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UAB Center for Emerging Infections and Emergency Preparedness (CEIEP)

Emergency Preparedness and Community Mitigation Symposium

December 6, 2007

- Recent History of Biodefense and Emerging Infections Research
- Importance for Emergency Preparedness
- Current efforts at UAB
- Future research and challenges

Chronology of Biodefense & Emerging Infections Research

- Federal Level
  - February 2002: NIH Blue Ribbon Panel (Category A Agents), announces $1.5 billion in new research dollars
  - May 2002: Second NIH Blue Ribbon Panel (Category B and C Agents)
  - October 2002: Planning of RCEs
  - September 2003: 1st RCE awards made

Category A

- Bacillus anthracis (anthrax)
- Clostridium botulinum toxin (botulism)
- Yersinia pestis (plague)
- Variola major (smallpox) and other related pox viruses
- Francisella tularensis (tularemia)
- Viral hemorrhagic fevers
  - Arenaviruses
    - LCM, Junin virus, Machupo virus, Guanarito virus
    - Lassa Fever
  - Bunyaviruses
    - Hantaviruses
    - Rift Valley Fever
  - Flaviruses
    - Dengue
  - Filoviruses
    - Ebola
    - Marburg

Category B

- Burkholderia pseudomallei
- Coxiella burnetii (Q fever)
- Brucella species (brucellosis)
- Burkholderia mallei (glanders)
- Chlamydia psittaci (Psittacosis)*
- Ricin toxin (from Ricinus communis)
- Epsilon toxin of Clostridium perfringens
- Staphylococcus enterotoxin B
- Typhus fever (Rickettsia prowazekii)
- Food and Waterborne Pathogens
  - Bacteria
    - Diarrheagenic E.coli
    - Pathogenic Vibrios
    - Shigella species
    - Salmonella
    - Listeria monocytogenes
    - Campylobacter jejuni
    - Yersinia enterocolitica)
  - Viruses (Caliciviruses, Hepatitis A)
  - Protozoa
    - Cryptosporidium parvum
    - Cyclospora cayatanensis
    - Giardia lamblia
    - Entamoeba histolytica
    - Toxoplasma
    - Microsporidia

- Additional viral encephalitides
  - West Nile Virus
  - LaCrosse
  - California encephalitis
  - VEE
  - EEE
  - WEE
  - Japanese Encephalitis Virus
  - Kyasanur Forest Virus

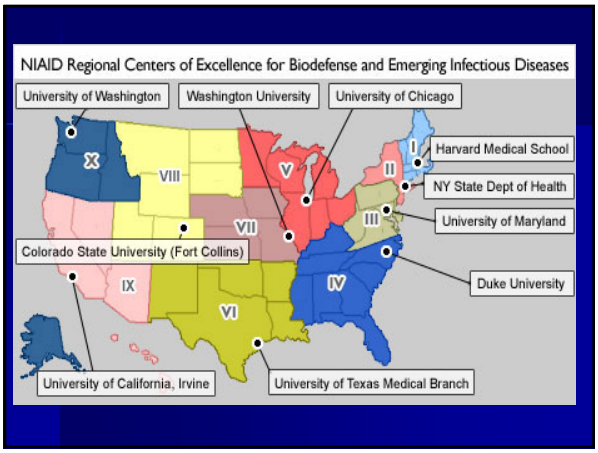
Category C

Emerging infectious disease threats such as Nipah virus and additional hantaviruses.
NIAID priority areas:

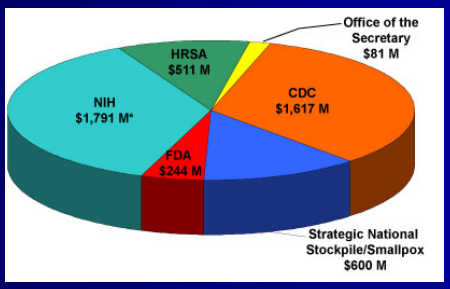
- Tickborne hemorrhagic fever viruses
  - Crimean-Congo Hemorrhagic fever virus
- Tickborne encephalitis viruses
- Yellow fever
- Multi-drug resistant TB
- Influenza
- Other Rickettsias
- Rabies
- Prions*
- Chikungunya virus*
- Severe acute respiratory syndrome-associated coronavirus (SARS-CoV)
- Antimicrobial resistance, excluding research on sexually transmitted organisms (see page 2)
- Antimicrobial research, as related to engineered threats*
- Innate immunity, defined as the study of non-adaptive immune mechanisms that recognize, and respond to, microorganisms, microbial products, and antigens*

Federal Level (cont.)

