# Summary Report

## Centers for Disease Control and Prevention
## Chronic Fatigue Syndrome Research Program
## External Blue Ribbon Panel Meeting

**January 30-31. 2007**

**Tom Harkin Global Communications Center**
**Atlanta, Georgia**

## Executive Summary

The Centers for Diseases Control and Prevention Chronic Fatigue Syndrome Research Program (CDC-CFSRP) External Blue Ribbon Panel met on January 30-31, 2007. This was the second of two meetings to discuss the activities and future placement of the CDC-CFSRP. The group was co-chaired and facilitated by Dr. Lisa M. Lee, Assistant Science Officer in Office of the Chief Science Officer, CDC Office of the Director, and Dr. Charles Raison, Assistant Professor in the Mind-Body Program and Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine. Members of the External Blue Ribbon Panel (EBRP), the CDC-CFSRP, the National Center for Zoonotic, Vector-Borne & Enteric Diseases (NCZVED), and the Coordinating Center for Infectious Diseases (CCID) and their affiliations are listed in Appendix A-EBRP.

The objectives of the meeting and charge to the EBRP members were the following:

1. Review the current collaborative intramural (i.e., within CDC's Coordinating and National Centers) and extramural (e.g., other federal government agencies, non-government professional organizations, clinicians, academic research scientists, and collaborators outside the CDC) research, educational, and community outreach activities of the CDC-CFSRP;

2. Review the portfolio of future research agenda options developed by the CDC-CFSRP Internal Planning Group, and identify and suggest prioritization for those which should be pursued and developed by the CDC-CFSRP; and

3. Identify successful and problematic lines of research, and suggest ways in which strategic research connections and synergies can be enhanced and problematic areas resolved.

Panel members were encouraged to share their ideas and information in open discussion without obligation to come to group consensus. More specifically, Panel members were to consider themselves a collection of individual consultants simultaneously gathered to exchange their individual advice and opinions. The responsibility of distilling the ideas and information shared at the meeting, and making subsequent decisions would rest solely with the CDC.

Dr. William Reeves, Chief of the CDC-CFSRP and the Chronic Viral Diseases Branch, Division of Viral and Rickettsial Diseases, NCZVED, CCID (CVDB, DVRD, NCZVED, CCID) provided an overview of the CDC-CFSRP, including its current activities, its fiscal, human, and collaborative resources, recommendations for future research activities, and placement of the CDC-CFSRP within CDC (see Appendix B-EBRP). This presentation was followed by a question and answer session between Panel members and CDC-CFSRP leadership.

Dr. Lisa M. Lee summarized the proceedings of the Internal Planning Group (IPG) meeting which occurred December 5-6, 2006. Dr. Lee's presentation focused on the content and prioritization of research agenda options developed by the IPG, recommended enhancements to strategic research connections and synergies, and the research and programmatic environment that the IPG felt would be most suitable for the CDC-CFSRP. The remainder of the two-day meeting focused on discussions amongst the EBRP regarding the research agenda the CDC-CFSRP should consider pursuing in the future, including continuation of current activities as well as development of new research and programmatic efforts. Discussions also focused on identification of limitations in the current CDC-CFSRP and how they could be resolved through potential intramural and extramural collaborations. The conclusions of the EBRP regarding the CDC-CFSRP were as follows:

- Surveillance activities within Georgia should continue;
- Work on further refining the case definition should take place;
- New interventions should be evaluated, especially those which have proven to be successful in other areas of medicine;
- Due to the multi-faceted nature of the CFS as a disease, research efforts must be multi-disciplinary in nature;
- To support long-term sustainability, the CDC-CFSRP should collaborate with internal and external partners; and
- To sustain its reputation for producing strong research outcomes, the CDC-CFSRP must preserve its organizational strengths (i.e., laboratory capacity, surveillance activities, modeling activities) and be placed in an organizational environment where collaboration and resource sharing are encouraged.

## ASSOCIATIONS BETWEEN CDC-CFSRP AND EBRP MEMBERS

The EBRP members were asked to describe any existing collaborations with the CDC-CFSRP as they introduced themselves. The following associations were noted:

| EBRP Member | Association with CDC-CFSRP |
|---|---|
| Dr. Charles Raison | Receives funding from CDC to conduct a research study using treatment with the cytokine interferon-alpha as a model system for understanding inflammatory contributions to the pathophysiology of idiopathic fatigue. |
| Dr. Nancy Klimas | Currently collaborating with CDC-CFSRP on a Gulf War Study through a Department of Defense grant. |
| Ms. K. Kim McCleary | 1) Contractor to the CDC-CFSRP for project that utilizes several integrated strategies to educate health care professionals, including primary care providers, nurse practitioners, and physician assistants (PA) about detection, diagnosis, and management of CFS;<br>2) Contractor to the CDC's National Center for Health Marketing for project that utilizes integrated marketing strategies to raise awareness of CFS and inform the public of the serious nature of CFS, its prevalence in the population, and its symptoms. |

## REVIEW OF CURRENT COLLABORATIVE INTRAMURAL AND EXTRAMURAL ACTIVITIES OF THE CDC-CFSRP

**and**

## PRIORITIZATION OF FUTURE RESEARCH AGENDA OPTIONS IDENTIFIED BY THE INTERNAL PLANNING GROUP

The EBRP discussed the current research activities of the CDC-CFSRP, and the research agenda options identified by the IPG.

