Biothreat and Emerging Infectious Disease Detection

Designing Novel Systems and Evaluating Current Methods

Richard E. Rothman, MD, PhD, FACEP
The Johns Hopkins University
Departments of Emergency Medicine and Medicine (Division of Infectious Diseases)
CEPAR, PACER, MARCE

Team: JHU SOM, JHU APL, USF CBD, CUBRC

Disclosures: *DM-3668, 3772 Patents: Cambrex, Inc.*

Research Objectives

- To describe currently available, developmental and potential technologies for rapid (bedside or point of care) detection of emerging and biothreat agents

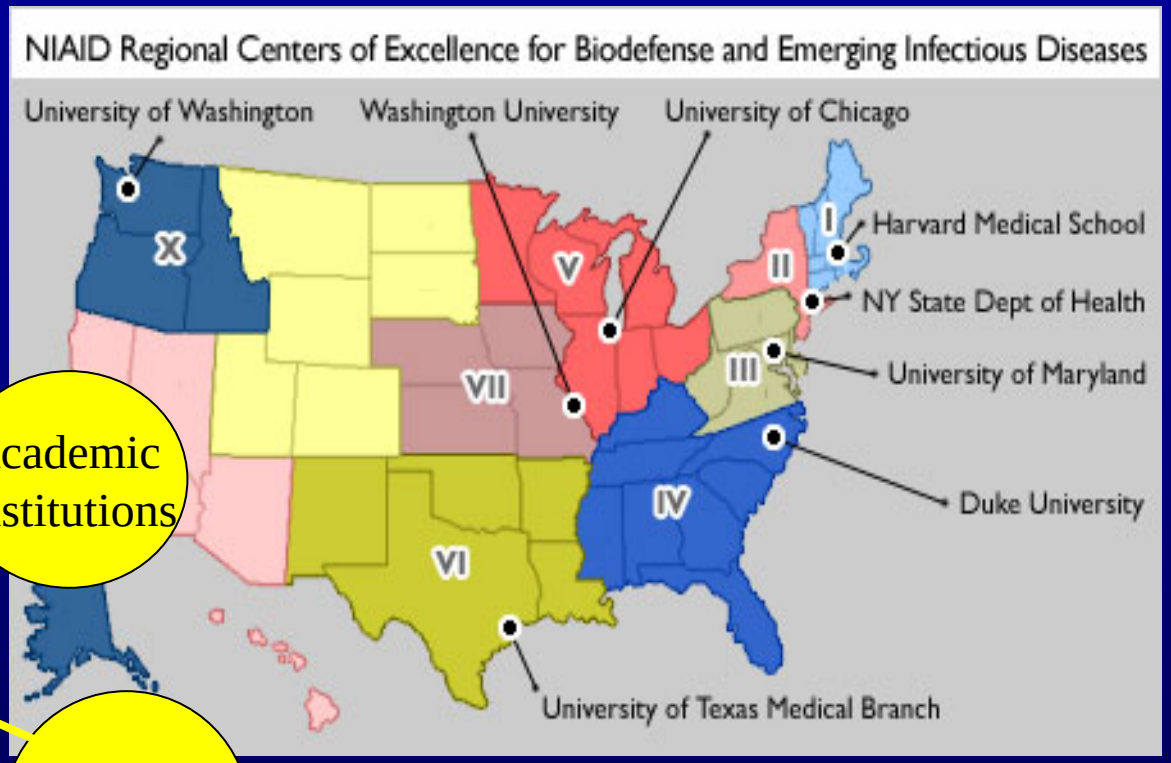
- To identify potential ways of improving laboratory response network with regard to surge capacity and integration of new technologies

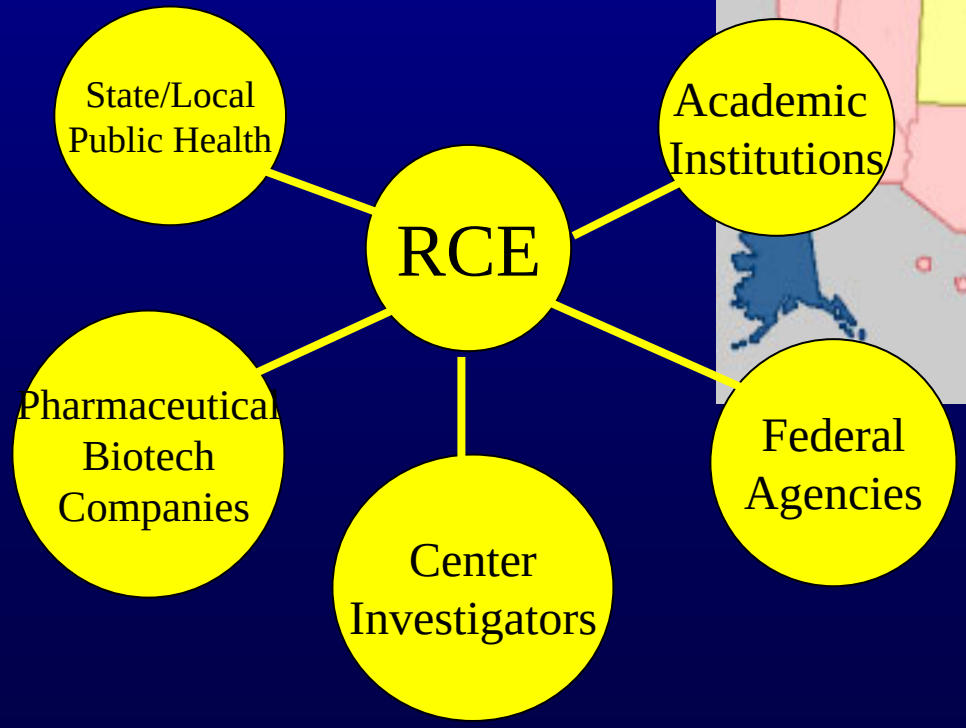
- To catalog existing syndromic surveillance methods in the 50 US and perform detailed description of select representative examples

Overview

- Describe regional organizations involved in disaster and biothreat preparedness (MARCE, CEPAR, PACER)
- Discuss potential routes for public health and medical interventions infectious disease outbreak preparedness (natural or manmade)
- Provide examples of potential diagnostic technologies under development
- Outline DHS studies in context of existing public health infrastructure

NIH: Regional Centers for Excellence



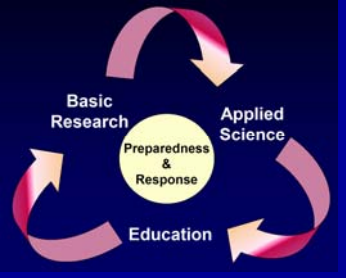


CEPAR

Center for Emergency Preparedness and Response

http://www.hopkins-cepar.org

- **Model Infrastructure for Johns Hopkins Enterprise (Incident Command)**
- **Integrated w/ Regional Assets**
- **Policy and planning**
- **Training and Exercise**
- **Funding and Grants**



CENTER FOR THE STUDY OF HIGH CONSEQUENCE EVENT PREPAREDNESS AND RESPONSE (PACER)

Program Goal:

Study how the nation can best prepare for and respond to potential large-scale incidents and disasters.

