

The Innovation I Need Now to Improve Sepsis Care

Sepsis Tech & Innovation
June 22-23, 2021

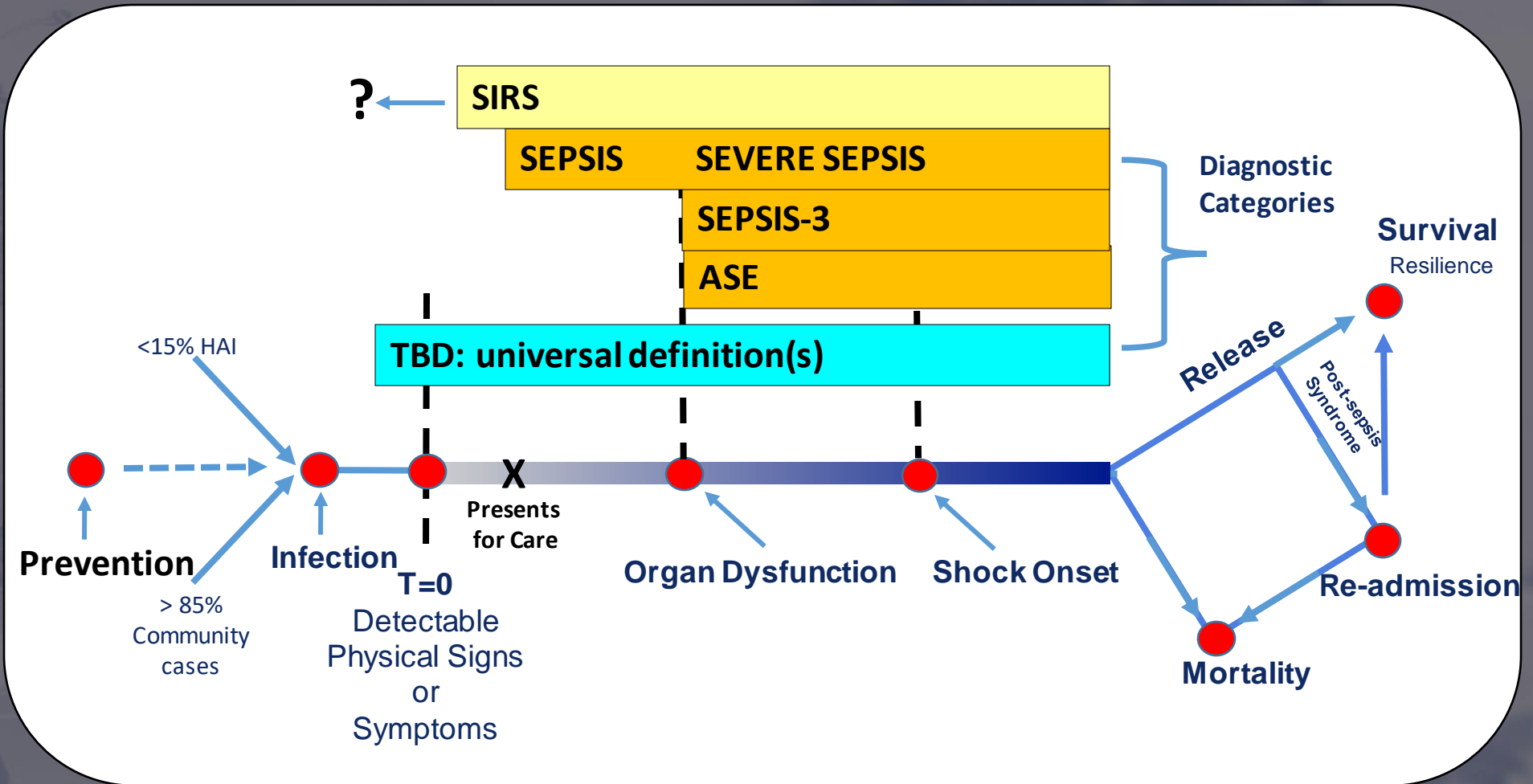




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A Conceptual Sepsis Patient Continuum



#1 Innovation I Need Now

A change from threshold-based, dichotomous thinking to a continuum-based concept of sepsis.