- Continuation of Georgia Surveillance Activities
  - Panel members recommended that both the population-based surveillance and Bibb County registry in Georgia be continued, particularly because these longitudinal surveillance activities could:
    - identify treatment interventions and their rates of use
    - identify critical patient sub-groups
    - provide information which could allow greater generalizability of findings
    - allow for comparisons between individuals who do and do not seek care
    - support the refinement of the case definition
    - identify risk factors associated with CFS and other conditions
    - long-term outcomes (i.e., functional status, co-morbid medical conditions, other occurrences such as auto accidents)
    - changes in knowledge, attitudes and beliefs of studied populations over time

  - Data from the Georgia surveillance activities is the first comprehensive data set collected using instruments which have been defined and accepted by a majority of CFS researchers

- Interventions
  - Panel members indicated attention should be placed on developing interventions which would address the variety of signs and symptoms observed among the diverse subgroups of CFS patients seen clinically
  - Interventions proven to be effective in addressing other illnesses should be examined as potentially new treatments for CFS
  - Intervention research could lead to new interventions and clinical support for many patients who experience symptoms beyond those captured in the current case definition
  - Clinicians need evidence-based guidelines:
    - that identify and validate treatment interventions
    - that identify intervention options besides those related to exercise and cognitive behavioral therapy (CBT)
    - because reimbursements are only allowed for evidence-based medicine

    - because they currently borrow evidence-based practices from other areas of medicine due to the lack of options available for treating CFS patients
  - Interventions that address CFS specifically may help minimize the misconception that the illness is not real (e.g., it is not just a sign of depression)

- Case Definition
  - The case definition and the methods used to categorize CFS patients should be consistent over time and across surveillance studies. This will allow for comparisons across studies and populations
  - The appropriateness of using the criteria of six months of fatigue to identify incident cases and antecedents should be reevaluated, especially because co-morbidities can develop over the intital 6 months (e.g., lost time at work; disenfranchisement; feelings of abandonment and isolation; mood symptoms)
  - Means of identifying cases at the earliest possible time would help with studies of pathogenesis

- Psych-Neuro-Immunological (PNI) Connections
  - PNI connections are critical to CFS research and can be studied through longitudinal surveillance of the type being carried out in Georgia
  - NI (neuro inflammatory disorder) connections should also be examined for potentially useful information and interventions

- Developing Tools/Measures for Diagnosis, Genomics, Functional Status, and Marker Identification[1]
  - Standardized measures are critical, particularly for implementing longitudinal studies
  - Identification of functional disease and vulnerability markers for diagnosing disease would be helpful. Clinicians lack objective markers on which to base disease or disability status; marker identification could provide information about sub-groups of patients
  - Studies that examine interventions would be beneficial

- Specimen Banks
  - Identification of all available specimen banks would provide substantial benefits:
    - savings in research costs
    - access to readily available specimens
    - support collaboration
    - increase opportunities to re-examine disease etiology with technological improvements

- Other IPG-identified research areas discussed
  - Provide an environment which will support synergistic laboratory activities
  - Examine disparities in incidence and prevalence of CFS
  - Support/encourage basic research collaborations

[1] This area was not discussed during the initial prioritization but garnered discussion among panel members.

- Other research areas discussed which were not identified by the IPG
  - Measure disease burden and initiate activities using a health utilities framework to determine and compare quality of life and quality of adjusted life years across illnesses
  - Separate CFS and Fibromyalgia co-morbidity issues
  - Support CDC-CFSRP as a model data sharing infrastructure (e.g., server; data management activities; laboratory platform) for groups conducting CFS research to emulate
  - Identify what CDC wants to do with the information identified by the CDC-CFSRP, especially given its transient funding environment:
    - apply CDC-CFSRP expertise to other “unwell” conditions/fatiguing syndromes that need definition, examination, and etiology
    - standardize methods used to determine case definitions and conduct surveillance
    - use a systems biology approach to continue progress made in identifying patient subgroups
  - Identify a medical home/specialty for CFS
  - Make use of military populations to study CFS and other related disorders where signs/symptoms/specimens are available pre and post onset

## STRATEGIC RESEARCH CONNECTIONS AND SYNERGIES FOR CDC-CFSRP ENHANCEMENT AND PROBLEM RESOLUTION

Internal Connections and Synergies - Collaborations within CDC:
(Caution was suggested concerning the potential of the CDC-CFSRP to lose capacity or be spread too thin)

- NCZVED
  - Post-Lyme Disease

- Chronic Disease Center
  - Develop and test treatment interventions, i.e., secondary prevention. For example, physical activity and exercise studies with the Division of Nutrition and Physical Activity
  - Collaborate on intervention genomics

- Occupational Health and Injury
  - Focus on early trauma (traumatic brain injuries [TBI]) resulting CFS-like illness
  - Examine outcomes of injury among patients with CFS and CFS-like conditions
  - Gulf War Syndrome and similar conditions related to the current war (this may also have implications for working with those in environmental health)

- National Center for Health Statistics (NCHS) and use of the National Health and Nutrition Examination Survey (NHANES)
  - Utilize existing data (information and biological specimens) from nationally representative studies (e.g., NHANES)
    - to identify and develop indicators of CFS that are reliable and valid
    - provide baseline measures for subgroups