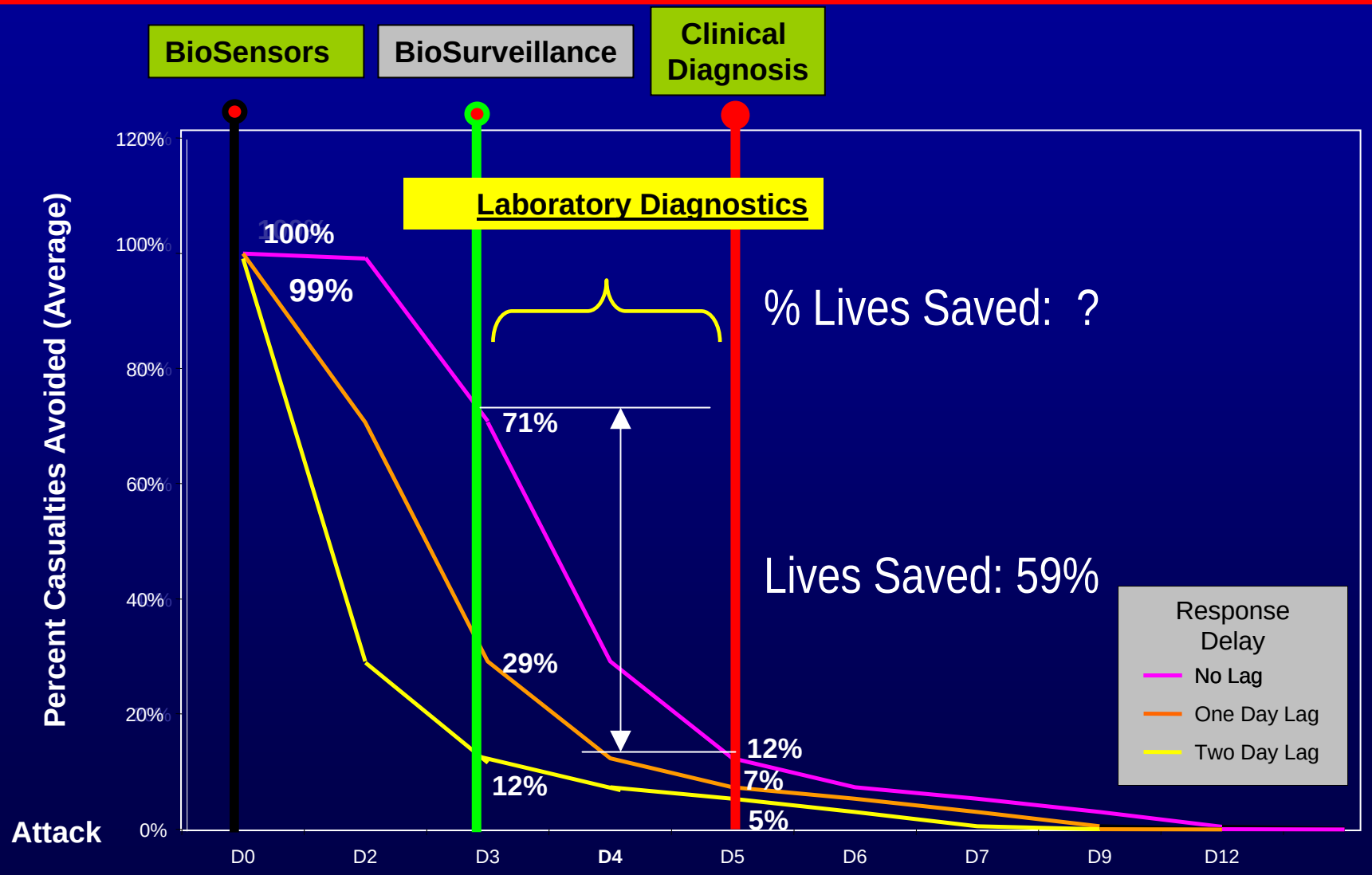
Team:

Multi-center cross state consortium drawing from experts in multiple disciplines

Research Domains

- Preparedness
- Response Networks
- Analysis, Modeling & Simulation
- Education
- Health Science & Technology

Laboratory Diagnostics and Syndromic Surveillance



Model from Kaufman, et al, 1997 Emerging Infectious Diseases

Clinicians Perspective on Diagnosis in Acute Care Settings

Key diagnostic questions which influence patient management can't be answered in a timely way…

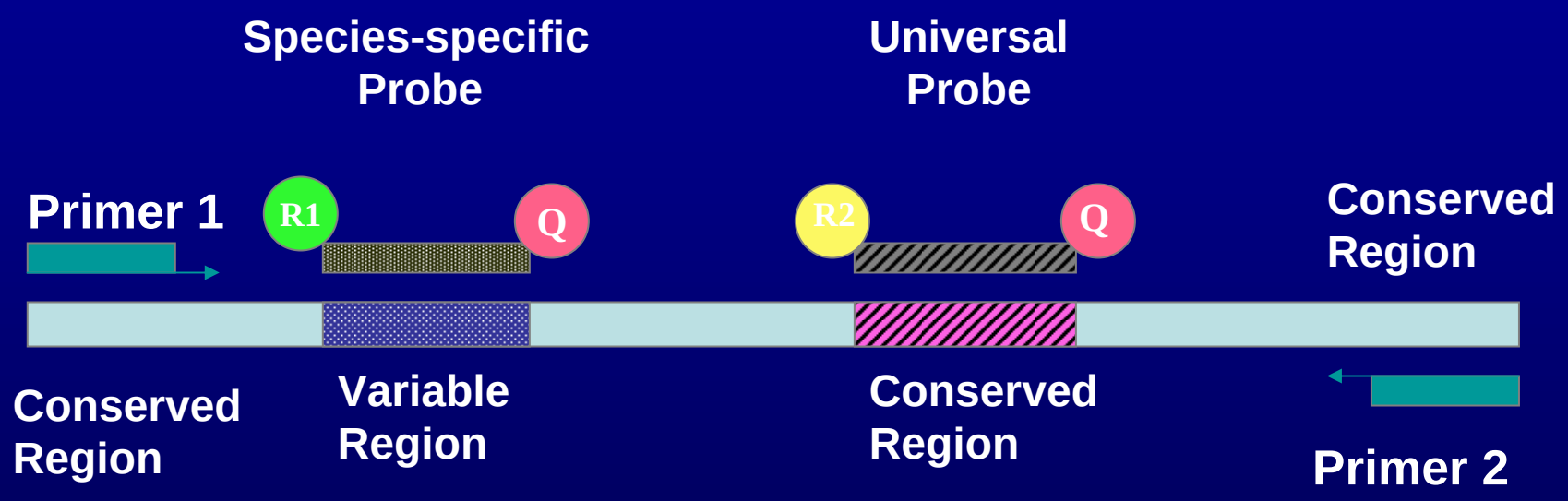
- **Is there systemic infection?**
- **What is the organism?**
- **Is there an uncommon organism?**
- **BT agent?**