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NATIONAL ACTION PLAN FOR COMBATING ANTIBIOTIC-RESISTANT BACTERIA

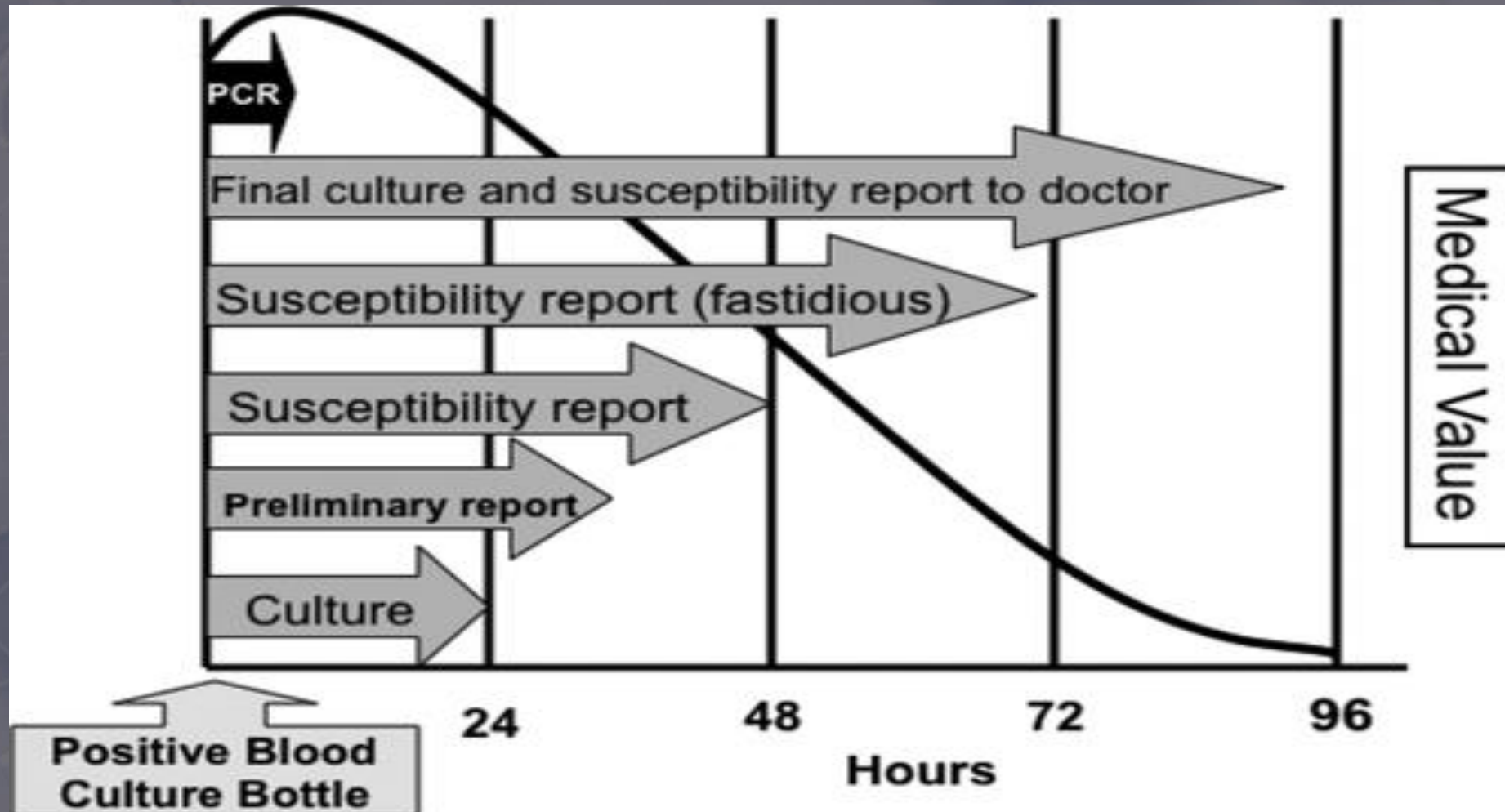
MARCH 2015



National Action Plan Highlights

- The plan sets 1-, 3-, and 5-year targets in each of the five overarching goals, which are to: slow the emergence of resistant bacteria and prevent the spread of resistant infections
- Strengthen national one-health surveillance efforts to combat resistance (the "one-health" approach to disease surveillance integrates data from multiple monitoring networks, according to the White House)
- **Advance development and use of rapid and innovative diagnostic tests for the identification and characterization of resistant bacteria;**
- Accelerate basic and applied research and development for new antibiotics, other therapeutics, and vaccines; and
- Improve international collaboration and capacities for antibiotic resistance prevention, surveillance, control, and antibiotic research and development