- Behavioral Risk Factor Surveillance System (BRFSS)
  - Identify opportunities to add questions that could be mutually beneficial to the CDC-CFSRP and others

External Connections and Synergies - Collaborations outside CDC:

- Department of Defense (DoD)
  - Benefits:
    - population in which incident CFS cases can be studied
    - largest population in which men can be studied
    - pre- and post-disease onset specimens can be collected and analyzed

International and global collaborative opportunities
- Dr. Anthony Komoroff (Harvard University) would like to establish a virtual network with Dr. Klimas (University of Miami/VA), Dr. Hanna (NIH), and Dr. Reeves (CDC-CFSRP) to create a virtual platform to include shared research hypotheses and findings
- Japanese officials have expressed interest in establishing research collaborations with US CFS researchers

- NIH
  - Collaborations could be achieved through Interagency Agreements with specific Institutes and Centers
    - release co-funded NIH-CDC Requests for Applications (RFAs) and Personnel Action Requests (PARs)
  - Intramural collaborations must be arranged with individual laboratories and are subject to the same review and IRB rules as all NIH intramural studies
  - Collaboration would allow for multiple, independent investigator-initiated, peer reviewed proposals to study the wealth of data that CDC has collected

- The Veterans Administration (VA)
  - Similarly to DoD, VA has a population in which co-morbidities could be studied
  - Can conduct intervention research and study the effectiveness of different treatments
  - Electronic medical records enhances the ability to search for undiagnosed patients (limitations in diagnoses will have to be addressed)

- Academia
  - Institutions currently conducting CFS research could collaborate with CDC

- Foundations
  - Public health focus (e.g., Robert Wood Johnson Foundation) for funding research or educational programs
  - The issue of unwellness could be used as a platform

- Health Maintenance Organizations (HMO) and Preferred Provider Organizations (PPO)
  - In an effort to decrease healthcare costs, some HMO and PPO are interested in funding research studies, especially intervention trials

- Medical Education
  - CDC can collaborate with other entities to create and develop a fertile environment to train new CFS investigators
  - CDC could garner support for a medical home for CFS (currently, patients are not seen by any one medical specialty)
  - Teach healthcare providers how to diagnose and differentiate between CFS patients and those feeling “unwell” and relieve suffering among the latter (42% “unwell” patients have a diagnosable or treatable condition)

Other general implications related to collaborations:

- CDC is considered the *thought* leader in CFS research
- - Use this position to leverage others into collaborative relationships on a variety of issues (e.g., intervention research; medical education)

- Public Health connection to CFS
  - While some panel members felt that the frequency of disease occurrence and the dearth of available treatment interventions warranted treating CFS as a public health problem, some felt that CFS is not currently seen as a priority for those dealing with multiple public health problems. More specifically, given the focus on clinical care for individual patients, Public Health Departments should use their limited resources to refer patients to appropriate CFS information and resources rather than provide direct services
  - CDC's strengths lie in its expertise in developing case definitions, conducting population-based studies, and surveillance activities, not clinical studies. Thus, the CFSRP should focus its activities in these areas

## PLACEMENT OF THE CDC-CFSRP

EBRP members discussed characteristics of the environment that would support the work of CDC-CFSRP. Discussions focused on factors which would support both the Program's current success and its diversification into new areas of research, and which would provide it an environment where continued funding opportunities would be most likely to exist. Below are summary comments relevant to this discussion.

### General considerations

- Support continued strong laboratory capacity
  - One of the major strengths of the CDC-CFSRP is its laboratory capacity. Continued support for laboratory capacity will be key to research activities, especially those focused on identifying interventions that work and subgroups of patients

- Create an infrastructure amenable to collaborations for interventions, testing, and treatment
  - The CDC-CFSRP should have an infrastructure and be located where it can seamlessly collaborate across organizational lines, take advantage of funding opportunities, and share expertise with other scientists in CDC. Because of the necessity for multi-disciplinary approaches and strategies to addressing research interests, an environment amenable to collaboration must be achieved

- Include strength in the behavioral sciences
  - Strength in the behavioral sciences has historically been citied as a contributing factor to the success of other CDC programs which address disorders or conditions of unknown etiology

- Include expertise in evaluating interventions developed through clinical trials
  - Expertise in clinical trials will be beneficial for designing research studies that can evaluate interventions (especially non-pharmacological treatments) that address multiple symptoms and outcomes
  - Interventions among a variety of subgroups of CFS patients can also be evaluated

- Embrace a systems biology approach
  - If systems biology is pursued in public health and within CDC, the CDC-CFSRP can serve as a model for this approach
  - The CDC-CFSRP has also been recognized for its leadership in linking community-based surveillance, clinical and molecular data. This expertise should be utilized by other groups at CDC

- Serve as source of expertise in studying disorders of unknown etiology for local, state, national, and international organizations

  - Panel members suggested that the CDC-CFSRP could be seen as a resource for other groups within CDC to emulate (e.g., applied to post-Lyme disease activities; other diseases of unknown etiology CDC is often called upon to investigate)

- Maintain strength in computational/statistical modeling
  - The CDC-CFSRP will require continued strong computational and statistical expertise to maintain its current level of activity; thus, the Program may benefit from collaborations with CDC-based statistical groups and may also be a resource to other groups working to develop bioinformatics expertise