Assay Design and evaluation

- **Rapid**
- **Sensitive**
- **Specific**
- **Reliable**

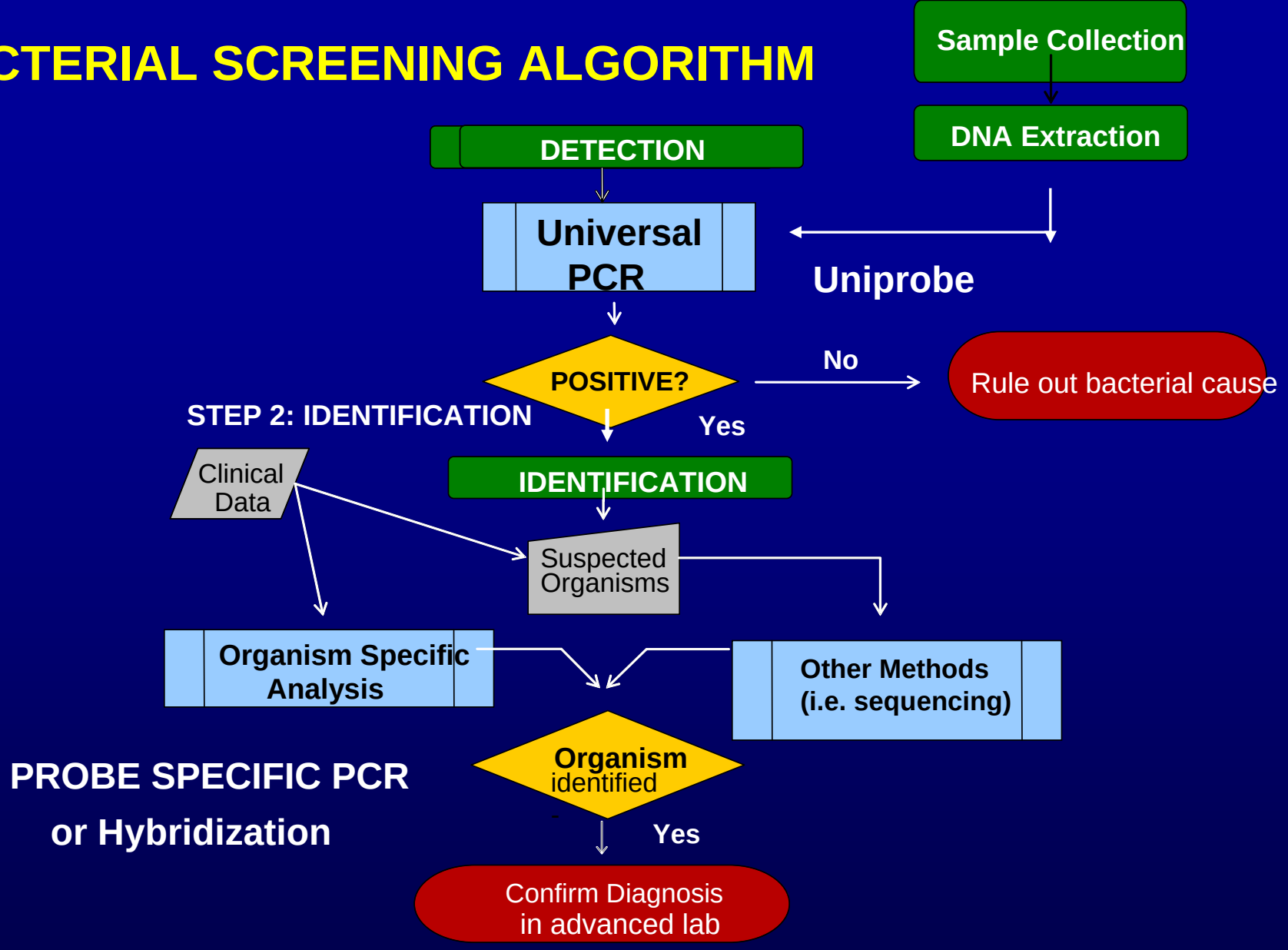
MULTIPROBE PCR ASSAY DESIGN

Yang, Rothman and Gaydos, JHU



16S rRNA gene

BACTERIAL SCREENING ALGORITHM



Time: < 6 hours
Clinical Testing: In progress (BT and nonBT agents)

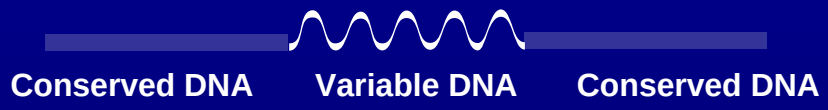
IBIS T-5000: Universal Biosensor:

D. Ecker et al, IBIS Technologies

STEP 1

Identify genomic regions for identification:

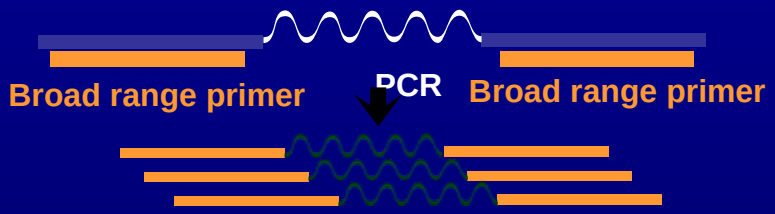
Variable DNA sequences flanked by conserved sequences



STEP 2

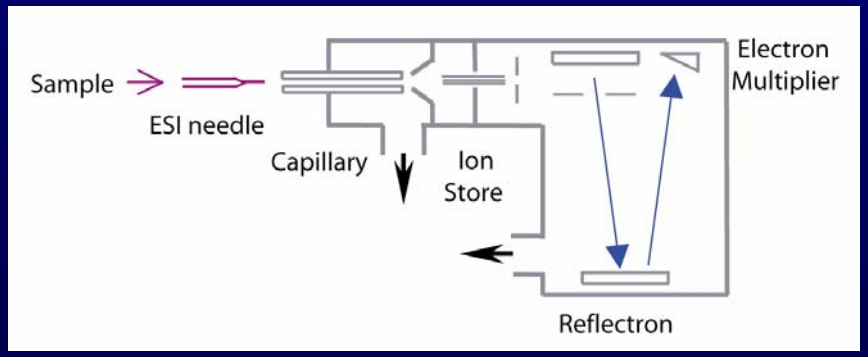
Amplify nucleic acids to measure:

Use broad-range, unbiased PCR primers



STEP 3

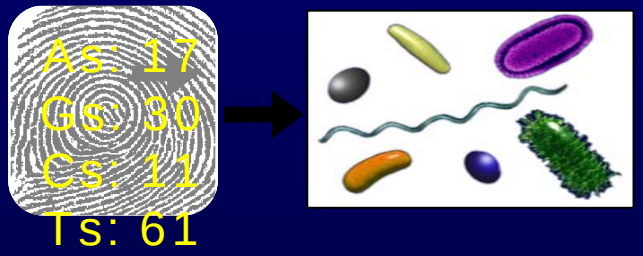
Measure nucleic acid: Highly-precise mass spectrometry



