**Department of Health and Human Service**

# Interagency Autism Coordinating Committee

**Meeting Highlights**
**May 24, 2002**
**National Institute of Health**
**Bethesda, Maryland**

## Introductions and Overview

*Dr. Richard Nakamura, Acting Director of the National Institute of Mental Health (NIMH) and Chair of the Interagency Autism Coordinating Committee (IACC),* opened this meeting with an announcement that a report of the last meeting is on the web site. He proposed that there be official minutes from the current and future meetings, which would be approved at the succeeding meeting. This was voted on and accepted by the committee.

Dr. Nakamura introduced *Dr. Yvonne Maddox, Acting Deputy Director of the National Institutes of Health (NIH).*

Dr. Maddox recalled that one year ago the Secretary of the Department of Health and Human Services (DHHS), Tommy Thompson, signed the order to establish the IACC. She and Dr. Steve Hyman (former Director of NIMH) got the first meeting off the ground. The IACC was formed as part of the implementation of the Children's Health Act of 2000. As of last week, the NIH has a new director, Dr. Elias Zerhouni. Dr. Zerhouni is committed to the coordination of research efforts in autism and plans to attend the next IACC meeting. Dr. Maddox emphasized that coordination of autism research and service efforts is crucial, and will be supported by Dr. Zerhouni as well as other new and current Institute directors. She also noted that interest from Congress is beneficial to these efforts. She noted that several Requests for Applications were issued in the past year by the participating federal agencies, and considerable progress was made as a result of recognizing the need and desire to get the various Centers programs off the ground. Dr. Maddox again emphasized the need for partnerships and collaboration, welcomed new partners to the IACC, and offered to be of help at any time.

Dr. Nakamura noted that NIH has been entrusted with a doubling of its budget, and that Congress wants assurance that it is going to be used wisely. NIH's job is to promote and manage the science and to make the results available to children and their families. This is a complex task that requires intense collaboration. He noted that competition is a key component to this task. The guiding idea behind peer review is that the strongest ideas and the strongest designs succeed, so that the result is reliable science. He asked the committee for help in determining how the science should be translated for use.

## Briefings from New IACC Members

Dr. Nakamura introduced new members of the IACC: Merle McPherson, M.D., Health Resources and Services Administration (HRSA); Sybil Goldman, M.S.W., Substance Abuse and Mental Health Services Administration (SAMHSA); Deidra Abbott, M.P.H. (for Thomas Scully), Centers for Medicare and Medicaid Services (CMS).

**Health Resources and Services Administration (HRSA)**
*Merle McPherson, M.D., Director, Services for Children with Special Needs, Maternal and Child Health Bureau, HRSA*

Dr. McPherson noted that her agency is involved with health resources and services provision and so she has an interest in how science is translated to services. Although HRSA does not have earmarked dollars for autism, there is a commitment to autism services. HRSA aims to get universal sustained service systems in place for all children with special health care needs, a national agenda that was initiated by Surgeon General Dr. Koop. The current plan is to incorporate the development of this agenda of comprehensive children's service systems into the President's New Freedom Initiative (http://www.disability.gov), which has the goal of reducing barriers to services for persons with disabilities and facilitating integration of service systems. HRSA (in collaboration with the American Academy of Pediatrics, Family Voices, and March of Dimes) has developed a 10-Year Plan, which is in final clearance stage in the Department, and will be implemented in all states by the year 2010.

Dr. McPherson noted that HRSA has block grants (Title V Block Grant Program) and demonstration projects that may include services for children with autism. She notes that there is increasing concern from states and demonstration projects about meeting the needs of these children. Dr. McPherson highlighted a program sponsored by Maternal and Child Health: the LEND Program (Leadership in Education and Neurodevelopmental Disabilities), formerly called UAP (University-Affiliated Programs). For example, the Children's Hospital of Philadelphia and Seashore House is a LEND program and has an active autism center. She also noted that the pediatric specialty in Behavioral and Developmental Pediatrics has moved to Board status, and that HRSA is funding a small program for training pediatricians in this specialty. They are also working with the AAP to meet the 2010 Health Goal of medical homes for all children with special health care needs. In summary, HRSA's autism efforts are part of a larger effort to try to get universal services in place for all children with disabilities.

**Substance Abuse and Mental Health Services Administration (SAMHSA)**
*Sybil Goldman, M.S.W., Senior Advisor on Children*

Ms. Sybil Goldman (SAMHSA) stated that since autism is not her area of expertise, she is here to learn as well. SAMHSA is the lead agency for provision of mental health and substance abuse services for children and adults. There is not a specific portfolio of activities related to autism, but children with autism are involved in SAMHSA programs, and their needs are posing challenges. The focus of the IACC, to bring science to practices, is a major commitment of Charles G. Curie M.A., A.C.S.W, the new Administrator of SAMHSA. When he was the Commissioner of Mental Health and

Substance Abuse in Pennsylvania, he worked hard on the issue of better serving this population. SAMHSA promotes mental health and substance abuse services across the age spectrum. SAMHSA focuses on risk and protective factors, has programs on prevention, rural provision of care, etc.