- Include expertise in surveillance
  - Surveillance expertise will be critical to the Program's continuing to address CDC's public health mission to monitor disease burden

- Include expertise in health marketing
  - Expertise in marketing will be important as the Program works to educate healthcare providers and the public about CFS in an effort to identify patients who currently remain undiagnosed
  - Surveillance expertise coupled with national public awareness campaigns and provider education programs will help minimize the total number individuals who remain undiagnosed with CFS

**Other Considerations**

- Implications of moving the CDC-CFSRP from its current organizational location within the CDC
  - Two main organizational locations emerged, infectious diseases and chronic diseases, both of which were favorably considered as potential options.
  - An additional suggestion was for CDC to create an office of complex disease investigations which deals with "unwellness" or diseases of unknown etiology, which could include the CFSRP
  - In the absence of a specific, proven, and clear link to infectious etiologies, some panel members felt retaining the CDC-CFSRP within an infectious disease environment (especially within a Branch dealing with viral exanthems, where the CFSRP currently resides) had the potential to convey an incorrect public health message
  - Alternatively, others felt that the public's perception of how CDC approached research and treatment of CFS would not be impacted by the Program's organizational location
  - Panel members felt that the CDC-CFSRP could be located in the part of CDC that dealt with chronic diseases given the chronic nature of the effects of the illness, as long as the laboratory component of the group's research was not compromised. Locating the program in the chronic disease center could be perceived as an acknowledgment of CFS as an actual illness, provide a rationale

for addressing interventions as a public health mission, and allow for a systems biology approach which could be applied to other chronic diseases

- Concern about decreased funding for the CDC-CFSRP
  - Panel members were concerned that projects initiated with the one-time funds are not sustainable with current base funding.
    *(NOTE: Dr. Steve Monroe, CVDB, DVRD, NCZVED, CCID, CDC confirms that base funding has remained relatively level from 2004 – 2008. The one-time restoration of funding was completed in 2005.)*
  - The Program is funded on a Congressional line-item
  - Resource constraints could be better addressed if the program is placed in a consultative role that allows expertise to be shared across programs at CDC

- Perception that CFS represents a public health crisis or problem which is not strongly connected to public health
  - While panel members referred to the current state of CFS as a public health crisis/problem, there is currently no strong link between public health and CFS because the illness is seen as a clinical issue and not one which limited public health resources can address
  - The launch of the national public awareness campaign in fall 2006 may generate opportunities for public health agencies and organizations to assess the connections between public health and CFS, especially regarding whether or not appropriate infrastructure and resources will be available to address the potential increase in patients diagnosed that may result

- Need for a medical home for CFS
  - CFS currently has no medical specialty whose practitioners consistently and routinely take responsibility for providing treatment to patients
  - With its influence within the health field it was suggested that CDC could assist in identifying the medical specialty(ies) which could take on primary responsibility for diagnosing and treating CFS patients

- Need to develop primary prevention interventions
  - Primary prevention studies could be conducted to assess health behaviors through longitudinal studies, comparing the healthy to the unhealthy. This information could be used to design instruments for CFS risk assessments
  - Aging is accelerated in CFS patients which has implications for premature onset of obesity and osteoporosis

- Need to develop secondary prevention strategies
  - Secondary prevention interventions should be developed and evaluated in conjunction with the chronic disease center
  - Evaluation of treatment interventions should be conducted to insure/inform evidence-based recommendations
  - Clinicians need assistance with prescribing and assessing the effects of physical activity, evaluating the risks for and effects of post-intervention (payback) fatigue, and evaluating nutrition and dietary interventions

- Other issues
  - Should CFSRP continue to exist at CDC; support was expressed for a CFSRP to continue at CDC and at NIH
  - There is a need to formalize collaborations external to CDC. With limited resources the question arose whether emphasis should be on developing the intramural program or on funding population-based studies with external collaborators?
  - Since there are many accomplished scientists within the program, consideration should be given to more shared communication and leadership duties within CDC-CFSRP
  - Concern that the CFSRP is somewhat insular and could be better integrated with and/or exposed to other CDC scientists

Appendix A-EBRP:

**CDC Chronic Fatigue Syndrome Research Program (CDC-CFSRP)**
**External Blue Ribbon Panel Members**

| | |
|---|---|
| Dr. Lisa M. Lee | Office of the Chief Science Officer,<br>Office of the Director,<br>Centers for Disease Control and Prevention<br>Atlanta, Georgia<br>**Co-Chair for EBRP** |
| Dr. Charles Raison | The Emory Mind-Body Program,<br>Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine<br>Atlanta, Georgia<br>**Co-Chair for EBRP** |
| Dr. Lucinda Bateman | The Fatigue Consultation Clinic<br>Salt Lake City, Utah |
| Dr. Charles C. Engel | Medical Corps, United States Army<br>Deployment Health Clinical Center at<br>Walter Reed Army Medical Center<br>Center for the Study of Traumatic Stress,<br>Department of Psychiatry, F. Edward Hébert School of Medicine, Uniformed Services University of the Health Sciences<br>Bethesda, Maryland |
| Dr. Eleanor Z. Hanna | Office of Research on Women's Health,<br>Office of the Director,<br>National Institutes of Health<br>Rockville, Maryland |
| Dr. James L. Hadler | Infectious Diseases Division,<br>Connecticut Department of Public Health<br>Hartford, Connecticut |
| Dr. Nancy Klimas | Department of Medicine,<br>University of Miami School of Medicine<br>Miami, Florida |
| Ms. K. Kim McCleary | Chronic Fatigue and Immune Dysfunction Syndrome (CFIDS) Association of America<br>Charlotte, North Carolina |