Time Required to Final Results



Rapid Molecular Methods

- Polymerase chain reaction (PCR)
- Multiplex PCR
- Nanoparticle Probe Technology
- Peptide Nucleic Acid Fluorescent In Situ Hybridization (PNA FISH)
- Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF)

Polymerase Chain Reaction

- Uses a fluorescently labeled probe with two primers
- These primers **target DNA that is specific to a species or resistance mechanism**
- The primers detect and then amplify target gene sequences
- Multiplex PCR uses many primers
- **Several devices commercially available for bloodstream infection detection**

Randomized Trial of Rapid Multiplex Polymerase Chain Reaction–Based Blood Culture Identification and Susceptibility Testing

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Testing Stewardship Meets Antimicrobial Stewardship

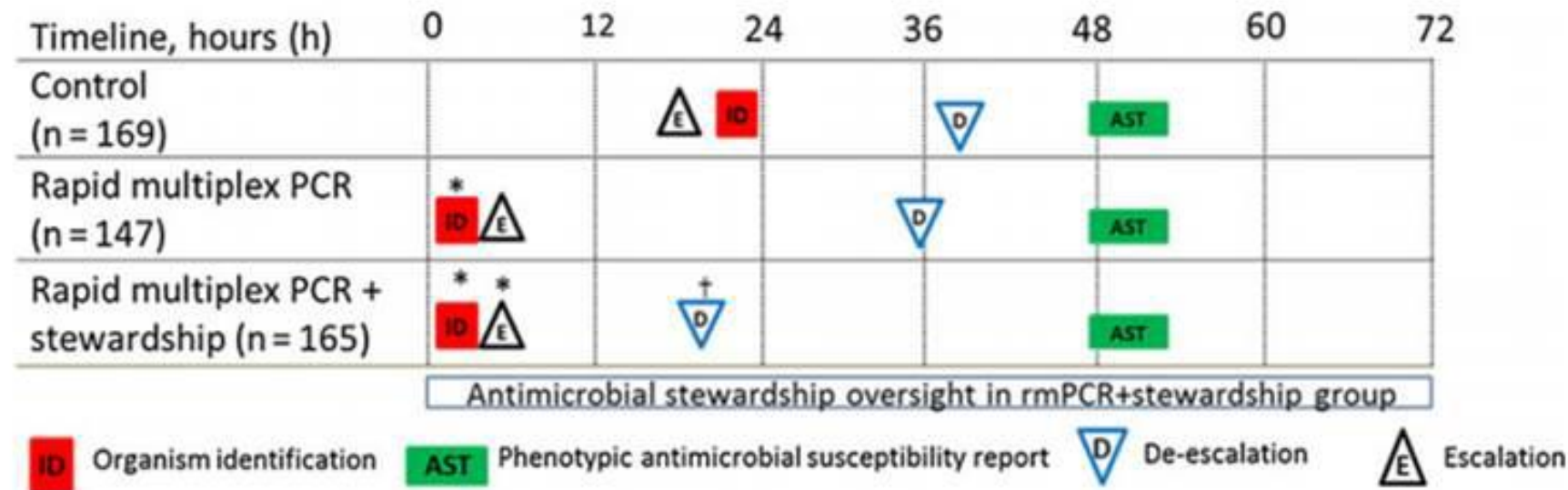


Figure 2. Comparison of time to organism identification, availability of phenotypic antimicrobial susceptibility results, and first appropriate modification of antimicrobial therapy for the subset of study subjects with organisms represented on the rapid multiplex polymerase chain reaction (rmPCR) panel (n = 481). Time 0 is when the positive Gram stain result was reported. Median time in hours (interquartile range [IQR]) to organism identification: control 22.3 (17–28), both rmPCR and rmPCR + stewardship 1.3 (0.9–1.6); de-escalation: control 39 (19–56), rmPCR 36 (22–61), rmPCR + stewardship 20 (6–36); escalation: control 18 (2–63), rmPCR 4 (1.5–24), rmPCR + stewardship 4 (1.8–9). **P* < .05 vs control; †*P* < .05 vs control and rmPCR groups.