Ms. Goldman presented information on the Comprehensive Mental Health Services Program, which was congressionally mandated in 1993. This program, funded by Congress, costs $97 million per year and is for building systems of care for children and their families. The last grantee meeting for this program focused on autism because of the increased need within communities. The targeted population is children under 22 years old with a mental health diagnosis (excluding substance abuse, V codes, and developmental disabilities unless there is a comorbid mental health diagnosis). To be eligible for this program, children with autism must have dual diagnoses. The average age is 12 years old. Most of the referrals to this program for children with pervasive developmental disorders are from schools and mental health systems, and a few come from departments of corrections. The children with pervasive developmental disorders are receiving case management, recreational activities, and family therapy and family support. A smaller number are receiving individual therapy.

Ms. Goldman spoke with a number of people in the state and community programs about their experiences with this population. One challenge identified was the fragmentation of care involving mental retardation and developmental disabilities (MRDD) administrations, in areas such as education, mental health, and other aspects of health. In most states, the MRDD system is more focused on children than on adults. Children may be identified in the education system or through Part B and Part C of Individuals with Disabilities Education Act (IDEA), or in the mental health system. Medicaid and school systems are the major payors for services. Also, services are being provided through managed care. There are significant issues concerning which entity pays for these types of services. The providers are also asking for information about prevalence and are also seeking information about effective treatments and service delivery packages, as well as guidance about how states should use their limited resources to best meet these needs.

*Discussion:*

Lee Grossman (Autism Society of America) noted that the number of people with autism presents a significant health care problem, and society is becoming increasingly overwhelmed by costs. He asked for the speakers' descriptions of what is being done now, as well as suggestions for the future.

Ms. Goldman responded that there is a need to learn more about what are effective services packages and suggested several areas of collaboration that are needed: CMS and community service providers need to work closely together to determine the best use of current funding streams. It will be important to coordinate with education systems, which are in many ways the lead providers but do not have resources to effectively tackle the coordination of services; work on ways to support the states and agencies with the federal resources to coordinate efforts; do a better job of disseminating information; work in

conjunction with State colleagues; work closely with our research colleagues. There is also a need for information about prevalence in order to plan for anticipated needs.

**Centers for Medicare and Medicaid Services (CMS)**
*Deidra Abbott, M.P.H., Technical Director, Division of Benefits, Coverage and Payment; Disabled and Elderly Health Programs Group*

Ms. Deidra Abbott passed along Mr. Thomas Scully's (the Administrator of CMS) regrets that he could not be at the meeting. She agreed that various federal and state efforts need to be coordinated. She described CMS as the federal oversight agency for the provision of health care services, and the financing of health care services for indigent populations, for elderly, for disabled people, and for children with special health care needs. The two financing authorities are Medicaid and Medicare. Medicaid is the primary funding source for children with special health care needs and disabilities. Ms. Abbott described two mechanisms that states can use to fund services for children with autism.

- The traditional Medicaid program, a medical model, provides states with the ability to provide mandatory and optional (e.g., case management) services. There were limitations of this model, so additional opportunities such as waiver programs have been added. The Home and Community-based Services Program (section 1915-C of the Social Security Act) was established as an alternative to institutional care. This is an optional program for states. There are about 264 Home and Community-based Services Programs throughout the country. States can establish specific programs for targeted groups, tailored to the needs of that particular group.

- The Managed Care Program (section 1915-B of the Social Security Act) is another optional waiver program for states that can be targeted to specific groups. Under this waiver, the services are provided in a managed care environment. However, these programs also have limitations.

Ms. Abbott also noted that the President's New Freedom Initiative is an ambitious plan, and that a number of the recommendations from the plan (report on the web at newfreedom.hhs.gov) relate to Medicaid waiver programs.

*Discussion:*

Mr. Jonathan Shestak (Cure Autism Now) emphasized that there is a large increase in the number of children with autism at very young ages that are going to need services, and it is important to anticipate this. Also, he emphasized the need for early screening programs.

Ms. Abbott acknowledged that the agency has not been aware of this need. She noted that CMS has a number of internal research initiatives going on to define/describe the

population. She reported that funding was appropriated by Congress (the Systems Change Grant) for grants to states to allow them to partner with advocacy groups and consumers, in order to establish integrated long-term care delivery systems.

Mr. Shestak noted that the Children's Health Act of 2000 made it very clear that DHHS was mandated to provide training for community providers.

Ms. Goldman noted that SAMHSA has convened a children's workgroup to assure that the needs of this population are addressed in some of the grants and technical assistance programs that are being funded. She noted that there is a need to look for science to provide the information to give to the Technical Assistance programs.

Dr. Barry Gordon commented that, while the ideal was to have rigorous scientific evidence in order to provide services, autism should not be held to a higher standard than is used in the rest of medicine or education. Rigorous evidence of efficacy is often scanty in other areas of medical and educational practice. So the decision to provide services, and what services to provide, often will have to be made on imperfect evidence and on plausibility.

There was a general discussion about the States being told to adopt programs that have an evidence base, but there are different types and variable levels of evidence.

Dr. James Battey (NIDCD) and Dr. Nakamura stated that the goal is for NIH to provide the best evidence available, to make the science as good as it can be, and to move it to practice as rapidly as possible.

**Break**

Dr. Nakamura stated that during the break, he had discussed with Dr. McPherson and Ms. Goldman the formation of a subcommittee on coordination of interventions services across agencies, possibly identifying State models that might serve as a basis for a national meeting. Such a subcommittee of the IACC will be established.