**Speakers:**

| | |
|---|---|
| Dr. William Reeves | CVDB, DVRD, NCZVED, CCID, CDC<br>Atlanta, Georgia |
| Dr. Elizabeth Maloney | Lead, Epidemiology Team<br>CDC-CFSRP, DVRD, NCZVED, CCID, CDC |
| Dr. Elizabeth Unger | Lead, Molecular Pathology and HPV Laboratory, CDC-CFSRP, DVRD, NCZVED, CCID, CDC |
| Dr. Suzanne Vernon | Lead, Human Genomics Program<br>CDC-CFSRP, DVRD, NCZVED, CCID, CDC |

**Observers:**

NCZVED,CCID, CDC:
Dr. J. Michael Miller
Dr. Steve Monroe

CCID-OD:
Dr. Pamela Ching
Dr. Joanne Cono

**Contract meeting recorder:**
Global Evaluation & Applied Research Solutions (GEARS) Inc.-
Ms. Bridget Hardaway

Appendix B-EBRP:

# PRESENTATION: CDC Chronic Fatigue Syndrome Public Health Research Program - What are we doing? Where should we go?

**Dr. William Reeves**

**Chronic Viral Diseases Branch,**
**Division of Viral and Rickettsial Diseases,**
**National Center for Zoonotic, Vector-Borne & Enteric Diseases,**
**Coordinating Center for Infectious Diseases,**
**Centers for Disease Control and Prevention**

## CDC Chronic Fatigue Syndrome Public Health Research Program

What are we doing?

Where should we go?

## CVDB Understanding:
Objectives of this Meeting

- Inform decisions as to placement of CVDB in CDC
- Suggest directions for this type of work at CDC

## Charge to the Panel

- Review current collaborative activities
- Review research portfolio
  - Suggest priorities
- Identify successful and problematic lines of research
  - Suggest enhancements
  - Suggest problem resolutions

## Tasked to CVDB

- Review current and proposed research activities
  - Collaborations within CDC
  - Collaborations outside CDC
- Review research partners
- How are CFS research activities prioritized?
- Have *Team Leads* speak specifically about projects

## CFS Program Objective

Devise control and prevention strategies for CFS

## CVDB CFS Research Program - Staff

| Management | PIs | Support | Post-docs | Pre-docs |
|---|---|---|---|---|
| W. Reeves | Epidemiology | I. Dimulescu | A. Smith | |
| J. House | *R. Malowey* | D. Rellis | M. Hollier | R. Craddock |
| | J. Lin | C. Meadows | V. Falkenberg | V. Emanuelle |
| | J. Jones | W. Lanugan | O. Nater | M. Tiller |
| | R. Bosovo | S. Narasimhan | M. Maier | B. Sherwell |
| | TBN | O. Morley | D. Brimmer | |
| | Laboratory | C. Chiang | | H. Tian |
| | *S. Vernon* | | | X. Chen |
| | *E. Unger* | | | |
| | M. Rajeevan | | | |
| | T. Whistler | | | |
| | TBN | | | |
| | Computation | | | |
| | *S. Vernon* | | | |
| | B. Carbonara | | | |
| | E. Addesso | | | |
| | G. Broderick | | | |

## CFS Research Program - External Collaborators

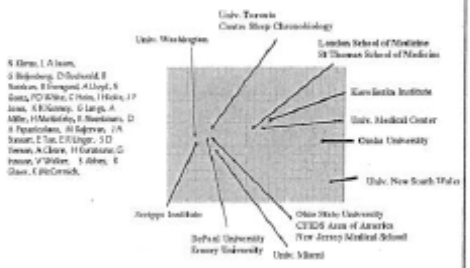
| Emory | UGA | DoD | Other |
|---|---|---|---|
| Psychiatry | Economics | Ft Benning | Abt Associates |
| A. Miller | P. Cozzo | WRAIR | CFIDS Association of America |
| C. Raison | | DARPA | Miami University |
| L. Wolberg | | | London School of Medicine |
| G. Pagnoni | | | Univ New South Wales |
| | | | Duke University - CAMDA |
| | | | NIH |
| | | | Nd Center Toxicological Research |
| | | | Biomind |
| | | | Univ Texas-MD Anderson |
| | | | Univ Alberta |
| | | | Weizmann Institute |
| | | | Univ Illinois |

## CFS Research Program - CDC Collaborations

| NCZVED | NCHM | NIP | NCIPC |
|---|---|---|---|
| West Nile | A. Forsyth | | J. Mercy |
| Lyme | | | |

## The International CFS Study Group

2000 - 2001 - 2003




## CFS International Targeted Workshops

2000
Discovery of Novel Pathogens

2003
Towards Understanding Cellular and Molecular Mechanisms for CFS

2004
Integrating Disparate Data to Simulate Lymphocyte Function

2005
Integrating Data to Make Sense of Biologic systems'

## CFS Program Objective

Devise control and prevention strategies for CFS

- Public health research leading to the control and prevention of medically unexplained chronically fatiguing illnesses -CFS-