Clinical Impact of Blood Culture PCR in Gram-negative Bacteremia (with Antibiotic Stewardship)

Decreased

- Time to optimal antibiotic therapy
 - 80.9h to 23.2h ($p < 0.001$)
- Length of stay from
 - 22.3 to 15.3 days ($p = 0.001$)
- Mortality from
 - 21% to 8.9% ($p = 0.01$)
- Hospital cost (per inpatient survivor) by \$26,298 ($p = 0.002$)

Take home points

- Rapid diagnostics can decrease diagnostic uncertainty
- To be effective, rapid diagnostics have to be actionable and tied to local stewardship program
- If effectively used, it can have direct impact on sepsis care and on patient clinical outcomes.



Lisa Shieh, MD, PhD
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Stanford University School of Medicine

Innovations we need now

Why do some patients with infection progress to sepsis and others do not?

- We need to better understand what triggers sepsis
- We need to prevent progression of infection to sepsis

Tanya Roberts died from urinary tract infection that caused sepsis

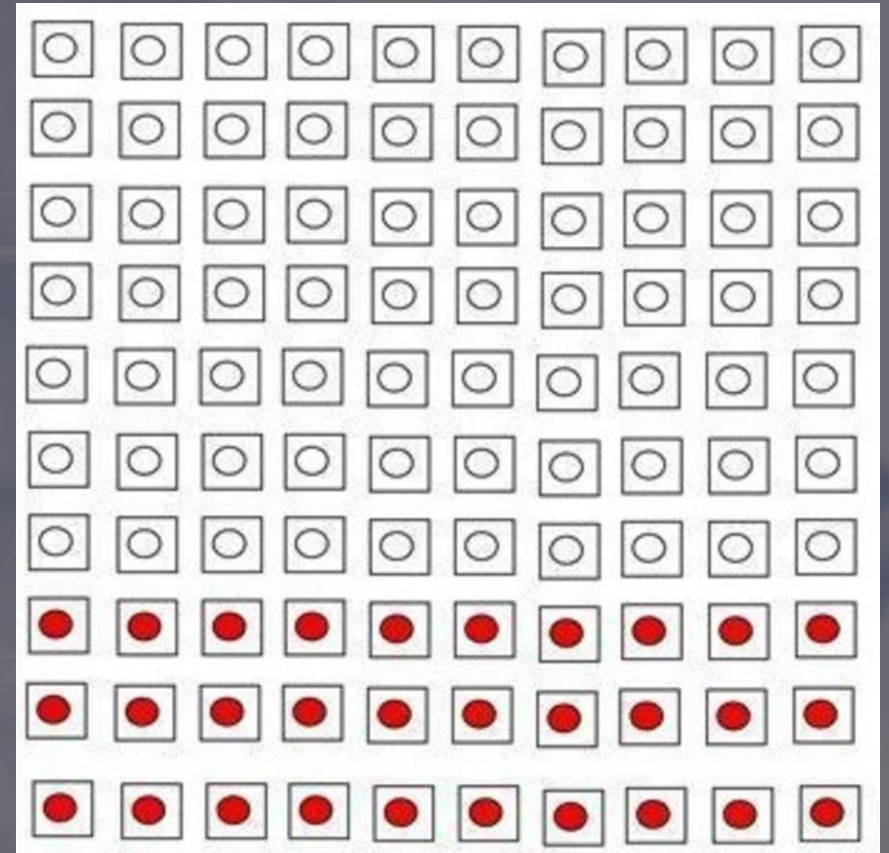


Up to 31 percent of sepsis cases start as urinary tract infections, leading to as many as 1.6 million deaths in the U.S. and Europe NBC News 1-7-21

It is hard to recognize sepsis

We need better diagnostics to recognize sepsis earlier

- Current screening tests do not work well in complicated hospitalized patients
- SIRS is only 30% specific
 - Can machine learning do better?
 - Can we develop fast turnaround diagnostic lab tests?



We need better treatments

Septic shock has a high mortality rate

- Despite being on antibiotics, some of our patients develop sepsis
- Many die in our ICU despite receiving current treatments available
- Many have other conditions (e.g. heart or kidney failure) that make giving fluids challenging



Dr. Septris



1 in 3

One in three patients who die in a hospital have sepsis.