## Progress Reports on Centers Programs

### Studies to Advance Autism Research and Treatment (STAART)

*Presented by Deborah Hirtz, M.D., National Institute of Neurological Disorders and Stroke (NINDS)*

Dr. Hirtz noted that the primary goal of the STAART Centers is for each center to bring together expertise to focus on major research questions in autism, e.g. early detection, treatment and prevention, or determining causes and risk factors. The intent is to bring together different disciplines including developmental psychology, developmental pediatrics, neuroimaging, and pharmacology. Another goal is to attract innovative approaches, collaborations within and among centers, and bring researchers from other fields into autism. The request for applications (RFA) asked for potential grantees to

propose at least three interrelated projects, including a treatment study, and a description of administrative cores. The centers will work collaboratively, particularly in the area of treatment research, in order to pool trial participants, etc. A steering committee and data management center will help to coordinate efforts.

The following institutes fund this initiative with NIMH taking the lead: NINDS, the National Institute of Child Health and Human Development (NICHD), National Institute on Deafness and Other Communication Disorders (NIDCD), and National Institute of Environmental Health Sciences (NIEHS).

Dr. Hirtz described the timeline for the STAART Centers initiative. An RFA for "developmental" grants was issued in April 2001, to provide one year of funding for potential center grantees to do preliminary work prior to applying for a full center grant. Applications were submitted in July 2001, the peer review occurred in August 2001, and review by the Institutes' Advisory Councils in September 2001. Six institutions were awarded developmental grants:

- The M.I.N.D. Institute, University of California, Davis; P.I. (Principal Investigator): David Amaral, Ph.D.
- Yerkes Research Center, Emory University; P.I.: Thomas R. Insel, M.D,
- University of Florida; P.I.: Mark Henry Lewis, Ph.D.
- University of Utah; P.I.: William McMahon, M.D.
- University of Missouri Hospitals and Clinics; P.I.: Judith Miles, M.D., Ph.D.
- Washington University; P.I.: Richard Todd, Ph.D., M.D.

Two competitions are planned for the full STAART Centers applications. Applications for Round 1 have been peer reviewed, and the Institutes' Advisory Councils were conducting their reviews during May 2002. Funding of successful applications will occur during the summer.

The second competition has a due date for applications of August 29, 2002. This would mean the applications would be reviewed in February or March of 2003, and would go to Advisory Councils in May 2003. Dr. Hirtz noted that there is an effort to see if it is possible to speed up the process so that the applications can go to the January/February Councils, but that depends on several factors including the number of applications. A big response to this round is expected, including the developmental grant awardees, revised applications from Round 1, and others.

The NIH commitment to the STAART Centers is $12 million a year. There is no funding overlap with the Collaborative Programs of Excellence in Autism (CPEAs). Funding will be for five years for each center, with a probable competitive renewal process. The funding mechanism is by cooperative agreement, with a cap of $1.2 million per year per center for direct costs.

**Collaborative Programs of Excellence in Autism (CPEAs)**
*Presented by Duane Alexander, M.D., NICHD*

Dr. Alexander described the background and status report of the CPEAs. These Centers are a joint project of the NICHD and NIDCD that have been ongoing for the past four years. Ten sites have been funded. The primary focus has been on neurobiology and genetics of autism. Because of the success of the network, and to maintain continuity of the families and investigators, it was decided to maintain the cohort, and all were invited to apply for competing renewal grants. The mechanism was changed to cooperative agreements to facilitate interaction and functioning as a network, and to increase the involvement of NIH staff. The applications for competitive renewal were reviewed in March, and will go to the NICHD and NIDCD Councils soon, with an anticipated funding level of approximately $10 million. There will also be a competition for a data management and coordinating center that will probably have the capability of also implementing these functions for the STAART centers.

*Discussion:*

Dr. Battey (NIDCD) asked whether there would be bridge funding for sites that need it while the applications are going through peer review, to avoid loss of continuity. Dr. Alexander confirmed that there is bridge funding available.

**Children's Centers for Environmental Health and Disease Prevention**
*Presented by Cindy Lawler, NIEHS:*

Dr. Lawler extended regrets from Dr. Kenneth Olden, Director of NIEHS, that he was unable to attend the meeting. Autism is a major new area of interest for NIEHS, and Dr. Olden is fully engaged and supportive of research in this area.

Dr. Lawler gave background information about the Centers for Environmental Health and Disease Prevention, which is a project jointly sponsored by NIEHS and the U.S. Environmental Protection Agency. The initial impetus for the program was an executive order signed in April 1997 that charged agencies to consider environmental risks to children and put in place policies and programs to address these risks. Eight centers were established in 1998, with foci on respiratory disease and general growth/development. The intent of the project is to foster multidisciplinary interactions among basic, clinical, and behavioral scientists. The Centers are coordinated programs that incorporate exposure assessment and health effects research to develop risk-management strategies. Each center supports at least two basic science projects and one community-based intervention project.

A new program was announced in 2000 to add additional centers to focus on environmental influences in a range of developmental disorders, including autism. Four centers were awarded in 2001. Dr. Lawler then gave examples of projects supported at two of the sites: University of California, Davis (UC-Davis); and University of Medicine and Dentistry in New Jersey (UMDNJ).

UC-Davis: A major component of this center is a large, case-control epidemiologic investigation to examine potential associations between autism risk, environmental

factors (vaccinations, heavy metals, pesticides), and genetic susceptibility. Another project at U.C.-Davis is working to establish animal models of autism, both in rodents and non-human primates. When those are established, neurotoxins can be evaluated for their influence on social behavior.