## CFS Control Strategy


**Surveillance**

- Prevalence, Incidence, Demographics
- Clinical Attributes
- Risk Factors
- Biomarkers
- Clinical Course
- Economics
- Access/Utilization - Health Care
- QAL

**Clinical Studies**

- Clinical Attributes
- Risk Factors
- Pathophysiology
- Biomarkers

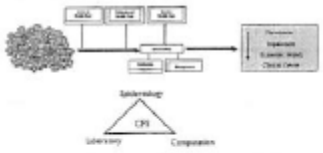
**Lab Studies**

- Clinical Attributes
- Risk Factors
- Pathophysiology
- Biomarkers

## CVDB CFS Research Program


## How are CFS research activities prioritized?

- Public health research leading to the control and prevention of medically unexplained chronically fatiguing illnesses -CFS-



## CFS Public Health Research Program Underlying Paradigm

### CFS is a Complex Illness

- Represents alterations in complex systems of homeostasis
- Not a result of a single mutation or single environmental factor
- Arise from a combined action of many genes, environmental factors and risk-conferring behavior
- A multidisciplinary approach is necessary
- Understanding CFS may elucidate the common pathways of other complex diseases


## CFS Public Health Research Program Underlying Paradigm

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Post-Infection Illness

Military Populations

DARPA

Chemotherapy Illness

Evolution of CFS Research Strategy
CFS in the Population

1989 - 1994 Physician Surveillance of CFS

Evolution of CFS Research Strategy
CFS in the Population

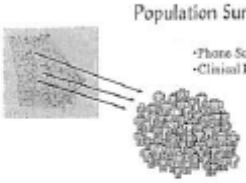
1994 - 2000 Population Surveillance of CFS

Evolution of CFS Research Strategy
CFS in the Population

2000 - 2001 Pilot National Survey of CFS

Evolution of CFS Research Strategy
CFS in the Population

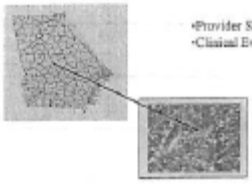
## CFS in Georgia
### Population Surveillance



•Phone Screening
•Clinical Evaluation

- Prevalence, Incidence, Demographics
- Clinical Attributes
- Risk Factors
- Biomarkers
- Clinical Course
- Economics
- Access/Utilization - Health Care
- KAB

## CFS in Georgia
### Provider Surveillance



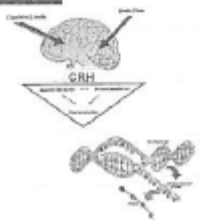
•Provider Screening
•Clinical Evaluation

- KAB Providers
- KAB Patients
- Pilot Registry
  - Prevalence, Incidence, Demographics
  - Clinical Attributes
  - Risk Factors
  - Biomarkers
  - Clinical Course
  - Economics
  - Health Care Utilization

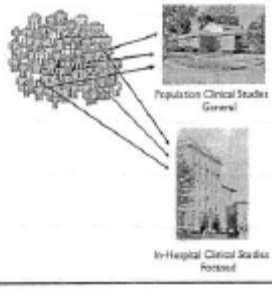
## In-Hospital Clinical Studies of CFS

- Surveillance studies
  - provide limited data
  - good cases and controls
- In-hospital case control studies
  - Hypothesis testing
  - Controlled environment
  - Sophisticated measurements