- June 2003: BSL-3 and BSL-4 Laboratory Construction Applications
- RBLs Awarded October 2003
- Biodefense and Emerging Infection Training Grants Approved in September, 2003
- 2004 – vaccine supply and development
- 2004 NIH Roadmap – Clinical and Translational Science Award: Emphasis on bench to bedside research.



HHS Civilian Biodefense Spending FY 2006 (Est.)



UAB level

- March 2002: Strategy Meetings begun
- September 2002: Submission of Pilot Center Application
- October 2002: Planning of SERCEB
- Late 2003 – SERCEB, SEBLAB, UAB Centers received funding
- 2003 – CASG began clinical trials on emerging infections
- 2006 – CEIEP created merging two existing centers

Importance of Basic and Clinical Research to Preparedness Efforts

- Federally mandated approach to develop medical countermeasures
- Need for vaccines (prevention), diagnostics, and therapeutics
- Determine type and amounts of products for national stockpile

UAB Projects

Basic Research (SERCEB)

Development of Therapies for Orthopox viruses

- Cores:
  - Structural Biology: DeLucas
  - Protein Expression: Luo
  - Monoclonal Antibodies: Accavitti-Loper
  - Small Animals: Kern/Quenelle
  - Policy and Ethics: Tilden

Basic Research (cont.)

- Drug Candidate Screening and Animal Models: Kern, Prichard, Whitley
- Drug Synthesis: Secrist and Maddry at SRI

Vaccinia virus UDG structure

Vaccinia (Green)

Structure has been determined to 2.3 Å Resolution. Currently R and Rfree Values are 29 and 32%. Approximately 86% of protein residues lie in the core region of Ramachandran plot.

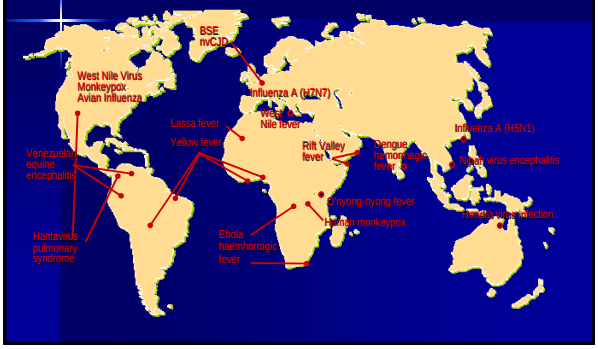
Clinical Trials

- Collaborative Antiviral Study Group (CASG): international multi-center group conducting trials at more than 70 institutions.
- Mandated by NIAID to study West Nile virus in 2003. Study closed in December 2006.
- Began pediatric study of Tamiflu in late 2006 (children 0-2 years old).
- Developed protocol templates for small pox and SARS.

Future of research- Federal level

- NIAID Strategic Plan for Biodefense Research – September 2007
  - Continued emphasis on vaccines, diagnostics and therapeutics, particularly drug discovery
- CTSA- NIH Roadmap initiative
  - More emphasis on interdisciplinary research to "speed up" bench to bedside process

Emerging Viral Diseases: 21st Century



Future of research- UAB level

- SERCEB – emphasis on drug discovery for the upcoming recompetition
- UAB Drug will be the first RCE developed drug in humans
- Compound will be studied through the NIAID CASG
- Increased emphasis on interdisciplinary efforts - CCTS

Challenges to Biodefense and Emerging Infections Research

- Understanding of Natural History and Pathogenesis of Disease
- Definition of Molecular Targets
  - Lack of Pharmaceutical Incentive
- Controlled Trial Evaluations during 'Outbreaks'
  - Lack of controlled trials
  - Compassionate release of unproven medications
  - Regulatory Impediments