UMDNJ: One component of this center is a basic science project to investigate adhesion and repulsion molecules as mediators in developmental neurotoxic injury (lead and methyl mercury). For example, the work is examining how methyl mercury mediates its effects on neuronal migration and synapse formation. A clinical project will involve 100 children with autism and will conduct an exhaustive exposure assessment of home and neighborhood environments, as well as potential variation in response to toxins and environmental substances.

*Discussion:*

Mr. Shestak asked whether NIEHS had set aside money to support a STAART center.

Dr. Lawler replied that NIEHS is committed to support STAART centers in this round and next. The amount of support is predicated on the types of applications that come in, and the type of projects that are going to be funded. They are also trying to leverage some funds to coordinate these NIEHS centers and STAART centers.

**Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE)**
*Presented by Jose Cordero, M.D., M.P.H., Centers for Disease Control and Prevention (CDC)*)

Dr. Cordero presented information about the CADDRE centers, and other programs at the CDC. He is the Director of the new National Center on Birth Defects and Developmental Disabilities that was created by the Children's Health Act 2000. This group has a staff of 130 and a current budget of about $90 million.

Dr. Cordero noted that Dr. Marshalyn Yeargin-Allsopp was present, and that she has put together the system that is used in the U.S. for conducting population-based surveillance of developmental disabilities. There is a network in a number of states conducting surveillance for autism. In addition, the CDC's Centers of Excellence in Autism and other Developmental Disabilities Epidemiology are currently funded in California, Colorado, Maryland/Delaware, Pennsylvania, and Atlanta. They are conducting surveillance, case-control and other special studies.

The surveillance of developmental disabilities began in 1991. It is population-based, based on record review, and started with the inclusion of mental retardation, cerebral palsy, vision and hearing impairment. Autism was added in 1996. Dr. Cordero presented a description of the prevalence rate of autism in a 1996 case ascertainment in Atlanta, which estimated there were 3.4 children (3-10 years of age) per thousand with diagnoses within the autism spectrum of disorders.

Dr. Cordero then described the CADDRE network that includes four centers funded by the CDC. Their main activity is to monitor trends in autism spectrum disorders and conduct epidemiological research on possible causes. They conduct multi-center collaborative studies, as well as center-specific activities and projects, community outreach, and education. Each center covers a population base of at least 30,000 live births per year, and are funded at a level of $500,000 per year for 5 years for each center. Activities and special projects include surveillance, biological markers, medical and psychological and developmental conditions, prenatal infections, HLA type, and school-based screening.

Dr. Cordero also talked about a CDC-Denmark collaboration conducting cohort and longitudinal studies. Denmark has a unique data infrastructure that cannot be duplicated in the U.S. Examples of projects completed through this collaboration include: validation of autism diagnosis; vaccination studies; analysis of archived tissue samples and blood-spot samples to look for biomarkers.

*Discussion:*

Dr. Yeargin-Allsopp answered some questions about the prevalence studies. Dr. Battey asked for clarification about race differences. She clarified that mental retardation is more prevalent in black children in Atlanta, and that the prevalence of autism combined with mental retardation appears to be greater in black children in Atlanta, but not autism without mental retardation. This difference is statistically significant. Ms. Abbott asked whether the increasing prevalence is due to better recognition on the part of family members, or systems? Dr. Cordero noted that both are factors. Dr. Yeargin-Allsopp noted that services became more available in the early 1990s, through the Individuals with Disabilities Education Act (IDEA), all of which helped to increase awareness.

Mr. Shestak stressed the importance of having prevalence/incidence data for public policy. He also asked for an update on the ongoing study in Denmark on potential effects of thimerosal, and an update on the CDC's cost-of-illness analysis.

Dr. Cordero responded that he did not have information on the cost-of-illness study. The Denmark study, and also one in Atlanta, are in the final stages of analysis and should be finished in the next few months.

A discussion about prevalence rates followed. Dr. Yeargin-Allsopp noted that she recently presented results from the Atlanta population at a meeting. The prevalence was much higher than had been previously reported from other U.S. studies. She clarified that a national prevalence rate is not currently available. CDC has studies underway to estimate prevalence from several geographic areas, because is the prevalence probably varies across the country. The prevalence rate in Atlanta was 3.4 per thousand for the spectrum, but not all of the milder phenotypes might have been ascertained. Also discussed were prevalence rates in Brick Township, New Jersey, which were found to be 4 per thousand for autism, and 6.7 per thousand for the entire spectrum. In the Atlanta

study, there are plans to do clinical evaluation of the cases identified, as well as look at children identified with other disabilities, to try to get a more accurate estimate of the rate of the entire spectrum and also validate the diagnosis of autism obtained from record review.

Dr. Cordero noted that school records supply about 44% of the data and that access to school records is key to our ability to monitor the prevalence of autism in this country.

**Mapping Autism: Issues and Efforts**

*Presented by Barry Gordon, M.D, Ph.D.., Public Member and Professor in the Departments of Neurology and Cognitive Science, Johns Hopkins University and Medical Institutions*

Dr. Gordon presented his efforts at "mapping autism" as a follow-up to the initial discussion of this topic at the previous IACC meeting. He noted that the goals he had in mind for this project were to help provide an overview of what is currently known about autism, integrated across sources and accessible to all, as well as to identify what remains to be discovered, with the capability for drilling down to more detail when those details were available. He emphasized that these basic goals are fundamentally unattainable, and even contradictory, but he still felt they would be useful to try to achieve. He went on to present a draft for comments. The prototype presented by Dr. Gordon was developed with Robert Glatzer (Infostructure, Yardley, PA; www.infostweb.com) who provided services free of charge.