## In-Hospital Clinical Studies of CFS



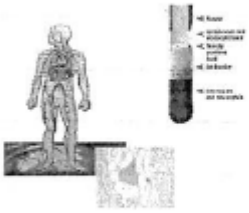
## Laboratory Studies of CFS




- Risk Factors
- Biomarkers
- Pathophysiology

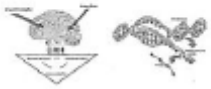
## Laboratory Studies of CFS

- What to sample?
  - Blood



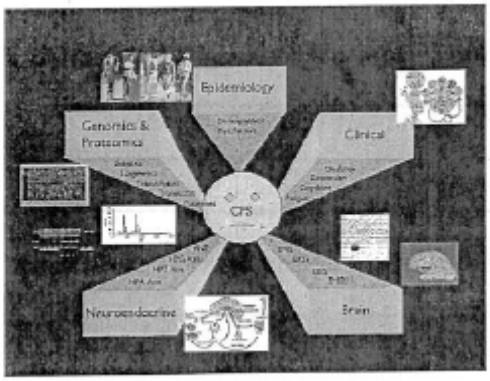
## Laboratory Studies of CFS

Plasma, Serum, PBMC



Hormones, Metabolites

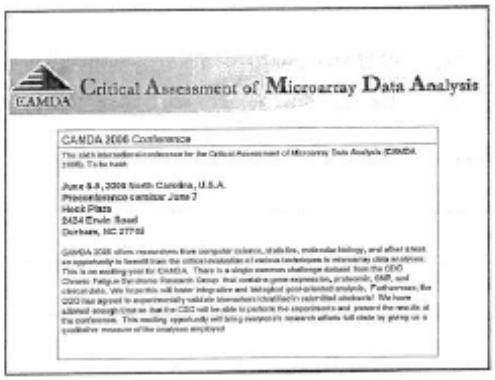
Active hormones
Circadian rhythm

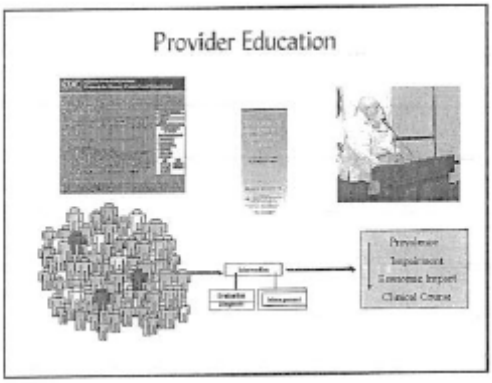


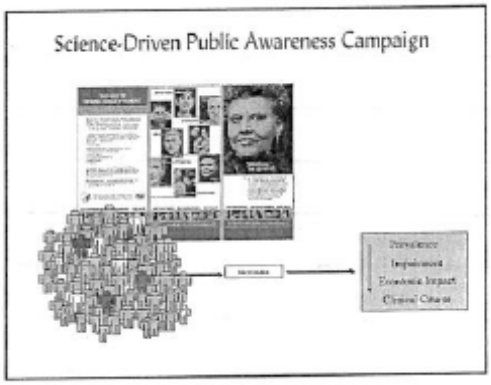
## Computation and Analysis

## Computation and Analysis

## $C^3$ – Results


CAMDA
Critical Assessment of Microarray Data Analysis
CAMDA 2006 Conference
June 8-9, 2006 North Carolina, U.S.A.
Preconference seminar June 7
Hotel Plaza
2424 Erwin Road
Durham, NC 27705


Provider Education
Prevalence
Impairment
Economic Impact
Clinical Course

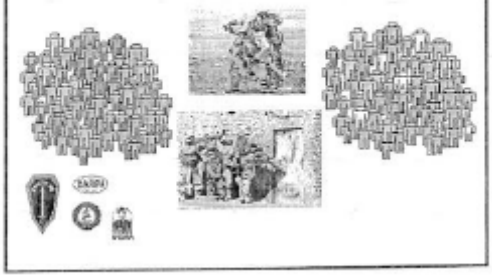

Science-Driven Public Awareness Campaign

## 2000-2005 - CFS Publications (n=635)

| | Pubs | % World Pubs | Cit Rate |
|---|---|---|---|
| CDC | 52 | 8.2% | 17.0 |

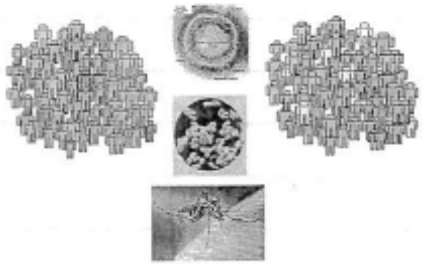
## Complex Illness Paradigm

Stress/Resiliency - Military Populations



## Complex Illness Paradigm

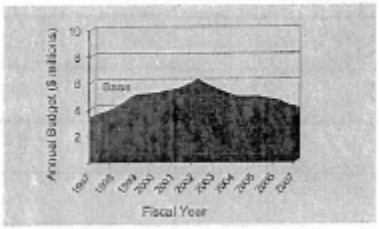
Post-Infectious Illness



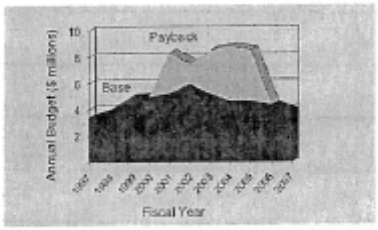
## Charge to the Panel

- Review current collaborative activities
- Review research portfolio
  - Suggest priorities
- Identify successful and problematic lines of research
  - Suggest enhancements
  - Suggest problem resolutions