STEP 4

Identify the organisms:

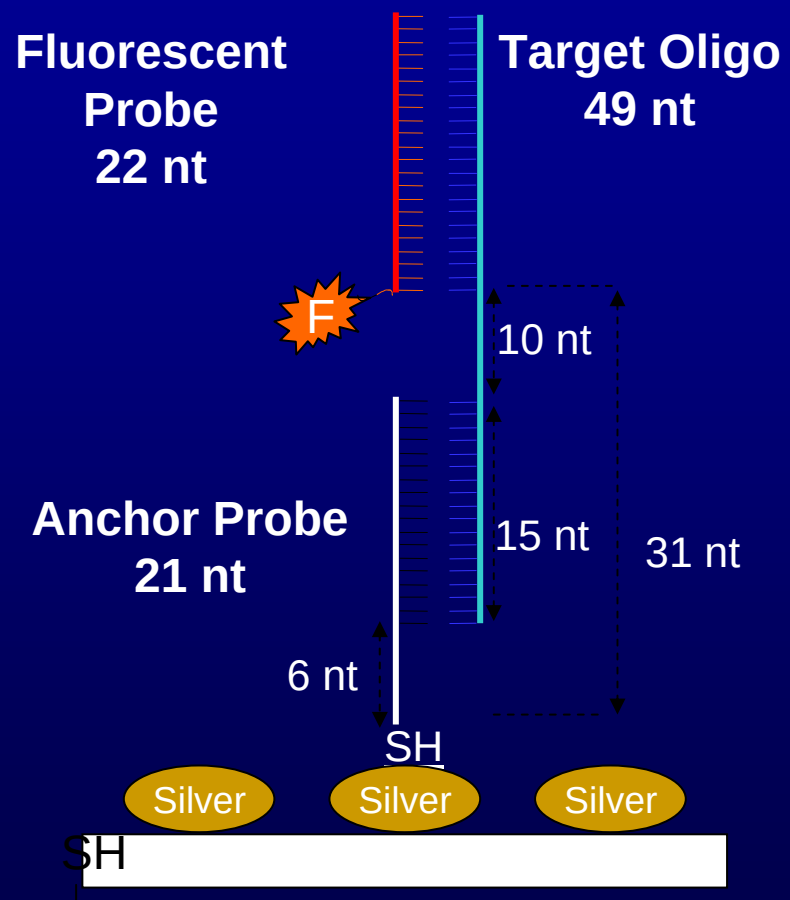
Base-composition fingerprints



High throughput (1500 PCR/day, ~300 samples/day)
Multiple deployments (CDC, NHRC, USAMRID)

Microwave-accelerated metal-enhanced Fluorescence Anthrax Assay

C. Geddes et al, UMBI



Assay construction

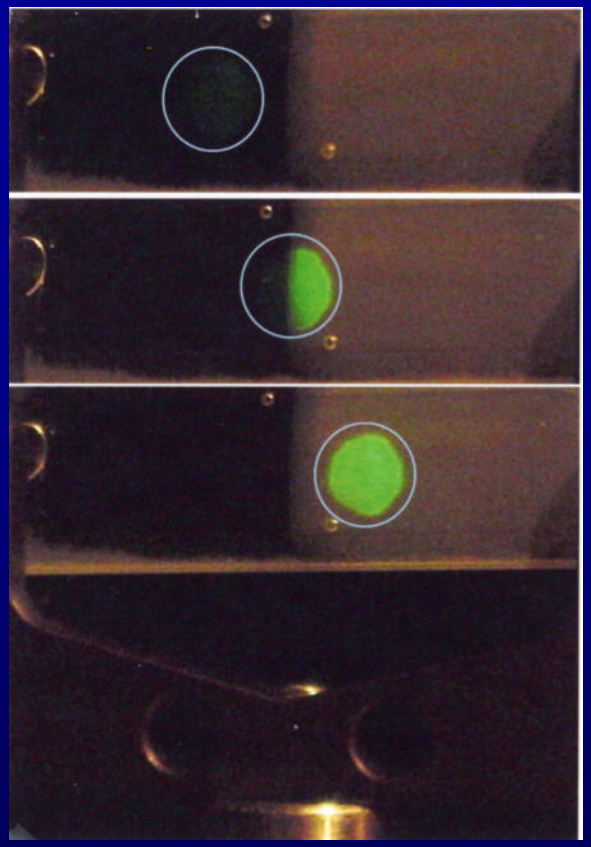
- Bioinformatically identify a conserved sequence of the PA gene
- Fluorophore is uniquely positioned for metal-enhanced fluorescence, only when the Anthrax target is present.

TAMRA

GTTTTTACCGTTATATATAAG `

TATAAGGTAAATGTATATGCTG

TGGCAATATATATTCATTAGGGTTAATATTCCATTTACATATACGAC



Combined technology of metal-enhanced fluorescence with low power microwave heating results in both ultra fast and ultra sensitive assay

Ultra sensitive detection of B. Anthracis in < 30 seconds

Breath Condensate Mass Spec Detection

J Jackman et al, APL and JHU

AIRBORNE MICROBES

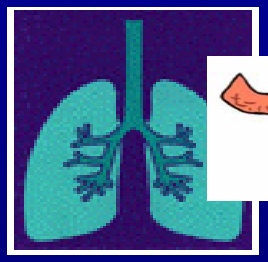
Bacteria

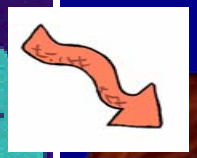
Toxin

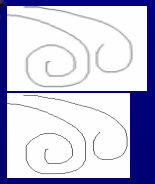
Virus

Unique Molecules Discriminate:
Infected vs Non-infected?
Bacterial or Viral?
Which microbe?