Dr. Gordon presented a web-based interface with several users in mind: parents and the concerned public, including advocates; researchers; educators and therapists; and public officials. Different users would be able to view different aspects of the information, and probe the data in different ways. The information used for the prototype was derived from public sources, mainly Cure Autism Now (CAN), the National Alliance for Autism Research (NAAR), and NIH web sites. Just from these examples alone, he identified several challenges and issues to be addressed: what information or data to present; how to present it; how to find it and update it, and how to get data from the different sources into conformity.

The prototype included several examples of how the data could be presented for different audiences and for different needs, and for how users could navigate through the web site and the data.

He noted that the next step was for feedback as to whether the presentation formats he suggested would actually be useful to the various groups of people involved in autism and related issues. He welcomed input as to what information was most desirable, and how this information should be presented.

*Discussion:*

Several committee members commended Dr. Gordon on his presentation. A discussion followed about other aspects that might be considered, including center-specific information and basic science. Dr. Gordon also noted the potential for this being an avenue to disseminate information from hearings, conference proceedings, etc., as well as a way to cross-reference literature from different disciplines, and information about services as well as evidence-based practices.

Dr. Cordero asked whether committee members could have copies of slides presented at the meeting, and Dr. Foote said that he would obtain and distribute them, with permission from the presenters.

Dr. Zeph added her congratulations to Dr. Gordon on his presentation, and emphasized that this format might be a way to disseminate information about services that are currently available. It could help families be informed about what is going on in their state, as well as other states, so that they can go to their legislatures and be effective advocates.

Dr. McPherson added that this is a method of transfer of information. Dr. Gail Houle of the U.S. Department of Education (DOE) agreed and noted that there is preliminary work by Carl Duntz that was funded in North Carolina a few years ago that is a system-mapping site. It is a demonstration project mapping, for a particular community, services for young children with disabilities that is used by service coordinators and families. She offered to get that information to people who are interested in learning more about it.

**NIH Autism Research Portfolio**

*Presented by Steve Foote, Ph.D., Interim Executive Secretary IACC, and NIMH*

Dr. Foote described the notebook that had been given to each committee member, containing lists, by institute, of autism research activities funded by NIH for fiscal year 2001. Included is an overall summary, by institute, of NIH autism expenditures. A sign-up sheet allowed committee members to request the document electronically. Another sign-up sheet at the registration desk permitted other attendees to request a copy. All of the information in the binder is public information.

*Discussion:*

Ms. Goldman asked if there was an attempt to cross-reference this information and connect it to the framework Dr. Gordon just presented.

Dr. Foote replied that there is not now, but that is why there is an interest in mapping. He noted that one can do a search of the NIH CRISP database using key words and combinations of words, but at this time there is not a way to outline relationships among topics.

Mr. Shestak emphasized the prevalence estimates and economic costs of the potentially large numbers of children with autism, and the costs of a lifelong disorder. He noted that

with the exception of Alzheimer's disorder, this is the biggest public health challenge our country faces. He commended the committee for its efforts. He said that he applauded the personal attention the Centers are receiving from staff, and that it looks as if all of the different centers eventually will be working together. He asked the NIH to be more aggressive next year, committing to funding a total of more than 5 STAART centers. He suggested that the data management center for the CPEAs also be used for STAART Centers. He asked for more effort in brain banking and gene banking, as well as intramural research. He also suggested that the figure NIH presents ($55 million for annual autism research expenditures) is not accurate, as this includes basic research that applies to other disorders as well, not exclusively targeting autism although tangentially related.

Mr. Shestak also emphasized that NAAR, CAN, the Autism Society of America (ASA) and other organizations are raising money to fund pilot studies that can then apply for grant support by federal agencies.

Dr. Nakamura responded that there is agreement that $55 million is not enough, and explained that NIH is presenting these figures this way in an attempt to be consistent across diseases, not to be deceiving. Basic research is an important key to future clinical research. He also discussed the need for expanding research capacity since there are not enough researchers for childhood diseases. Efforts to expand the number of quality researchers include a loan-repayment program and other new mechanisms to try to build up the field. Currently, capacity is so limited that we are having difficulty finding reviewers for the center applications.

Mr. Shestak asked about the NIH commitment to funding STAART Centers, if there are more than five qualified applications. Dr. Nakamura responded that five is the lower limit.

Dr. Penn also noted that research training is crucial, and emphasized the importance of the loan repayment program. She observed that the advocacy groups have done much to highlight the need for researchers so more people will consider going into the field.

Mr. Grossman stated his appreciation for the fact that the institutes and agencies around the table are struggling with complex issues, but feels that there is a lack of federal commitment regarding autism. He is very concerned that the burden on our society will be huge when these children are adults. We need a concerted, coordinated effort to address this problem.