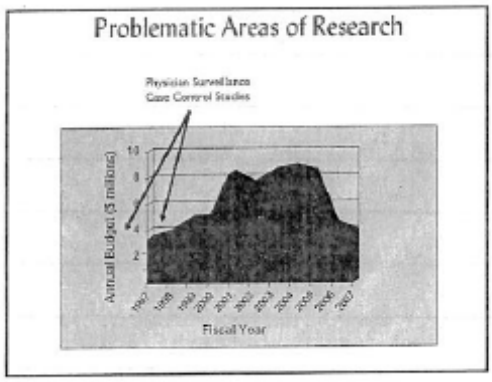
## Problematic Areas of Research



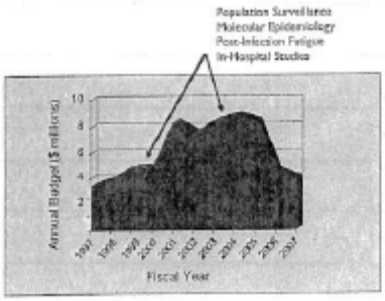

## Problematic Areas of Research



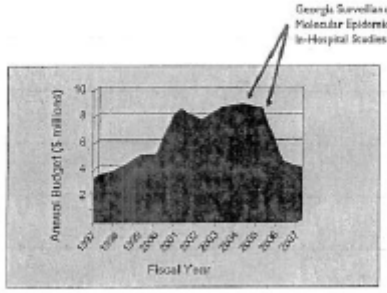
## Problematic Areas of Research



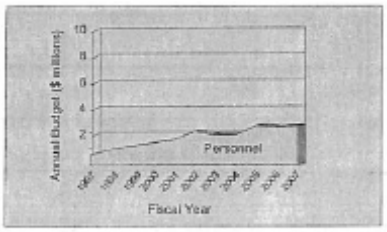

## Problematic Areas of Research



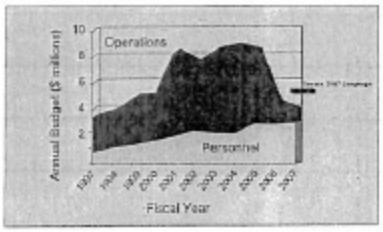

## Problematic Areas of Research



## Problematic Areas of Research

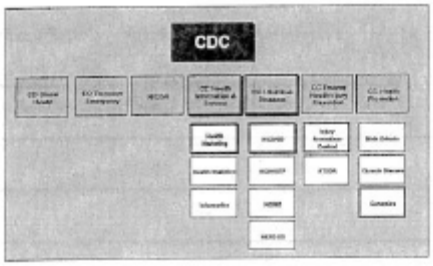


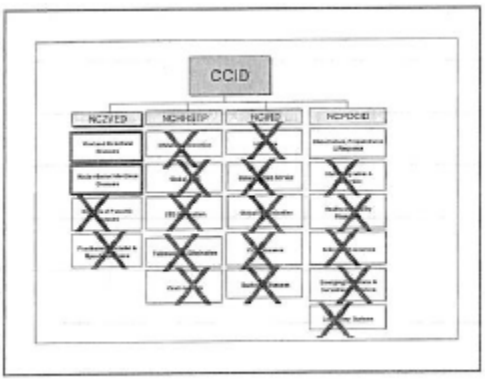

## Problematic Areas of Research




## CFS – Where Should We Go?

- Inform decisions as to placement of CVDB in CDC




## Where should we go?

CFS Public Health Research Program Should Remain in NCZVED

Program is a model NCZVED effort

- Integrated epidemiology – laboratory – computation program

Primary technical synergies are infectious disease laboratory

- Technical synergies – genomics/proteomics/targeted assays
- Technical support – reagents/equipment/maintenance
- Technical analytic issues

Effectiveness and productivity reflect current placement in NCZVED

## Charge to CVDB

- Review current and proposed research activities
  - Collaborators within CDC
  - Collaborators outside CDC
- Review research partners
- How are CFS research activities prioritized?
- Have Team Leads speak specifically about projects

Dr. Maloney
Dr. Vernon
Dr. Unger

Appendix C-EBRP:

**PRESENTATION: Summary Report: Centers for Disease Control and Prevention Chronic Fatigue Syndrome Research Program Internal Planning Group Meeting**

**Dr. Lisa M. Lee**

**Office of the Chief Science Officer,**
**Office of the Director,**
**Centers for Disease Control and Prevention**

# Summary Report: CFS Internal Planning Group

Lisa M Lee, PhD
Assistant Science Officer
Chair, CFS IPG

## CFS Internal Planning Group (IPG)

- CDC scientists and Center leaders
- 5-6 Dec 06, Atlanta
- Charge
  - Understand CFSRP core activities
  - Identify research areas and opportunities for intra- and extramural collaborations
  - Suggest approaches to encourage a collaborative program

## Subject Matter Experts

- Dr Anthony Komaroff
  - Causes of CFS
- Dr Nancy Klimas
  - Recent Advances in CFS
- Ms K Kimberly McCleary
  - Research Program of CFIDS
  - National CFS Awareness campaign
- Dr William Reeves
  - CDC's CFSRP Activities

## Major Conclusions: 1

- Build on multidisciplinary strengths by performing intervention research
- Research disease burden (e.g., economic research)
- Explore psychiatric, neurological, and immunologic connections

## Major Conclusions: 2

- Collaborate internally with CDC programs
- Collaborate externally with other federal agencies
- Consider options for placement of CFSRP within CDC

## Recommended Research Areas: 1

- Develop tools for genomics, diagnostics, measuring symptoms and functional status
- Standardize data collection techniques
- Provide cooperative environment for laboratories
- Maintain specimens in bank

## Recommended Research Areas: 2

- Conduct surveillance data collection
- Standardize case definition
- Continue to search for etiology
- Identify biologic subgroups
- Conduct intervention studies
- Measure disease burden
- Examine disparities

## Recommended Research Areas: 3

- Study pyschiatric, neurologic, and immunologic connections
- Conduct clinical trials on interventions
- Examine differences between persons who seek and do not seek treatment
- Collaborate for basic research

## Placement Within CDC

- CFSRP has strong multidisciplinary approach and needs an environment that can support diverse work teams
- Gaining experience in brain-body connections
- Should a group with expertise in psyco-neuro-immunologic conditions be established?
- Could such a group be a resource for other/new conditions?

## Today's Charge

- Suggest priorities for research areas/agenda
- Suggest ways to enhance strategic research connections and synergies
- Describe research and programmatic environment best suited for these activities