1. Microorganism enters lungs and triggers an inflammatory response.







2. Breath (droplets and water vapor) collected

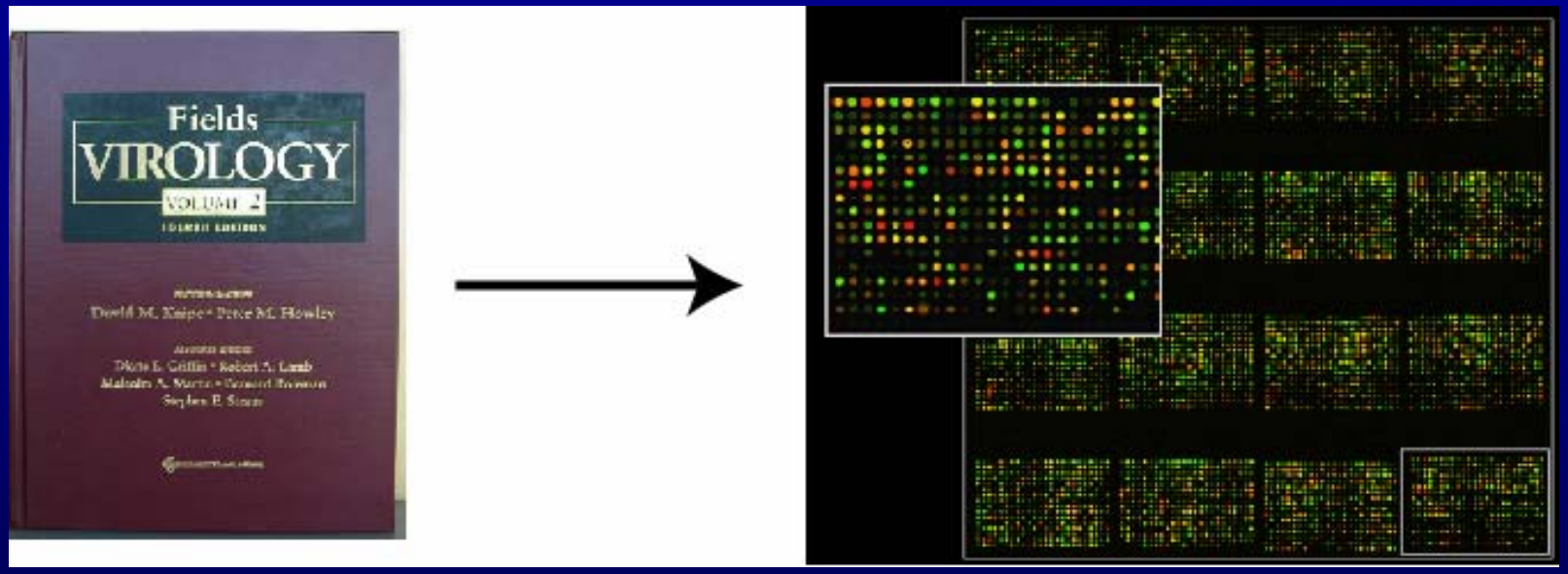
3. Collected products analyzed for presenc of host response molecules

Reliably identifies bacterial pathogens in animal models

Human protocols in progress

Virochip

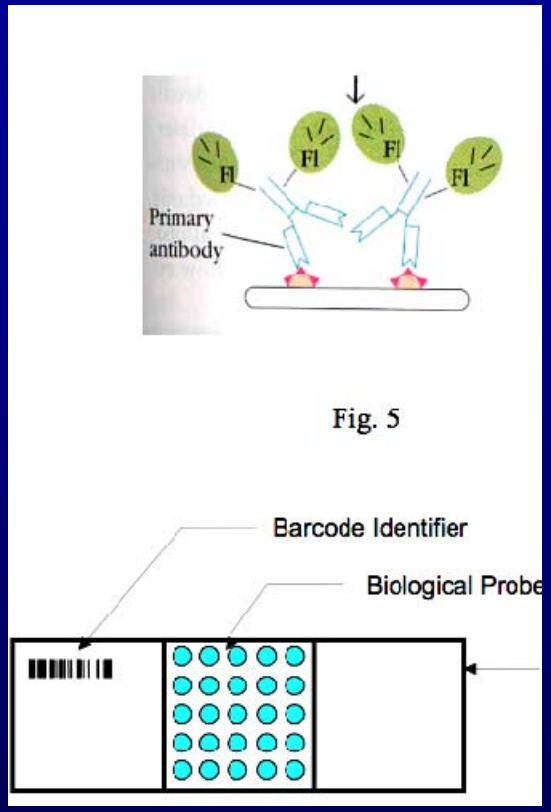
D. Wang et al, St. Louis University



Microarray allows for simultaneous screening of ALL known viruses

NanoDetection Technology (NDT) for Molecular Signatures

Malak Kotb et al, Univ Tenn



Disposable slides w/DNA or Antibody probes
Computer chip for detection
PDA for wireless result transmission/analysis

Integration of new technologies into public health infrastructure: Laboratory Response Network (LRN)

The LRN and its partners will maintain an integrated national and international network of laboratories that can respond quickly to acts of chemical or biological terrorism, emerging infectious diseases and other public health threats and emergencies.

Mission in Action

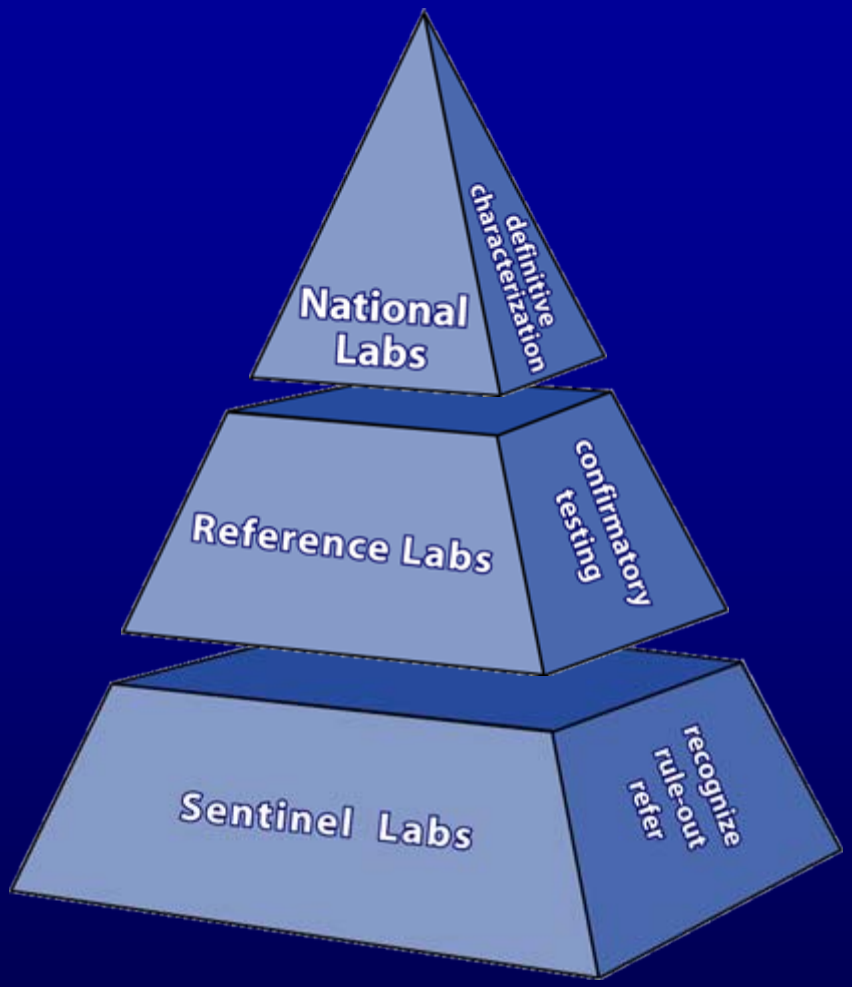
Bioterrorism Preparedness

- Timely detection of *Bacillus anthracis* during anthrax attacks in 2001

Public Health Emergency Response

- Developed rapid tests for detection of Severe Acute Respiratory Syndrome

CDC
Centers for Disease Control and Prevention



National responsible for specialized strain characterizations, bioforensics, select agent activity, and handling highly infectious biological agents.