**Lunch Break (12:15 – 1:15)**

**NIH Strategies to Improve Coordination of Gene and Tissue Banking, Data Sharing and Interactions with Voluntary Organizations**

*Presented by Steve Foote, Ph.D., Interim Executive Secretary of IACC, and NIMH*

*Participating: James Battey, Jr., M.D., Ph.D. (NIDCD); Kenneth Olden, Ph.D. (NIEHS); Audrey Penn, M.D. (NINDS); Lisa Freund, Ph.D. (NICHD); Richard Nakamura, Ph.D. (NIMH); Jonathan Shestak, Vice President Cure Autism Now (CAN).*

Genetic data sharing:

Dr. Foote reminded members that this topic came up at the last meeting and was considered a high priority. Genetic and tissue sharing activities were specifically mentioned in the Children's Health Act, and are critical for determining the pathophysiology of autism, for identifying which individuals would benefit from specific interventions, and for determining outcomes.

Dr. Foote indicated that the STAART Centers RFA specifically stated that the funded centers would be required to participate in sharing genetic data and clinical information; that is, they will be required to deposit in the NIMH repository both biological material (including blood samples) and clinical information about the subjects from which the samples were collected. NIMH will bear the cost of the banking activities. Similar data sharing will occur in the CPEAs (as discussed later by Lisa Freund)

Dr. Foote also stated that NIMH recently funded an award to Dan Geshwin as the Principal Investigator (P.I.) at the University of California Los Angeles, for an effort to expand the Autism Genetics Resource Exchange (AGRE) database that was started by, and supported by, CAN. NIMH will now fund the database and some associated activities for five years. NIMH also has a genetics repository that is used to house and distribute genetic data, including autism data and samples. A notice was recently published in the NIH Guide announcing the availability to the scientific community of the genetic materials and data that were collected for a project at Stanford.

Also worth mentioning are mouse genetic studies, as these are the source of many of the more promising hypotheses about the genetic bases of autism and its pathophysiology. Many of the institutes have funded a large number of mouse genetic activities that have rigorous sharing protocols built into them. NIH intends to create a centralized resource for mice, mouse lines, and well-characterized data about phenotypes (http://www.nih.gov/news/pr/may2002/nhgri-06.htm).

*Discussion*

Mr. Shestak stated that NIMH has been a leader at NIH in encouraging sharing of raw data and samples. This was started by Dr. Hyman, carried on by Dr. Nakamura, and has had strong leadership from Dr. Foote. He emphasized the importance of having one very large data set, and asked what the CPEA policy is in this regard.

Dr. Freund stated that this would be developed as the CPEAs start coordinating with the STAART Centers. She noted that there is an active genetics sub-committee in the CPEAs already doing candidate gene work, but it will be beneficial to have a large data

set to be able to look at interactions among candidate genes, and the collaboration between STAART and CPEA centers will be an excellent opportunity for this.

Dr. Gordon asked about criteria used for identifying the phenotype, in terms of the crucial characteristics of a child that should be identified, how they are identified, and how they are entered.

Dr. Freund responded that there have been common protocols in the CPEAs, often using the ADOS-G (Autism Diagnostic Observation Schedule – General), ADI-R (Autism Diagnostic Interview – Revised), etc., which have already been standardized. They are also standardizing a medical history and demographic interview. It would be important to coordinate to the extent possible with other centers.

Mr. Shestak reminded the committee that the legislation talked very specifically about data banking and tissue banking. He advocated accelerating the project, and expanding efforts across institutes.

Several members noted the importance of characterizing the phenotype given the polygenetic nature of the disorder. This is absolutely critical to genetic studies.

Dr. Hirtz emphasized that everyone is committed to this collaboration. Having large samples gives us the opportunity to use population-based approaches and extensive natural history information. Dr. Penn stated that we also desperately need biomarkers, and sharing of resources will help this as well.

Dr. Shestak suggested that the centers that are going to study genetic susceptibility to heavy metal effects could be encouraged to obtain their DNA from the NIMH repository, in order to minimize the time needed to complete the studies or, that they could circulate specifics about the type of information they need to people who are collecting samples.

D. Foote summarized this discussion by stating that the goal is increased collaboration, and in the near term the coordination of autism efforts at NIH will include coordination of the STAART Centers and CPEAs. The intent is to maximize the consolidation and standardization of materials, both the information and the biological materials, and to have as close to "one-stop-shopping" for investigators as possible.

<u>Tissue Banking</u>:

Dr. Foote stated that tissue banking is much more problematic, in terms of getting to the "one-stop-shopping" goal from where the resources are now. The infrastructure and start-up costs are enormous for collecting and banking materials. It makes sense for an entity like NIH, or maybe advocacy groups in the early stages, to support non-hypothesis driven collection of materials so that later they are available for cost-effective, rapid testing of a wide variety of ideas. We now have the technology to test molecular hypotheses in post-mortem tissue, something that we did not even envision 10 or 15 years ago.

The Autism Tissue Program, funded by advocacy groups and NIH, draws from tissue banks funded by NIMH, NINDS, and NICHD. However, there is variability in the protocols, operations, and capabilities of these banks, making it difficult to implement standardized, centralized capabilities. There is a lot of work to be done here. The STAART Centers are also required to participate in sharing of materials, but judging from the applications, there seems to be less representation of projects and cores involved with this type of activity than with genetics.

Dr. Foote stated that basic science developments are critical to this work. The neurosciences institutes are involved with the Molecular Neuroanatomy Project (formerly called the Brain Molecular Anatomy Project or BMAP). A number of efforts are underway to develop the ability to map and precisely localize the distribution of specific molecules in the brain. The goal is to map this complex information onto a standardized map so that investigators can find out where a specific molecule is expressed in the brain, and at what stage of development. This would be a very crucial tool in autism studies.

