

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