Carol A. Cunningham, MD, FAAEM, FAEMS
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Ohio Department of Public Safety
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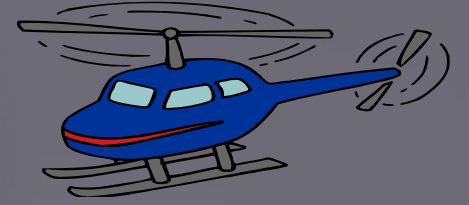
Facts of Foundation

- Emergency medical services (EMS) is a practice of medicine
- The specialty of EMS was unanimously approved by the American Board of Medical Specialties on September 23, 2010
- Emergency medical services (EMS) providers encompasses emergency medical responders (EMRs), emergency medical technicians (EMTs), advanced EMTs (AEMTs), and Paramedics
- The practice of EMS and emergency medicine is contemporarily dynamic and requires rapid decision-making and nimble and flexible protocols

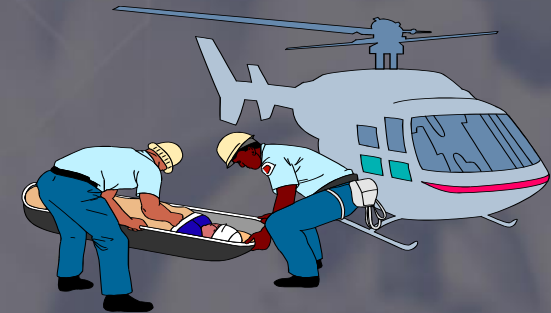




Facts of Foundation



- The scope of practice, available resources, and depth of manpower are limited for EMS
- A significant percentage of communities in our nation are served by rural and/or volunteer EMS agencies
- Many rural communities have long transport times and do not have Paramedics in their EMS systems



Facts of Foundation

- Initial patient triage, treatment, and transport are based on signs and symptoms rather than definitive diagnoses
- Our pace of medical decision-making and provision of medical care is faster than the growth in a Petri dish and often is performed at the speed of light



The Spectrum of Illness



STABLE

- Normal vital signs
- Appears well



The Grim Reaper is Coming

- Mildly abnormal vital signs
- Nonspecific symptoms



SHOCK

- Hypotension
- Appears ill

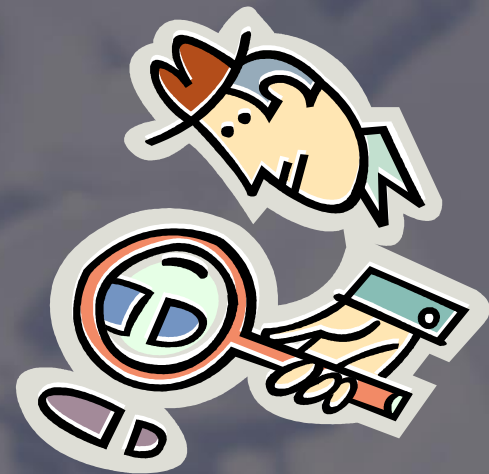
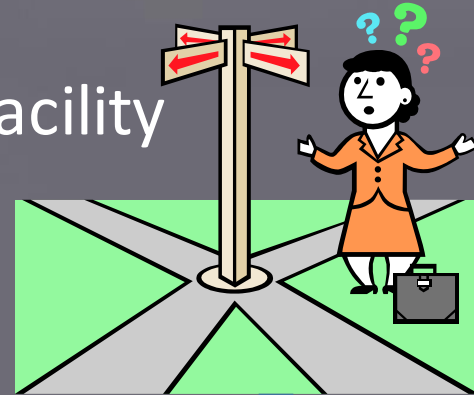
Early Recognition: Challenges and Opportunities

- **CHALLENGES**

- ❖ Transport times and distances to an appropriate healthcare facility
- ❖ Limited scope of practice (especially EMRs and EMTs)

- **OPPORTUNITIES**

- ❖ Designated tiered hospital centers for sepsis care
- ❖ Improve early recognition of “The Grim Reaper” in the neonatal and geriatric patient populations
- ❖ Handheld point-of-care testing devices suitable for EMS
 - Multiple parameter testing with one small sample of blood
 - Affordable and durable
 - Develop testing for other body fluids, e.g. saliva





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Thank you!