Ms. Jane Pickett, Coordinator of the Autism Tissue Program (ATP) said that there are 40 donors, supporting 24 projects, two of which are large-scale projects. So far, activities have primarily been pilot projects, although they are starting some large-scale projects, which she called the Autism Atlas Project, and a more comprehensive gene project. Archive tissue is also becoming more important since it is now possible to do gene expression studies from tissue samples. Some of the exciting new research is in the area of brain structures, where some specific structural differences have been found in tissue from individuals with autism. This is being done with archive tissue that has been kept by Margaret Bauman, and more recently in NIH samples. The ATP participated in the NIH International Brain Banking Conference this spring.

ATP launched a NAAR-funded project this month, to develop better collection at medical examiner sites around the county. They are also partnering with the M.I.N.D. Institute. They are doing extensive phenotyping and are also genotyping tissue. They will be presenting their pilot data at the International Meeting For Autism Research–IMFAR–meeting in November.

Dr. Pickett emphasized the importance of service providers giving information to parents regarding tissue and brain donation to facilitate collection efforts. She has brochures available in English and Spanish, and they can translate into other languages.

She reported some data from the ATP that suggests a higher mortality rate in children with autism than the general population in California. She said that they had not anticipated this as an area of investigation. They hope to do a similar investigation in another geographic region.

Mr. Grossman reiterated his question about ways to promote collaboration among programs with regard to tissue banking. He asked if there is a way to have the ATP collaborate with the STAART Centers.

Dr. Foote replied that NIH must develop a course of action to boost activities in this arena with the help of other groups (e.g., current brain banking activities, the ATP, online banks). Dr. Nakamura noted that increasingly, the assumption is that data will be shared. NIH expects data sharing, and P.I.s have to include data sharing plans in their applications, or explain why their data would not be shared. NIH is still in the process of working out the logistics of how this will be done.

**Strategic Planning for Treatment Development**

*Presented by Steve Foote, Ph.D., Interim Executive Secretary IACC, and NIMH; and Mr. Lee Grossman, Public Member and President Autism Society of America (ASA)*

Dr. Foote stated the need to systematically evaluate treatments and to have these evaluations available to consumers. He presented an overview of these types of activities currently ongoing at NIH, as well as upcoming activities, and described what are the biggest areas of need. Ann Wagner, Ph.D. in the NIMH Division of Services and Intervention Research assisted in pulling this information together. Current activities include: investigator-initiated grants, such as R01s, RUPP (Research Units in Pediatric Pharmacology) and RUPP-PI (Psychosocial Interventions) networks, CPEA/MRDDRC (Mental Retardation And Developmental Disabilities Research Centers) centers, 7 NIH grants awarded in response to the Innovative Treatments RFA, services research grants (by end of year, NIMH will have funded the first two services research grants). Some institutes are also using small business grants or SBIRs to fund some types of intervention research such as web-based interventions and the use of computer-assisted technology to deliver or support interventions.

Upcoming activities: The STAART Centers are required to have at least one treatment project each. NIH is optimistic about coordinating enrollment of subjects into studies, using common assessment and outcome measures. In the Fall, a workshop is being organized by Ann Wagner in collaboration with the NIH/ACC to facilitate psychosocial/behavioral treatment research.

Recognizing the need for treatments in all areas, Dr. Foote identified some areas to particularly highlight, including intervention discovery for core symptoms; testing currently used interventions; interventions for adults; effectiveness evaluation (i.e., how well does a given intervention work in the real world); and research on the factors that facilitate the adoption of effective interventions by community service providers.

In his presentation, Mr. Grossman explained that as a businessman, he has taken a business strategic approach when conducting a review of the problem of autism. He identified agencies that ought to be involved in this strategic plan. He noted that although autism shares many common threads with other disorders, it is a unique disorder. Three common threads in autism, despite the heterogeneity of the disorder, are: 1. problems with generalization; 2. communication difficulties that can be manifested as behaviors that are often looked upon negatively; 3. and disparate abilities (i.e., uneven functions – excels in one area, but impaired in another).

Mr. Grossman also described the parents' experience. Parents seeking diagnosis and treatment are frequently frustrated by negative prognosis. In terms of early intervention, parents often need to secure services on their own and out of their own pocket. Secondary school programs are virtually non-existent. Schools may maintain that there is no research evidence to support the intensive therapies parents ask for and refuse to provide them. He noted a dramatic shift during transition between school age and adulthood in parents' level of optimism. There is a severe lack of services and parents are often struck by abysmal lack of support. He likens this to removing the wheelchair for someone with physical disabilities when they turn 21. Finally, parents must deal with issues related to long-term care (e.g., when parents die).

Mr. Grossman highlighted the economic impact of autism and stated that the lifetime cost of autism can be diminished by 2/3 with early intervention.

With regard to what needs to be done, Mr. Grossman referred to a recently published book by National Research Council (NRC) (with contributions from Gail Houle from the Department of Education), Educating Children with Autism, which outlines recommendations for services. He encouraged the committee to review the report and implement the recommendations. He also suggested that a review of the recommendations might be an appropriate item for the next IACC meeting.

Research, early intervention, school-age and adult issues are the four key areas in autism that needs to be addressed, and several of the federal agencies around the table should be involved in this effort.