Reference laboratories responsible for investigation and/or referral of specimens (>140 state and local public health, military, federal, and international laboratories)

Sentinel laboratories provide routine diagnostic services, rule-out and referral steps in the identification process (not equipped to perform the same tests as LRN reference laboratories).

How and when are new technologies integrated?

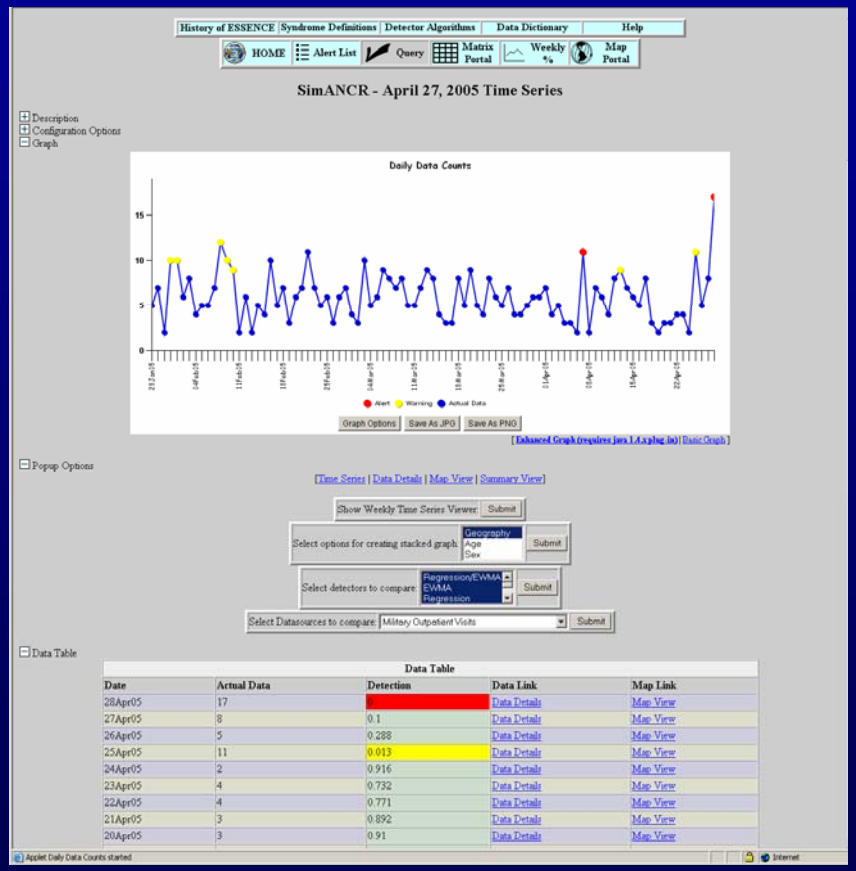
Syndromic Surveillance:
Early warning systems

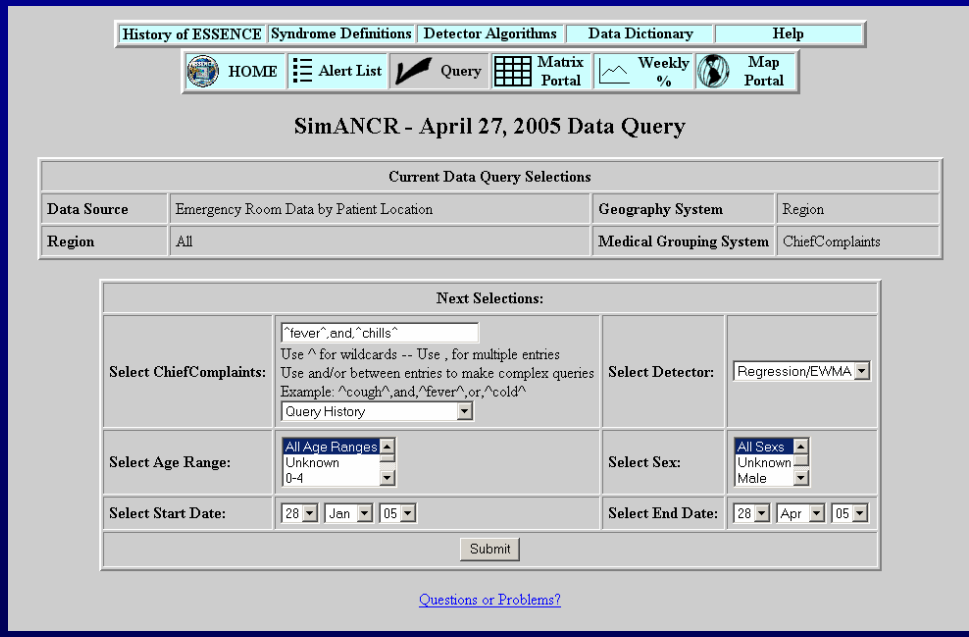
- Multiple systems
- Different temporally/different investigators
- Different data source evolution

International Society for Syndromic Surveillance
(http://www.syndromic.org)

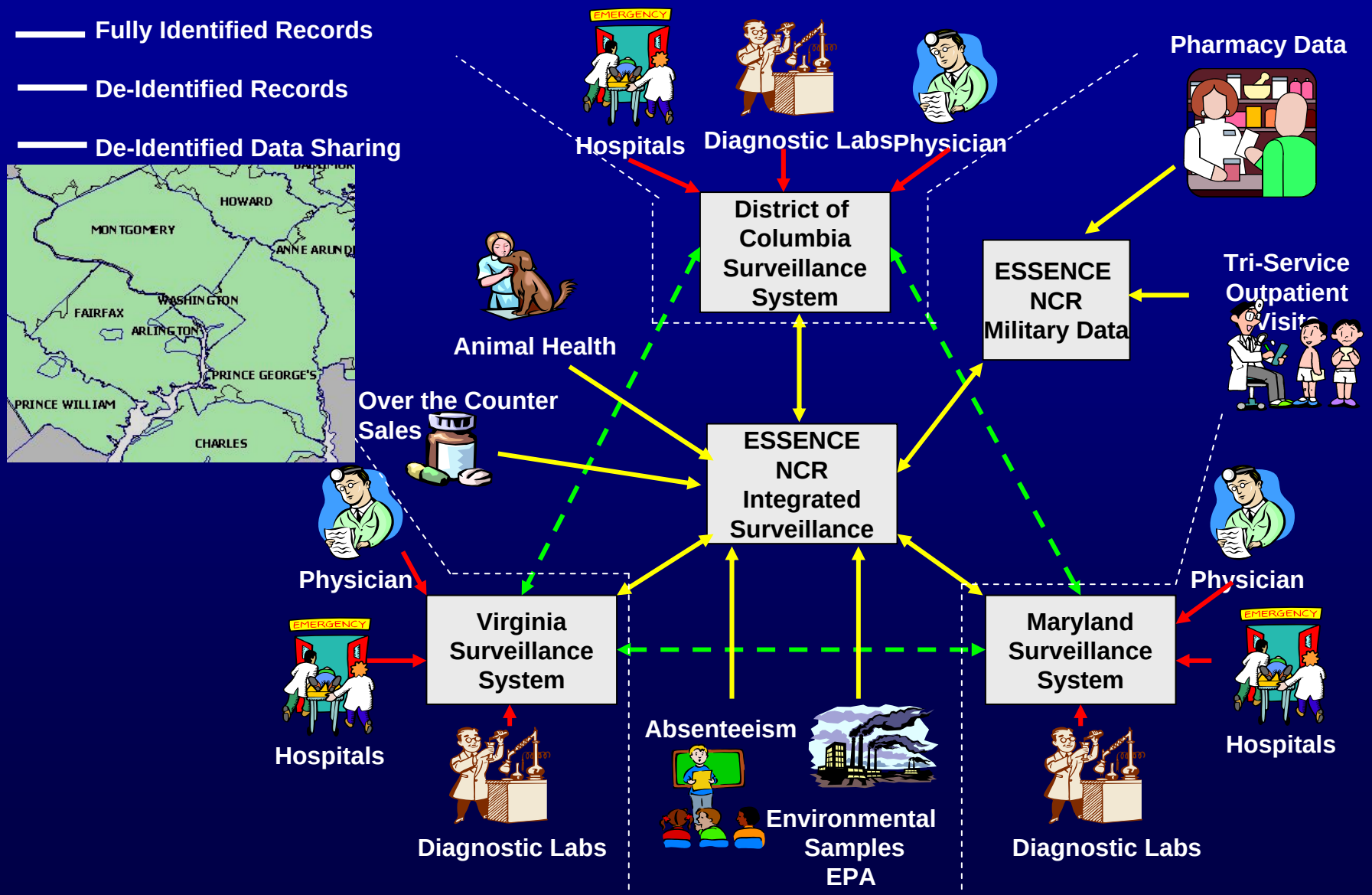
1 EXAMPLE: ESSENCE:

Web based disease surveillance information system to alert Health Authorities of infectious disease outbreaks, including possible bioterrorist attacks





National Capital Region (NCR) Network:
IDEAL MODEL for a Disease Surveillance:



BioSense

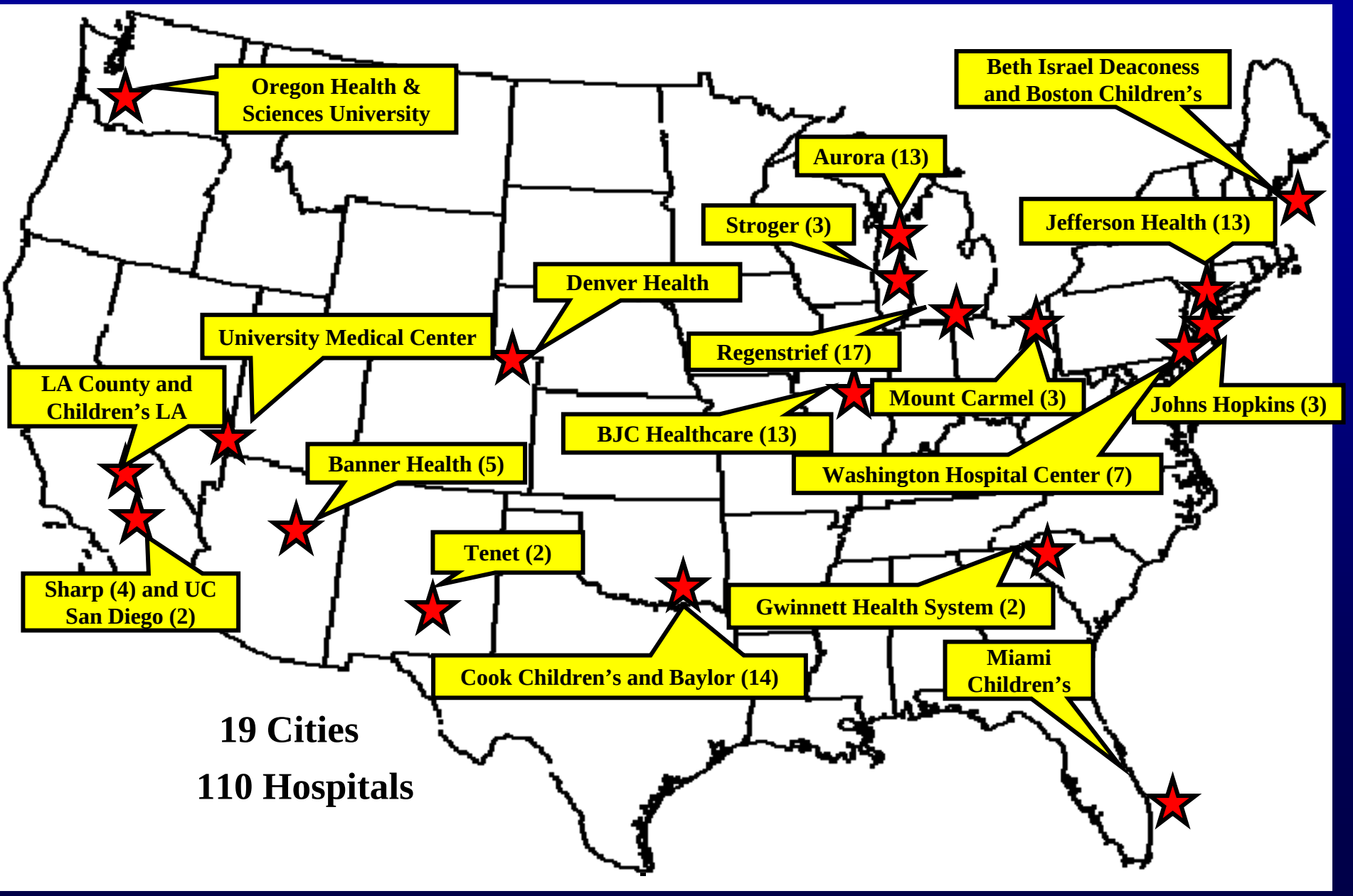
Vision

- **Provide national situational awareness** for suspect illness and possible cases before, during, and after a health event
- Help confirm or refute the existence of an event, monitor its size, location, rate of spread, and cessation

Approach

- **Real-time delivery** of emergency room and acute care data from hospitals to BioSense and **local** public health <u>aggregated and sent every 15 minutes</u>
- Electronic "views," analytics, and reports for national, state, and local public health, hospital, and government officials provided through **a secure web site**

Hospital Commitments to BioSense, 2005



PACER Research Objectives

- **To describe currently available, developmental and potential technologies for rapid (bedside or point of care) detection of emerging and biothreat agents.**
  - Systematic reviews, multiple sources: peer reviewed literature; scientific conferences; experts interviews (industry and military)

- **To identify potential ways of improving laboratory response network with regard to surge capacity and integration of new technologies**
  - Semistructured surveys (LRN and hospital laboratories) directors

- **To catalog existing syndromic surveillance methods in the 50 US and perform detailed description of select representative examples for detailed evaluation**
  - Semistructured surveys: state, city and county epidemiologists

Conclusions

- Preparedness for disasters (infectious disease outbreaks) is complex, involves multiple levels of planning

- Funding from DHS will help to scientifically evaluate existing and potential technologies and methods related to detection and surveillance of natural and manmade biothreats