Other important considerations include: 1. Medical insurance coverage – autism is a medical disorder that needs to be recognized; 2. Congressional support needs to turn into legislative action; 3. Public awareness campaign (especially through implementation of the Children's Health Act Section 104); and 4. Closer working relationship with volunteer organizations.

*Discussion:*

Dr. Carbone, of the Food and Drug Administration, asked what direction should be taken with regard to pharmacologic treatments versus behavioral treatments, or combined treatments. Mr. Grossman replied that he sees interdisciplinary scientific efforts as being critical; he would like to see it proven that pharmacological treatments can be effective for some core autism symptoms. We know that there are behavioral treatments that work (outlined in the NRC report) – we need to be better at implementing them.

Dr. McPherson commended Mr. Grossman for his call for interagency cooperation. She noted that many of these issues are addressed in the HRSA 10-year plan. She also acknowledged that services integration is a key issue, especially continuity of care over the life span. She agreed that training needs to be conducted, but also restructuring of the provider's work environment for services to be effective (e.g., 6-minute appointment

not effective). She also noted that the CDC helped to fund the American Academy of Pediatrics (AAP) initiative to develop practice guidelines.

Dr. Cordero commented on the CDC's work, through cooperative agreements with the AAP and other academies to train pediatricians and other personnel in the pediatrician's office to be sure children with autism are identified early. He cited his experience with training pediatricians in immunization procedures as an example of how well pediatrician training can work. Mr. Grossman responded that this is critical, as is the larger issue of public awareness in general.

Mr. Shestak suggested that training in identification of the disorder is probably one of the easier things to address in this field. Dr. Yeargin-Allsopp commented on her experience at a meeting of the Pediatric Academic Societies, where she did a training workshop on early identification and diagnosis. She noted that there were 3 or 4 sessions devoted to autism, and they were all standing-room only. She also noted that there have been about eight practice parameters for pediatricians put together by various academies (AAP, The American Academy of Child and Adolescent Psychiatry (AACAP), American Academy of Neurology) in the past two years. Audiotape training is being developed which will be on the AAP website when it is available. One key guideline: Listen to parents. Parents know that there is something wrong even though they may not know what is wrong.

Dr. McPherson reinforced the above comments, and added that the AAP is working on a national training program co-funded by Shriner's Hospitals, which will emphasize clinical skills and communication with the family (family-based medicine).

Dr. Hirtz called attention to the practice parameters that were a product of the American Academy of Neurology and the Child Neurology Society. These are evidence-based and emphasize a two-stage process: screening for developmental abnormalities at well-baby visits and actual diagnosis by an autism expert.

Dr. Battey added the comment that proper developmental diagnosis takes time and we need to convince payors to cover that. Dr. McPherson noted that the 10-year Plan is trying to address this issue as well.

Ms. Goldman noted that similar issues are confronted in mental health screening and diagnosis. The training piece is one thing. The next step, i.e., connecting the families to intervention services, is key. Pediatricians are concerned that they identify a need but have no place to refer.

Mr. Shestack agreed that the next step is key, but it is also the most expensive. He emphasized that early identification should not be deterred just because services are difficult to obtain.

Dr. Cordero summarized that a key issue is how to restructure the pediatric visit and use that time most efficiently. Most children have 6-8 visits to pediatricians per year.

Opportunities are there, but they have to be used to screen kids appropriately and have them appropriately referred.

**Open Session for Public Comment**

Cathy Rookard from the Delaware Biotechnology Institute noted that autism is described as a neurological or developmental disorder, and this may be where it falls through the cracks. She suggested that the co-morbid pathologies that are associated with autism (e.g., GI problems) should be emphasized.

Margaret Dunkle from George Washington University stated that she is undertaking a project about funding streams and policies and programs that affect children with autism and their families, focusing especially on low-income children from Los Angeles County. She suggested that the genetic and tissue banking efforts give consideration to whether their samples represent the ethnic and socioeconomic diversity of the community.

**Closing Comments and Next Steps**

Dr. Nakamura asked the committee for suggestions for next steps. Several suggestions were offered.

1. A subcommittee concerning integration of services across agencies will be formed including representatives from key federal agencies on Mr. Grossman's list: HRSA, SAMHSA, DOE, CMS, the Agency for Healthcare Research and Quality (AHRQ) and State and community people.

2. A subcommittee on instituting a national screening policy was recommended. Dr. McPherson said that she would be willing to work on this, as did Dr. Hirtz, Dr. Cordero, Mr. Shestak.

3. Dr. Gordon is willing to continue working on the mapping project. Dr. Houle will send Dr. Gordon information about the North Carolina system-mapping site.

4. A recommendation was made to post information about each Federal agency's mission on the IACC web site.

5. A recommendation was made to distribute the HRSA 10-Year Plan after it is finalized.

Potential items for the next meeting:

1. Description of the new NIH centers (STAART and CPEA updates).

2. Description of NIH Intramural activities related to autism. What can the IACC do to foster additional efforts?

3. Discussion of how advocacy groups can effectively interface with federal agencies.

4. Strategic planning: can the IACC set an agenda for what the committee would like to accomplish for the future?

5. A report on clinical and research training. And what is being done at NIH to recruit and retain researchers.

6. A report from the newly organized services and national screening subcommittees.

Dr. Nakamura noted that there would be ongoing email communications to refine these suggestions and facilitate the formation of subcommittees.

Meeting was adjourned at 3:30 p.m.