PACER

A. Preparedness Theory & Practice
Lead: G.Green (CEPAR)

- **A.1. Threat & Vulnerability Analysis**
  Lead: M. Moskal (UB/CUBRC)
  Partners: APL, CBRTA (Black and Veatch)
- **A.2. Deterrence & Prevention**
  Lead: Dan Hamilton (SAIS)
  Partners: SAIS Faculty
- **A.3. Decision Paradigms**
  Lead: K. Kohri (JHU- APL)
  Partners: CEPAR, Morgan (SB)
  - -Command & Control
  - -CONOPS
  - A.3.i. Situation Awareness
    Lead: D.P. Glock (JHU-APL)
    Partners: UB/CUBRC, SAIS
    - -Recognition
- **A.4. Regional Integration**
  Lead: R. Vogel (MEMA)
  Partners: CBRTA, CEPAR,OHSU, DHRMCRH MCA, FSU, ARC
- **A.5. Surge Capacity**
  Lead: Tom Kirsch (CEPAR)
  Partners: DHRMCRH, OHSU, MD-DHMH, ARC, BSI
  - --Mass Casualty Handling
  - --Mass Population Handling
  - --Mass Distribution Strategies
- **A.6. Policy, Ethics, Law**
  Lead: S. Teret (BSPH Ctr for Law and PH)
  Partners: SAIS, SPSBE, FAMU, Govt Aff,BSPH
- **A.7. COOP/COG**
  - A.7.i. Continuity of Gov't
    Lead: R. Vogel (MEMA)
    Partners: SAIS, FSU, Brookings, JHU-Gov
  - A.7.ii Business Continuity
    Lead: S. Greenberg (JHU SPSBE)
    Partners: JHHS, Morgan, FAU, SPSBE
- **A.8. Forensics**
  Lead: C. Whitcomb (UCF)
  Partners: SPSBE-PSLP

B. Response Networks
Lead: T. Terndrup (UAB)

- **B.1. Informal Networks:**
  Lead: K. Denninghoff (UAB)
  Partners: Morgan, Tusk, BSPH, FSU, ARC
  - -Cultural Outreach
  - -Faith Based Initiatives
  - -Teachers
- **B.2. Formal Networks:**
  Lead: P. Pons (DHRMCMR)
  Partners: MEMA, JH Gov Aff, ARC, MIEMSS
  - -Interagency Coordination
- **B.2.i. International Integration**
  Lead: D. Hamilton (JHU-SAIS)
  Partners: SAIS
- **B.3. Health Systems Integration**
  Lead: J. Williams (AHCC)
  Partners: UAB, OHSU, DHRMCMR, FSU, CE
- **B.4. Leadership Behavior**
  Lead: S. Greenberg (JHU SPSBE)
  Partners: SAIS, FAMU, SPSBE
- **B.5. Civilian Behavior**
  Lead: D. Washington (ARC)
  Partners: Morgan, Brookings,

C. Analysis, Modeling, and Simulation
Lead: J. Epstein (Brookings)

- **C.1. Physical Effects M&S**
  Lead: M. Bruneau (UB-MCEER)
  Partners: FAMU, FAU, UAB, APL, CUBRC
  - -CBRN Environment Transport and Fate
  - -Infrastructure
- **C.2. Behavior Modeling**
  Lead: J. Epstein (Brookings)
  Partners: FSU, FAMU,
- **C.3. Economic Impact Assessment**
  Lead: J. Epstein (Brookings)
  Partners: FAU
- **C.4. CBRN Health Effects Modeling**
  Lead: J. Epstein (Brookings)
  Partners: BSPH, CEPAR
- **C.5. Integrated Modeling**
  Lead: J. Coolahan (JHU-APL)
  Partners: Brookings, UB, UAB
- **C.6. V V& A**
  Lead: J. Coolahan (JHU-APL)
  Partners: UAB

D. Science, Technology and Engineerin
Lead: Jose Latimer (JUH-APL)

- **D.1. Infrastructure Integrity**
  Lead: N. Yazdani (FAMU)
  Partners: FAMU, UAB, UB(CUBRC, MCEER) Morgan, CBRTA
  - D.1.i. Enviromental Remediation
    Lead: D. Canter (APL)
- **D.2. Information Assurance**
  Lead: G. Masson (WSE)
  Partners: APL, UB(CMIF), FSU SAIT, WSE
  - D.2.i. Communications
    Lead: M. Sudit UB (CMIF)
- **D.3. Detection & Sensors**
  Lead: J. Pournoor (CBRTA)
  Partners: UB/CUBRC, APL
  - -Standards Development
  - -Surveillance Technology
- **D.4. Test and Evaluation**
  Lead: C. Latimer (JHU-APL)
  Partners: APL, UB/CUBRC, Morgan
- **D.5. Health Science & Technology**
  Lead: R. Rothman (JHU-SOM)
  Partners: USF, UAB, APL, JHU BSPH, UB/CUBRC, UCF, CBRTA,
  - --Syndromic Surveillance Techniques
  - --Technology Development
  - D.5.1 PPE and Decon Methods
    Lead: P. Bryesse (JHU-BSPH)
    Partners: UAB, DHRMCMR, OHSU

E. Education
Lead: M. Ofusu (Morgan)

- **E.1 Primarly and Secondary Education**
  Lead: P.Welch (Morgan)
  Partners:
- **E.2. Higher Education Institutions**
  Lead: J. Links (JHU-BSPH)
  Partners: Morgan, UAB, Jacksonville, FSU
- **E.3. Leadership Training**
  Lead: S. Greenberg (JHU-SPSBE)
  Partners: ARC
- **E.4. First Responder Training**
  Lead: S. Cantrill (DHRMCMR)
  Partners: MIEMSS, OHSU, FCCJ, ND, SPSBE AHCC, MEMA, BSPH, ARC
- **E.5. Health System Continuing Educati**
  Lead: T. Thomas (Loma Linda)
  Partners: AHCC, CEPAR, TAHEC
  ---Prof Employees, first receivers, other HS Employe
- **E.6. Civilian/Public Training & Outreach**
  Lead: Darcy Ravndal (USF)
  - E.6.i. Disaster Training Courses
    Lead: D. Ravndal (USF)
    Partners: I UAB, ARC , Morgan
  - E.6.ii. Public Awareness (Media)
    Lead: W. Evans (UACC)
    Partners: JHU, Tusk, ARC
  - E.6.iii. Underserved Populations
    Lead: I. Griffin (UAB)
    BSPH, Morgan, ND, ARC, FAMU,Tusk, SPSBE, LL
  - E.6.iv. Teachers
    Lead: Welch (Morgan)
    Partners: I ARC, FSU
- **E.7i. Cultural Competence (Populations**
  Lead: R. Rowell (Morgan)
  Partners Tusk, FAMU, ND, LL, USF
- **E.7ii. Cultural Competence (Interagency**
  Lead: M Ferrer (JHU-SPSBE)
  Partners: BSPH
- **E.8. Education Science**
  Lead: Spector (FSU)
  Partners: CEPAR, ARC